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Nosocomial infections in the Intesive Care Unit, Univerisity Hospital for Infectious and Tropical Diseases, Belgrade, Serbia

Bolničke infekcije u Odeljenju intenzivne nege Univerzitetske klinike za infektivne i tropske bolesti, Beograd

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Abstract

Bacground/Aim. Nosocomial infections (NIs) are an important cause of morbidity, mortality and prolonged hospitalizations. Fifty percent of NIs have been reported in Intensive Care Units. The aim of this study was to determine the frequency and type of NIs among critically ill patients treated in the University Hospital for Infectious and Tropical Diseases, Clinical Centre of Serbia, as well as risk factors for acquiring them. **Methods.** This prospective cohort study included 52 patients treated in the Intensive Care Unit from January to June 2004. The diagnosis of NI was established according to the Centers for Disease Control and Prevention (CDC) definition, based on clinical presentation, radiological and microbiological findings, etc. Statistical data processing was done by using the electronic data base organized in SPSS for Windows version 10.0. The level of statistical significance was defined as $p < 0.\ 05$. **Results.** NIs were found in 33 (63.4%) of 52 inpatients. Urinary tract infections (UTIs), pneumonia, and soft tissue infections, the most common nosocomial infections in our setting, were recorded in 41.0%, 25.6%, and 23.1%, of patients, respectively. Several factors contributed to a high incidence of these infections: chronic comorbidities ($p < 0.01$), the presence of indwelling devices such as urinary tract catheters ($p < 0.01$), endotracheal tubes ($p < 0.05$) along with mechanical ventilation ($p < 0.05$). **Conclusion.** The majority of patients with NIs had chronic underlying comorbidities. All the patients with UTIs had urinary catheters. The most important risk factors for the development of nosocomial pneumonias were endotracheal intubation and mechanical ventilation. The patients with pneumonia had the highest mortality.

Key words:
cross infection; risk factors; comorbidity; urinary catheterization; intubation, intratracheal; respiration, artificial; mortality.

Apstrakt

Uvod/Cilj. Intrahospitalne infekcije su važan uzrok morbiditeta i mortaliteta, kao i produžetka bolničkog lečenja. Polovina svih bolničkih infekcija javlja se u jedinicama intenzivne nege. Cilj ove studije bio je da se utvrde učestalost i vrsta bolničkih infekcija kod bolesnika lečenih u Odeljenju intenzivne nege Klinike za infektivne i tropske bolesti Kliničkog centra Srbije, kao i faktori rizika od obolevanja. **Metode.** Ovom prospektivnom kohortnom studijom bilo je obuhvaćeno 52 bolesnika koji su lečeni u Odeljenju intenzivne nege u Klinici za infektivne i tropske bolesti u periodu od januara do juna 2004. Dijagnoza je postavljana na osnovu definicije bolničkih infekcija Centra za kontrolu i prevenciju bolesti (CDC), kliničke slike, radioloških, mikrobioloških i drugih nalaza. Statistička obrada podataka urađena je pomoću statističkog paketa SPSS za Windows verziju 10.0. Nivo statističke značajnosti bio je $p < 0,05$. **Rezultati.** Intrahospitalne infekcije nađene su kod 33 (63,4%) od ukupno 52 lečena bolesnika. Infekcije urinarnog trakta (41,0%), pneumonije (25,6%) i infekcije mekih tkiva (23,1%) bile su najčešće bolničke infekcije. Nekoliko faktora doprinosilo je visokoj učestalosti ovih infekcija: hronične komorbidne bolesti ($p < 0,01$), prisustvo stalnih pomagala, kao što su urinarni kateter ($p < 0,01$), endotrahealni tubus ($p < 0,05$), kao i mehanička ventilacija ($p < 0,05$). **Zaključak.** Većina bolesnika sa bolničkim infekcijama imala je i neku hroničnu bolest. Svi bolesnici sa infekcijama urinarnog trakta imali su urinarni kateter. Najznačajniji faktori rizika od razvoja intrahospitalne pneumonije su endotrahealna intubacija i mehanička ventilacija. Bolesnici sa pneumonijom imali su i najveću smrtnost.

