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NOSOCOMIAL INFECTIONS AND MICROBIOLOGICAL AGENTS IN AN INTENSIVE CARE UNIT

GORANA ĆOSIĆ[1], JELENA ĐEKIĆ[1], SMILJANA RAJČEVIĆ[1], M. RISTIĆ[1] and N. IKONIĆ[2]

[1] *Institute of Public Health of Vojvodina, Center for Control and Prevention of Diseases,* 21000 Novi Sad, Serbia
[2] *Clinical Centre of Vojvodina,* 21000 Novi Sad, Serbia

Abstract - Hospital environments provide a special setting for the interaction of microbiological agents of infection and a host of patients and healthcare workers. Although the basic tenets about the spread of infections in hospital have not changed, new issues have emerged that make infection control more problematic. The aim of this paper was to provide the epidemiological characteristics of nosocomial infections and pathogens among patients in an intensive care unit (ICU), the department with the highest risk of the infections associated with medical devices and healthcare.

Key words: Intensive care unit, nosocomial infections, hospital-acquired infection

INTRODUCTION

Nosocomial infections are those acquired in a hospital. Although less frequently, infections can be acquired in other institutions of healthcare practice as well. Because of this it is more accurate to call them healthcare-associated infections (Coffin et al., 2008). The hospital environment provides a special setting for the interaction between the agents of infection and the patients and healthcare workers as hosts. Over the years, the very character of hospitals has changed. Patients are sicker, underlying diseases are more compromising, invasive procedures are more common, new varieties of microorganisms are responsible for a wider spectrum of nosocomial infections, bacterial isolates are becoming more resistant to standard antibiotic therapies, patients are clustered in specialized units and a greater variety of caregivers are directly involved in the care of patients, increasing the number of potential reservoirs of infections. Within hours of admission, a patient's flora begins to acquire the characteristics of the surrounding bacterial pool. Infections that are clinically evident 48 h after admission to the hospital are considered as healthcare-associated infections (HAI). Those that are evident within the first 48 hours after admission are classified as community-acquired or interhospital infection if they are transmitted from another healthcare institution (Mayhall, 1999). Patients in intensive care units are at a higher risk of acquiring HAI due to severity of the underlying diseases and the invasive medical technology and devices used in therapy. Most published studies of ICU-acquired infections have come from developed countries (Cooke et al., 2004, Safdar et al., 2001). Relatively few data have been reported from developing countries (Rosenthal et al., 2006) and even fewer from this country (Jovanović et al., 2006). Herein, we present the findings of a seven-year surveillance study of infections associated with medical care and therapy in the ICU of the University Hospital in Novi Sad, Serbia.

MATERIALS AND METHODS

Surveillance was performed on patients in a combined medical-surgical ICU of the tertiary-care

university-affiliated hospital in the period from 1 January 2004 to 31 December 2010, as a prospective cohort study using a designed questionnaire. Among the patients admitted to the ICU, only those hospitalized for at least 48 h were included in the study. The following data were collected: demographic data, admission diagnoses, origin of the patient, data regarding the type and duration of applied invasive procedures, surgical operation and physical status expressed according to the traditional American Society of Anesthesiologists (ASA) Score (No author listed, 1963), endotracheal intubation, intravascular catheter and urinary tract catheter. For patients with developed infection additional data were required: date of onset, anatomical localization of the infection, result of microbiological examination. CDC definitions were used in setting up the diagnosis of hospital infection (Garner et al., 1996). The results were analyzed using descriptive and standard statistical methods and are presented in tables and graphs.

RESULTS

Over a seven-year period, 3209 patients out of 3576 were included in the survey based on the criterion that they had been hospitalized for at least 48 hours after admission to the ICU. The average age was 55.3 years (ranging from 18 to 92), and the male-female sex ratio was 1.8:1. The average length of stay in ICU was 8.1 days. Patients with HAI stayed in hospital for 11.6 days longer than patients without HAI. The frequency of invasive procedures applied are shown in Table 1.

A total of 1073 HAI was registered with the mean incidence rate of 33.4% and incidence density of 33.8 per 1000 ICU patient-days.

The annual incidence of HAI had a decreasing trend, with the highest incidence density recorded in 2005 (41.5/1000 ICU patient-days) and the lowest in 2009 (17.1 per 1000 ICU patient-days) (Fig. 1).

The most common infection was pneumonia (29.4%), followed by urinary tract infections (23.4%), infections of the lower respiratory tract (19.7%) and blood infections (17.4%) (Table 2).

