Original Article

Hospital infections in a neurological intensive care unit: incidence, causative agents and risk factors

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Abstract

Introduction: Hospital infections (HIs), which are frequently associated with hospital treatment, increase morbidity, mortality and treatment costs. The aim of this study was to establish the incidence of HIs in a neurological intensive care unit (nICU), and to determine the most prevalent causative agents and risk factors for HIs.

Methodology: A cross-sectional study with nested case-control design was conducted between 1 July 2009 and 30 June 2010 at an 18-bed neurological intensive care unit at the Clinical Center Kragujevac, Serbia.

Results: In total, 537 patients were enrolled in the study, with 6,549 patient-days. There were 89 patients with 101 HIs. The incidence of patients with HIs was 16.57%, and incidence of HIs was 18.81%, while density of HIs was 15.42 per 1,000 patient-days. The most frequent anatomical sites of HIs were urinary tract (73.27%), blood (10.89%), and skin and soft tissues (10.89%). The following risk factors were identified: co-morbidity (OR=3.9; 95% CI=1.9-7.9), surgical intervention in the last 30 days (OR=5.6; 95% CI=1.5-20.4), urinary bladder catheterization longer than seven days (OR=3.8; 95% CI=1.8-8.2), value of Glasgow coma scale ≤ 9 (OR=3.7; 95% CI=1-6.9), and longer hospital stay (OR=1.1; 95% CI=1.1-1.2).

Conclusions: Hospitalization in an nICU bears high risk of HIs, especially of urinary tract infections caused by Gram-negative bacteria, in patients with longer hospital stay or co-morbidities, and in those who have had surgical interventions or prolonged use of a urinary bladder catheter. Special attention should be paid to these patients to prevent HIs.

Key words: hospital infections; intensive care unit; neurology; risk factors

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Introduction

Hospital infections (HIs), a treatment complication found in hospitalized patients, are considered an important factor for increased hospital morbidity, mortality, and total treatment costs. HIs constitute a significant health challenge in developed countries, and the problem is worse in developing countries where proven preventive measures may be unobtainable [2,3,4].

Frequency of HIs varies among different hospital departments and depends on hospital type, patient characteristics, and diagnostic criteria. Numerous studies have shown they are most frequently found in patients from intensive care units (ICUs) and comprise 25% of all HIs, even though ICUs occupy only 10% of hospital bed capacities [5]. Risk of HI development is primarily dependent on the type and severity of the underlying disease, as well as exposure to invasive diagnostics and treatment methods.

Characteristics of patients from the neurological ICUs ensue from the underlying disease (altered sensorium and state of consciousness, impaired protective reflexes, muscle weakness, etc.) and make them more prone to acquisition of His, which suggests that specific risk factors may lead to the development of HIs in these patients [6-8].

Microorganisms that cause HIs are usually of endogenous origin as a part of the permanent or transient patient flora, and are rarely disseminated from some existing focus or transferred from the hospital environment, medical staff, devices or equipment that were previously contaminated. The most common pathogens that cause the HIs are *Escherichia coli, Klebsiella, Proteus, Enterobacter* and *Acinetobacter* [9].

The aim of this study was to review the incidence of HIs in a neurological Iintensive care unit (nICU), and identify the most prevalent causative agents and risk factors for HIs.

Methodology

A cross-sectional study with nested case-control design was conducted between 1 July 2009 and 30 June 2010 in an 18-bed neurological intensive xare unit, Clinical Center Kragujevac, Serbia.

The study enrolled all patients hospitalized for more than 24 hours and over 18 years of age. Patients with a fatal outcome occurring within the initial 24 hours, or whose length of ICU stay was shorter than 24 hours, were excluded from further research. Following admission to the ICU, each patient was examined and underwent laboratory tests. Information about each patient was entered into a questionnaire that contained the following data: change in body temperature; data on physical examination of each patient; laboratory findings; data on invasive procedures used; and treatment modalities. All patients were followed until final disease outcome, *i.e.,* cure and discharge or death. After discharge from the ICU, patients were followed for an additional 48 hours to determine whether HI development occurred within that period.