Ključne reči:
infekcija, intrahospitalna; faktori rizika; komorbiditet; kateterizacija urinarnog trakta; intubacija, endotrahejna; disanje, mehaničko; mortalitet.

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Introduction

Nosocomial infections (NIs) are a global health problem, present in all health systems, irrespective of a health service level. NIs cause a variety of medical, ethical, economical and legal consequences. These infections cause substantial morbidity and mortality, prolong hospitalization, and increase direct patient-care costs and the number of hospital staff [1, 2].

According to the Centers for Disease Control and Prevention (CDC) definition, nosocomial or hospital-acquired infections are manifested 48 hours after hospital admission, during the course of receiving treatment for other conditions within a healthcare setting. They are neither present nor incubating at the time of admission, but are acquired in hospital, and even manifest after discharge. NIs are more common in large university hospitals and intensive care units (ICUs), where critically ill patients are treated. According to the published studies, even in the developed countries, 5–10% of patients treated in hospitals are going to be infected. Although ICUs usually account for less then 10% of hospital capacity, over 25% of NIs develop in these departments [3]. The prevalence rate of ICU-acquired infections reaches up to 20% [1]. Multiresistant bacteria cause most of the infections in ICUs [4].

The aim of this study was to determine the frequency and type of NIs in the ICU in our setting along with risk factors for acquiring them.

Methods

This prospective cohort study was established according to the CDC metodology [5]. We investigated NIs in the patients admitted to the ICU in Infectious and Tropcal Diseases University Hospital in Belgrade, from January to June 2004. The patients admitted to the ICU in our setting suffered mostly severe central nervous system (CNS) infections, septicemia, and/or bacterial endocarditis, and less frequently tetanus and botulism. The patients with several severe non-infectious disesases were occasionaly hospitalized due to differential diagnosis. NIs were considered if diagnosed at least 48 hours after the admission, based on clinical, radiological and microbiological findings. Data from patients' charts and by interviewing hospital staff were collected. Radiological examinations included chest X-ray and chest computed tomography (CT) scan when needed. Specific bacteral NIs were confirmed by using standard microbiological methods for cultivation and identification of microorganisms. Infection rate (IR) was expressed as the total number of NIs *per* 1,000 patient days. We calculated device utilization rates by dividing the total number of devices days by the total number of ICU patients days, and device utilization NI rate by dividing the number of device associated NIs by the total number of device days [6].

All analyses were performed using an electronic database organized in the SPSS (version 10.0) statistical package. Non-parametric variables were analyzed using Chi-square or Fisher's exact test, as appropriate. The same method was used to access association between the appearance of NIs and possible risk factors, while One way ANOVA test was used to compare means. The level of significance was 0.05.

Results

Fifty-two patients, representing 1,116 patients-days, were treated in the ICU during 6-month study period (January – June 2004) (Table 1). The mean patients age was 50.5 ± 18.2 years, and they were predominantly male (44.2%).

The most prevalent diagnoses on admission were various CNS infections, septicemia, and/or endocarditis, as well as fever of unknown origin (Table 1). Other less common diagnoses were: ostemyelitis, cavernous sinus thrombosis, paraparesis, tetanus and stroke, recorded in one patient each, respectively. Thirty-two (61.5%) of the patients had comorbidities.

Table 1

Patients treated in the Intensive Care Unit (ICU) during a 6-month period (January – June 2004)

Parameter	Value
Male, n (%)	29 (55.8)
Female, n (%)	23 (44.2)
Age, (years), $\bar{x} \pm SD$	50.52 ± 18.21
Admission diagnosis	
neuroinfections, n (%)	33 (63.5)
sepsis, n (%)	7 (13.5)
fever of unknown origin, n (%)	5 (9.6)
endocarditis, n (%)	2 (3.8)
other, n (%)	5 (9.6)
Comorbidities n (%)	32 (61.5)
cardiovascular diseases, n (%)	15 (29.0)
diabetes mellitus, n (%)	7 (13.5)
malignancy, n (%)	2 (3.8)
connective tissue diseases, n (%)	2 (3.8)
chronic obstructive pulmonary disease, n (%)	2 (3.8)
hematological disease, n (%)	2 (3.8)
cerebrovascular disease, n (%)	2 (3.8)
Total, n (%)	52 (100)

Out of 52 observed patients, 33 (63.4%) acquired 39 different NIs (Table 2). Of those, 24 (46.2%), and 6 (11.5%) patients had one, and two concomitant infections, respectively, while one (1.9%) patient had even three NIs.