The highest incidence rates were in critically ill patients (ASA score 4 and 5; 31.2% and 42.8%, respectively). Pneumonia among patients with mechanical ventilation was more common than among patients without this risk factor ($p<0.0001$). The higher risk of ventilator-associated pneumonia (VAP) was at the beginning of the study period (33.8 per 1000 days on ventilation in 2005) in comparison with 2010 (12.2 per 1000 days on ventilation) (Table 3).

Tables 4, 5 and 6 show the microbiological agents responsible for the most typical device-related nosocomial infections: ventilator-associated pneumonia, blood stream infections and urinary tract infections. Eighty-four percent of *Staphylococcus aureus* infections were caused by methicillin-resistant strains, while 2% of *Enterococcus* spp. isolates were resistant to vancomycin.

DISCUSSION

The mean incidence rate of ICU-acquired infections in our study was 33.4 per 100 admitted patients, and the absolute risk of infection was 34.8 per 1000 ICU patient-days. Since the 1980s, it has been recognized that ICU patients acquire nosocomial infections at a much higher rate than patients on other wards. The risk for patients in an ICU is as much as 5 to 10 times greater than for those at medical wards (Weber et al., 1999, Ćosić et al., 2005, Jovanović et al., 2006). The increased risk of nosocomial infection results from a patient's intrinsic factors, such as severe underlying disease, trauma, multiple illnesses, immunosuppression, invasive medical devices such as endotracheal tubes, intravascular and urinary tract catheters, and environmental factors such as crowding, substaffing, animate and inanimate reservoirs of infection. Our study showed that the highest incidence rates were in critically ill patients (ASA score 4 and 5) with 31.2% and 42.8%, respectively. The most common infection was pneumonia with a relative frequency of 29.4%, followed by urinary tract infections (23.4%), infections of the lower respiratory tract (19.7%) and

Table 1. Characteristics of patients in the ICU, Clinical Center of Vojvodina, Novi Sad, Serbia, 2004-2010.

Patient characteristics	Results
Number of patients hospitalized in ICU	3576
Number of patients hospitalized in ICU ≥48 h and included in the study	3209
Average age (years) of patients (SD)	55.3 (11.2)
Male/female ratio	1.8 : 1
Total number of bed days	26704
Mean duration (days) of hospital stay in ICU (SD)	8.1 (5.3)
Mean duration (days) of hospital stay in ICU for patients with HAI (SD)	17.4 (11.4)
Mean duration (days) of hospital stay in ICU for patients without HAI (SD)	5.8 (4.9)
Number and proportion (%) of patients with an operation	3009 (93.8)
Number and proportion (%) of patients with ASA score ≥3 (N=3009)	2922 (97.1)
Number and proportion (%) of patients with mechanical ventilation	2719 (84.7)
Number and proportion (%) of patients with central vascular catheter (CVC)	2644 (82.4)
Number and proportion (%) of patients with urinary tract catheter (UTC)	2898 (90.3)
Number of healthcare associated infections (incidence %)	1073 (33.4)
Number of ventilator-associated pneumonia (incidence %)	311 (11.4)
Number of blood stream infections among CVC patients (incidence %)	185 (7.0)
Number of urinary infections among patients with UTC (incidence %)	247 (8.5)