HI diagnosis and anatomical localization were established on the basis of the standard definitions of Centers for Disease Control and Prevention (CDC), Atlanta, USA, modified for our setting [10]. In accordance with above definitions, all infections present at admission or incubating at the moment of patient's admission were not considered as HIs, but as externally acquired infections. An infection was considered hospital acquired if it developed in hospital and manifested 48 hours (typical incubation period for most bacterial HIs) or more following a patient's admission to hospital. Relevant HI data were obtained from the logbook used in the Microbiological Laboratory of the Clinical Center Kragujevac patient's records (medical history, temperature charts, lab results, etc.), and from direct contact with patients and treating physicians. Identification of HI causative agents was performed using a standard chemistry panel, while antibiotic resistance testing was done using the disk-diffusion method.

Information on potential risk factors for development of HIs was collected on patients' admission and during their hospital stay, and all data were recorded in a specially designed epidemiological questionnaire which included the following information: gender; age; previous stay in other departments (other wards, intensive care units or other hospitals); diagnosis and presence of infection at admission; admission urgency status; presence of other diseases or conditions (diabetes mellitus, cancer of various localizations, injuries, chronic heart disease, chronic obstructive lung disease, hypertension, chronic hepatic and renal disease); date of admission and discharge; diagnostic and treatment procedures used (inserted venous catheters, urinary catheters, intubation, mechanical ventilation); performed surgery; and final treatment outcome. At admission, all patients had their Glasgow Coma Scale (GCS) score determined to assess damage to the central nervous system, where the values < 8 indicated severely impaired consciousness at the level of sopor and coma [11,12].

Incidence rates of patients with HIs and all recorded HIs were calculated as a ratio of the number of patients with HIs or number of recorded HIs to the number of patients in the study (x100). To calculate the density of HIs, the ratio of the total number of HIs recorded in the ICU in the observed period to total number of patient days (x1000) was determined.

Primary data were analyzed using descriptive statistical methods, methods of statistical hypothesis testing, and analysis of outcomes and potential predictors. Data analysis was performed using SPSS (Statistical Package for Social Sciences software - SPSS Inc, version 11, Chicago, IL, USA). Descriptive statistical methods used included measures of central tendency (mean), measures of variability (standard deviation), and relative numbers. Hypothesis testing of difference in incidence was performed using chi-squared distribution and Fisher's combined probability test, while difference of means was tested using the Wilcoxon rank-sum test. Logistic regression was used to analyze the relation of binary outcomes and potential predictors. The level of statistical significance used to test statistical hypotheses was 0.05.

Results

During the study period, 537 patients met all eligibility criteria for the study, with a total of 6,549 days of hospital stay. Gender structure included more female (n = 310; 57.73%) than male subjects (n = 227; 42.27%). The average age of patients was 72 ± 11.5. Out of the total number of subjects, 282 (52.51%) had cerebral hemorrhage or infarction, 192 (35.76%) had hemiplegia, while other diagnoses accounted for

Table 1. Representation of hospital infections in the neurological intensive care unit according to anatomic sites and rates per 100 patients and 1,000 patient-days

Anatomical site	Number of Infections	%	Rate of infections per 100 patients	Rate of infections per 1,000 patient-days
Urinary tract infections	74	73.27	13.78	11.30
Blood infections	11	10.89	2.05	1.68
Skin and soft tissue infections	11	10.89	2.05	1.68
Pneumonia	4	3.96	0.74	0.61
Surgical site infections	1	0.99	0.19	0.15
Total	101	100	18.81	15.42

11.73% of cases (cephalea, encephalopathia, aneurysm, arteriosclerosis, dementia).

There were 89 patients with 101 HIs. The incidence rate of patients with HIs was 16.57%, while the incidence rate of HIs was 18.81%, with HI density of 15.42 per 1,000 patient-days. Distribution and rates of HIs are shown in Table 1.