Table 2

Nosocomial infections in ICU patients

Infection	Patients, n (%)
Urinary tract infections	16 (41.0)
Pneumonia	10 (25.6)
Skin and soft tissue infections	9 (23.1)
Stomatitis	2 (5.1)
Enterocolitis	1 (2.6)
Blood stream infection	1 (2.6)
Total	39 (100)

ICU – Intensive Care Unit

The development of NI was not associated with reported admission diagnosis ($p > 0.05$).

There was no statistical difference in the distrubution of NIs in relation to the patients' gender and age. Comorbidities had a significant association with the acquisition of NI ($p < 0.01$). Endotracheal intubation, mechanical ventilation and the presence of urinary catheters were also associated with the development of NIs (Table 3).

Out of 39 NI cases, etiological diagnosis was established in 21 patients (Table 4). In all 16 urinary tract infection (UTI) cases, always associated with indwelled urinary catheters, causative agents were identified, including Gram-negative bacteria such as *Pseudomonas aeruginosa, Klebsiella-Enterobacter, Escherichia coli* and *Citrobacter freundii*, recorded in 4, 2, 4 and 1 case, respectively. All *Escherichia coli* and *Klebsiella-Enterobacter* isolates were extended spectrum beta-lactamase producing bacteria (ESBL). The remaining five UTIs were caused by *Enterococcus* spp, a Gram-positive bacteria susceptible to vancomycin. The average duration of urinary bladder catheterisation was 19.71 ± 11.32 days (range 5–52 days).

A total of 10 patients developed bilateral intrahospital pneumonia, however without etiological confirmation. Eight out of 10 patients with pneumonia were intubated and mechanically ventilated. The mean length of hospital stay for patients with nosocomial pneumonias was 18.3 ± 8.12 days (range 8–50 days). Even 80% of patients with nosocomial pneumonia died.

Skin and soft tissues infections were recorded in 9 patients. Methicilin resistant *Staphylococcus aureus* (MRSA) was cultured from skin lesions in 2 out of 9 patients.

One of the patients acquired bacteriemia caused by *Enteroccocus* spp*.,* while two patients had oropharyngeal candidiasis. In one enterocolitis case no causative pathogen was cultured from the stool.

The mean overall nosocomial infection rate (IR) was 29.5 infections *per* 1,000 patient-days (Table 5).

The device utilization rate in patients on mechanical ventilation was 0.37 (160 device days, 427 patient days) and 0.65 in the patients with urinary catheters (Table 6) (662 device days, 1,026 patient days).

The device utilization nosocomial IR for nosocomial pneumonia in the patients on mechanical ventilation was 50 *per* 1,000 patient-days. The device utilization nosocomial IR for urinary tract infection in the patients with urinary catheters was 24 *per* 1,000 patient-days.

Out of 52 observed patients, 15 (28.8%) succumbed, while remaining 37 were discharged recovered. Age and gender did not influence the mortality ($p > 0.05$). Comorbid-

Table 3

Factors associated with the development of nosocomial infections (NI)

Parameter	NI	Without NI	*p*
Age (years), $\bar{x} \pm SD$	52.21 ± 12.3	49.18 ± 10.1	0.357
Male (n)	16	13	
Female (n)	11	12	0.336
Comorbidities (n)	22	10	
Without comorbidities (n)	11	9	0.008
Intubation, mechanical ventilation (n)	15	5	
Without intubation (n)	18	14	0.028
Urinary tract catheter (n)	14	6	
Without urinary tract catheter (n)	0	32	0.011