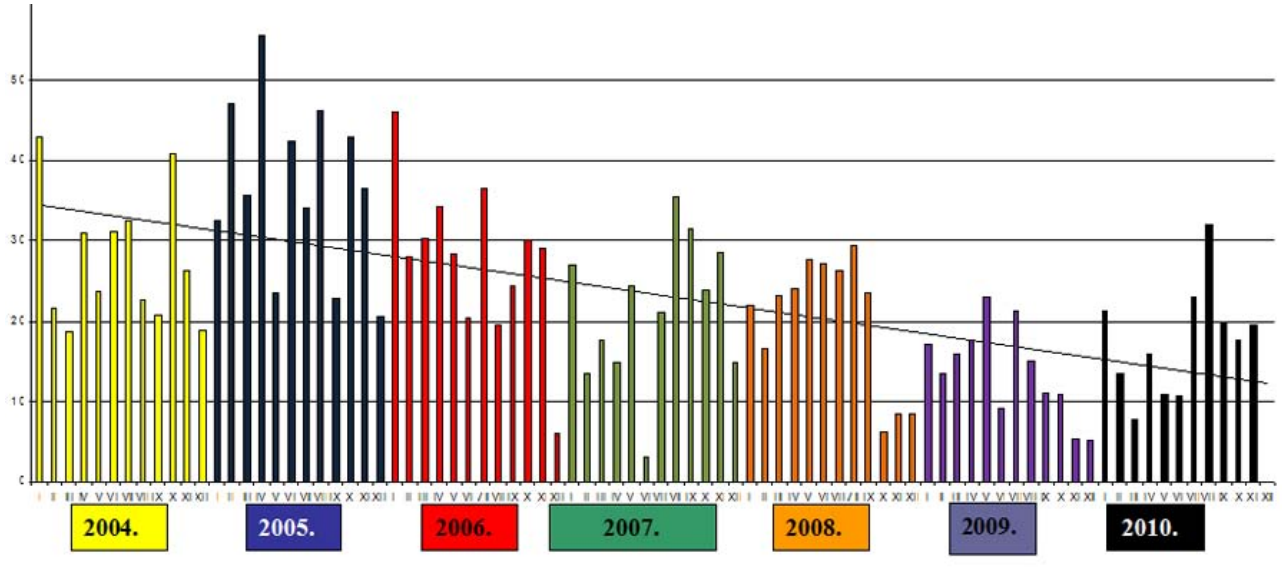

Fig. 1. Incidence rate of nosocomial infections in the ICU, Clinical Center of Vojvodina, Novi Sad, Serbia, 2004-2010.

bloodstream infections (17.4%). The frequency of these sites of infection was found to be different in the large prospective epidemiological study carried out in 125 Italian intensive care units (Malacarne et al., 2010). The most frequent infections in this study were pneumonia and blood stream infections, but with the higher frequency than in our study (48.7% versus 29.4% and 24.4% versus 17.4%, respectively). The frequency and absolute risk of infection vary by type of ICU (Richards et al., 2000). In an NNIS System report, the highest risk was registered in the burn ICU (24.1 per 1000 ventilator days), and neurosurgical and trauma ICU (18.3 and 17.2 per 1000 ventilator days, respectively). The combined medi-

Table 2. Frequency (%) and incidence rate (%) of HAI at different anatomical sites in the ICU, Clinical center of Vojvodina, Novi Sad, Serbia, 2004-2010.

Anatomical site of HAI	N (%)	Incidence (%) N=3209
Pneumonia	316 (29.4)	9.8
Urinary tract infection	251 (23.4)	7.8
Infections of lower respiratory tract (except pneumonia)	212 (19.7)	6.6
Blood stream infection	187 (17.4)	5.8
Surgical site infection	55 (5.1)	1.8
Skin and soft tissue infection	29 (2.7)	0.9
Gastrointestinal infection	10 (0.9)	0.3
Cardiovascular tract infection	7 (0.6)	0.2
Central nervous system infection	5 (0.5)	0.1
Genital tract infection	1 (0.1)	0.0
Bone infection	0 (0.0)	0.0
Eye ear and nose infection	0 (0.0)	0.0
Systemic infection	0 (0.0)	0.0
Total	1073 (100)	33.4

Table 3. Incidence of pneumonia associated with mechanical ventilation in ICU, Clinical Center of Vojvodina, 2004-2010.

	Number of patients hospitalized in ICU ≥48 h	Number of patients with mechanical ventilation (%)	Incidence of pneumonia on 1000 ventilator days	Incidence of pneumonia among patients with mechanical ventilation (%)	Incidence of pneumonia among patients without mechanical ventilation (%)
2004	486	364 (74.9%)	30,6	12,4	1.6
2005	457	380 (83.1%)	33,8	15,0	6.5
2006	433	376 (77.8%)	19,5	13,6	4.7
2007	482	397 (82.4%)	20,7	10,3	1.2
2008	467	421 (91.9%)	24,1	13,5	2.7
2009	454	410 (90.3%)	17,1	8,5	0.0
2010	430	371 (86.3%)	12,2	6,7	1.7
Total	**3209**	**2719 (84.7%)**	**34,6**	**11,4**	**2.6**
				RR 4.3 (95% CI 2.5 – 7.4), p<000.1	

Table 4. Microorganisms isolated from patients with pneumonia in the ICU, Clinical Center of Vojvodina, Novi Sad, Serbia, 2004-2010.