Table 4

Etiology of nosocomial infections in Intensive Care Unit patients

Etiologic agent (confirmed)	Patients, n (%)
Gram-positive infections	8 (38.1)
Enterococcus spp.	6 (28.6)
Staphylococcus aureus	2 (9.5)
Gram-negative infections	11 (52.4)
Pseudomonas aeruginosa	4 (19.1)
Esherichia coli	4 (19.1)
Klebsiella-Enterobacter	2 (9.5)
Citrobacter freundii	1 (4.7)
Candida spp	2 (9.5)
Total	21 (100)

Table 5

Monthly distribution of patients, nosocomial infections (NI) and infection rates

Month	Patients (n)	Patient days (n)	NI (n)	Infection rate
January	7	94	4	42.5
February	17	255	5	19.6
March	18	279	5	17.9
April	10	145	4	27.6
May	10	157	5	31.8
June	13	186	10	53.7
Total	75	1116	33	29.5

ities and duration of treatment were significantly related to the poor outcome (Table 6). No statistical difference was recorded between the subgroups with, and without NI regarding survival ($p > 0.05$). Nosocomial pneumonias, intubation and mechanical ventilation were significantly related to the lethal outcome. Indwelling urinary catheters were also associated with poor outcome (Table 6). None of the causative agents affected survival ($p > 0.05$).

Table 6

Clinical outcome in Intensive Care Unit patients

Parameter	Patients (n)		*p*
	survived	died	
Male	23	6	
Female	14	9	0.218
Age (years), $\bar{x} \pm SD$	48.24 ± 11.95	56.13 ± 15.04	0.159
Previous comorbidity	19	13	
No previous comorbidity	18	2	0.027
Duration of treatment (days), $\bar{x} \pm SD$,	29.84 ± 14.11	15.67 ± 11.95	0.001
NI	21	12	
Without NI	16	3	0.203
Urinary tract infection	8	1	
Pneumonia	0	7	
Skin /soft tissue infections	9	3	
Other	4	1	0.003
Intubation and MV	7	13	
Without intubation	30	2	0.000
UC	23	14	
Without UC	14	1	0.019

NI – nosocomial infections; MV – mechanical ventilation; UC – urinary catheter.

Discussion

We analyzed NIs in 52 patients treated in the ICU in the University Hospital for Infectious and Tropical Diseases in a 6-months period. The patients with various CNS infections and neurointoxications (tetanus, botulism) were included, as well as several patients with severe non-infectious diseases, and indeed even 63.4% of the admitted patients developed NI, without a relationship between initial diagnosis and prevalence of specific NI. Among the observed series of patients, the most prevalent were UTIs, pneumonias and skin and soft tissues infections, with rather high mortality rate among those with pneumonia.

There are many factors that contribute to the high incidence and unfavorable outcome of NIs: ICU patients have more frequent and more difficult comorbidities as well as more profound pathophysiological disturbances than patients in other hospital's departments. In these patients physiological barrieres to infections are often disturbed by using various medical devices, urinary catheters, endotracheal tubes, central vasular catheters, which allow direct breakthrough of microorganisms into the tissues and blood stream. In addition, indwelled catheters demand frequent contacts with hands of health-care workers which can lead to colonisation and infection with hospital pathogens. It is well-known that hospital and especially ICU hygiene and infection control practice are more problematic in developing countries [7], where Serbia belongs. This is why the prevalence of NIs in our setting has reached this high prevalence of over 60%.

Multi-resistant pathogens, such as MRSA, vancomycin-resistant *Enterococci* (VRE), ESBL-producing *Enterobacteriaceae* ect. are more common in ICUs [8]. This is in concordance with our findings.

The patients' gender and age had no influence on the development of NIs, although it had previously been shown that patients' age was important factor in susceptibility to infection, especially for infants, young children, and elderly.

In our series of patients comorbidities were associated with a higher prevalence of NI, which is in concordance with the National Nosocomial Infection Surveillance System (NNIS) report [9].