Microorganisms	Total	
	N	%
Acinetobacter spp.	156	42.5
Pseudomonas aeruginosa	85	23.2
Klebsiella pneumoniae	71	19.3
Staphylococcus aureus	13	3.5
Citrobacter spp.	9	2.5
Proteus spp.	8	2.2
Enterobacter spp.	8	2.2
Pseudomonas spp.	4	1.1
Candida albicans	3	0.8
Escherichia coli	3	0.8
Others	7	1.9
Total microorganisms isolated	367	100

Table 5. Microorganisms isolated from patients with blood stream infection in the ICU, Clinical Center of Vojvodina, Novi Sad, Serbia, 2004-2010.

Microorganisms	Total	
	N	%
Coagulase-Negative Staphylococci	96	44.6
Acinetobacter spp.	50	23.3
Klebsiella pneumoniae	23	10.7
Enterococcus spp.	12	5.6
Pseudomonas aeruginosa	6	2.8
Enterobacter spp.	6	2.8
Escherichia coli	4	1.9
Serratia spp.	4	1.9
Candida spp.	3	1.5
Staphylococcus aureus	2	0.9
Candida albicans	2	0.9
Others	6	2.8
Total microorganisms isolated	215	100

Table 6. Microorganisms isolated from patients with urinary tract infection in the ICU, Clinical Center of Vojvodina, Novi Sad, Serbia, 2004-2010.

Microorganisms	Total	
	N	%
Klebsiella pneumoniae	55	22.2
Pseudomonas aeruginosa	30	12.1
Acinetobacter spp.	24	9.7
Escherichia coli	19	7.7
Enterococcus spp.	74	29.8
Proteus spp.	5	2.0
Candida albicans	2	0.8
Candida spp.	23	9.3
Morganella morganii	3	1.2
Others	4	1.6
Total microorganisms isolated	248	100

cal/surgical ICU in the NNIS System report had a risk of infection at the same level as our surveilled ICU (11.8 and 11.4 per 1000 ventilator days, respectively).

Device-associated infection rates focused on endotracheal tubes for mechanical ventilation. The rates of ventilator-associated pneumonia decreased over time from 33.8 per 1000 ventilator days in 2005 to 12.2 per 1000 ventilator days in 2010 after targeted interventions were introduced, including an educational program focused on respiratory care. In 2010 in our ICU a lower rate was reached than in other developing countries, such as Argentina, Brazil, Mexico, India or Turkey, where the rates ranged from 10 to 52.7 per 1000 ventilator days (Rosenthall et al., 2006), but they were still higher than pooled the United States' National Nosocomial Infection Surveillance (NNIS) System rates of 1.2 to 9.9 per 1000 ventilator days or than the Italian study with 8.9 episodes of pneumonia per 1000 ventilator days (No author listed, 2004, Malacarne et al., 2010).

Of reported isolates in patients with pneumonia, 65.7% were Gram-negative non-fermentative bacteria, and 27% were enterobacteria. *Staphylococcus aureus* was the only Gram-positive causative agent of pneumonia with a relatively low frequency of 3.5%.

On the other hand, *Staphylococcus aureus* was the leading causative agent of VAP in Italy (33.5%) and USA (17%) (Malacarne et al., 2010, Richards et al., 2000). In patients with primary blood stream infections, coagulase-negative staphylococci were dominant (44.6%), as reported in the literature, and second most frequent Gram-positive bacteria was *Enterococcus* spp. The high percentage of methicillin-resistant *Staphylococcus aureus* MRSA (84%) infections in our study, as in studies of other developing countries, should immediately put this issue in the first line of hospital antibiotic control programs in order to prevent the spread of antibiotic resistance (Rosenthall et al., 2006, McGowan, 1994). In hospitals, concern about drug-resistant pathogens has focused on methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Enterococcus* spp. (VRE), expanded-spectrum β-lactamase-producing Gram-negative bacilli, multidrug resistant *Mycobacterium tuberculosis* as well as fluconazole-resistant *Candida* spp. (No author listed CDC, 1998). Although in our country there are laws mandating healthcare-associated infection programs, funds and resources for infection control and up-to-date investigation of sensitivity to antimicrobials in laboratories are limited, leading to sub-registration of multidrug resistance. The most important elements in an effective infection control program include a surveillance system, hand hygiene before and after contact with each patient and the patient's nearby surroundings, appropriate isolation of patients with transmissible agents, adherence to standards on disinfection and sterilization of instruments and equipment, immunoprophylaxis and the management of exposed healthcare workers (No author listed CDC, 2003). Infection control programs in hospitals, in targeted high-risk units such as an ICU, should be implemented as part of the global strategy to surveille and prevent the emergence and spread of antimicrobial resistance (Goldmann et al., 1996).

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