UTIs were shown to be the most prevalent NI [9]. In addition, it was previously demonstrated that indwelled urinary catheter was the leading risk factor for the acquisition of nosocomial UTIs and bacteremia (70–80%), followed by cystoscopy or other urological procedures [10]. These infecions

were also the most frequent in our series of patients. And indeed, all the patients with UTIs had indwelled urinary catheters. Similarly, Crouzet et al. [11], demonstrated that the duration of urinary catheterization had a great impact on catheter-associated UTI. During the first 3 days of catheterisation, urinary tract infections are rare if closed method of urinary drainage is used, but the risk for acquiring catheter-associated infection increases by additional 5% for every single day of catheterization afterwards. Reported IRs vary widely, ranging from 1–5% after a single brief catheterization to virtually 100% for patients with indwelling urinary catheters draining into an open system for longer than 4 days [11]. The average duration of catheterisation among our patients was even 19 days, so it is not suprising that all of them developed UTIs.

Likely, etiological diagnosis was established in all 16 UTIs. These infections were caused mostly by Gram-negative bacteria, and far less freqent were infections caused by Gram-positive cocci, such as *Enterococcus* spp, that were susceptible to vancomycin. One patient also had *Enterococcus* spp. bacteriemia/septicemia. Fortunately, all the patients from our series experienced favourable response to antibiotic therapy.

Pneumonia was reported to be the second most common NI in the USA, associated with the high morbidity and mortality rates among all hospital-acquired infections [12]. This is also in concordance with our data. Both intubation and mechanical ventilation were significantly associated with NI. Safdar et al. [13] showed the incidence of 1.3% nosocomial pneumonias per day, counting from the time of endotracheal intubation, with the highest incidence from the day 5 to 15. Similarly, most of our patients developed pneumonia about 2 weeks after admission to the hospital. No causative agents were demonstrated in our patients with pnumonia. Bronch aspiration and cannula swab cultures were performed in two patients, without results. However, these specimens are not recommended for etiological diagnosis of nosocomial pneumonia [14], since these techniqes are not capable of distinguishing "colonisations" from infection. Recommendations for the diagnosis of pneumonia include: the protected specimen brush (PSB) with quantitative cultures, bronchoalveolar lavage (BAL), and protected BAL (pBAL) [14]. Since these techniques were not available in our ICU, no etiological diagnosis for patients with pneumonia were established.

Skin and soft tissue infections were the third most common NIs in our series of patients. Most of them were localized around vascular access lines. MRSA was isolated from two swab cultures of skin lesions. MRSA has been common in our ICU. According to European Prevalence of Infection in Intensive Care (EPIC) study data, MRSA was present in 86% of isolated *Staphyloccoci* [3]. Pittet et al. [15], showed that prevention strategy for reducing colonisation and MRSA transmission, such as introducing mandatory handwashing in hospital personnel, was followed by dramatic reduction of NIs at the University Hospital in Geneva.

The mean overall NI rate was approximate or even lower but the device utilization NI rate for ventilator associated pneumonia and catheter-associated UTI was higher compared to other studies [16, 17].

It is very important to understand the significance of NIs in order do decrease their rate in hospitals. The mortality rate in our group of patients treated in the ICU was 28.8%. An EPIC study demonstrated quite similar results in Mediterranean countries [3]. Even though it was not possible to demonstrate with a small number of patients that ICU-acquired infections increased mortality rate in critically ill, we did find that certain NIs (nosocomial pneumonias) were associated with an increased risk of death in the ICU. The comorbidities, duration of hospitalization, the acquisition of nosocomial pneumonia, endotracheal intubation and mechanical ventilation along with prolonged urinary bladder catheterisation had significant influence on clinical ouctome of patients treated in the ICU.

Conclusion

In a series of 52 patients treated in the ICU, Serbian University Hospital for Infectious and Tropical Diseases, UTIs were the most common NIs, and easy to treat. On the contrary, among those with pneumonia, associted with endotracheal intubation and mechanical ventilation, the mortality rate was as high as 80%.

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