The presence of one HI was found in 77 (86.51%) subjects, while 12 (13.49%) patients had two HIs. According to anatomical site, the most frequent infections were found in the urinary tract (73.27%) and blood (10.89%), followed by the skin and soft tissues (10.89%); in addition, 4 cases of pneumonia and one surgical site infection were found (Table 1).

The presence of microorganisms as causative agents for HIs is shown in Table 2. Most causative agents belonged to Gram-negative bacteria (89.76%), the following having the largest number of isolates: *Enterobacter cloacae* (19.69%), *Klebsiella spp* (15.75%), *Proteus mirabilis* (12.60%), *Pseudomonas aeruginosa* (11.02%), and *Escherichia coli* (10.24%).

The results of the univariate analysis of risk factors for development of hospital infections in patients treated in the neurological ICU are shown in Table 3. According to the univariate analysis, previous stay in another department (other wards, intensive care units, or other hospitals) ($p < 0.001$), presence of infection at admission ($p < 0.001$), comorbidities ($p < 0.001$), surgical intervention within the past 30 days ($p < 0.002$), inserted urinary catheter ($p < 0.015$), urinary catheterization longer than 7 days ($p < 0.001$), intubation ($p < 0.001$), GCS ≤ 9 ($p < 0.001$) and prolonged hospital stay ($p < 0.001$) were significant risk factors for the development of hospital infections.

Multivariate logistic analysis identified five risk factors independently associated with the development of hospital infections: comorbidity (OR = 3.9; 95% CI = 1.9-7.9; $p < 0,001$); surgical intervention within the past 30 days (OR = 5.6; 95% CI = 1.5-20.4; $p < 0,008$); urinary catheterization longer than 7 days (OR = 3.8; 95% CI = 1.8-8.2; $p < 0,001$); Glasgow coma scale score ≤ 9 (OR = 3.7; 95% CI = 1-6.9; $p < 0,001$); and prolonged hospital stay (OR = 1.1; 95% CI = 1.1-1.2; $p < 0,001$) (Table 4). The entire model was statistically significant (chi-square test = 153.85; DF = 8; $p = 0.001$).

Adverse treatment outcomes occurred in 44 (49.44%) patients with HIs and in 202 (45.09%) without His; however, the difference was not reached statistically significant ($p = 0.452$).

Discussion

There have been few studies worldwide that examined incidence, prevalence or characteristics of HIs in the neurological ICU, despite their specific traits stemming from the nature of patients' disease as well as the medical procedures utilized. In Serbia, studies of incidence of hospital infections were limited to surgical wards. Incidence of HIs in a Serbian urology department was 22.4%, with density of 12.4 on 1,000 patient-days [13], in a cardiovascular surgery department about 2.6% [14], and in general surgery departments up to 3.4 on 1,000 patient-days [15]. On the other hand, prevalence studies were conducted on the hospital level only, showing values from 4.6% [16] to 7.1% [17].

In our study, the incidence of HIs in a neurological ICU was 18.81%, with density of 15.42 on 1,000 patient-days of hospital stay, a result similar to the rates found in developed countries. Countries with limited resources, or those at the early phases of HI surveillance, have much higher rates of HI incidence. In a study conducted at a neurological ICU in Turkey, Buke *et al*. [18] determined an HI incidence rate of 30.89% and density of 46.1 per 1,000 patient-days of

Table 2. Microorganisms found in isolates of hospital infections in the neurological intensive care unit

Causative agent	Number	%
Gram-negative (n = 114)		
Enterobacter cloacae	25	19.69
Klebsiella spp	20	15.75
Proteus mirabilis	16	12.60
Pseudomonas aeruginosa	14	11.02
Escherichia coli	13	10.24
Klebsiella oxytoca	12	9.45
Acinetobacter spp	4	3.15
Proteus vulgaris	3	2.36
Klebsiella pneumoniae	2	1.57
Other	5	3.94
Gram-positive (n = 13)		
Staphylococcus aureus	6	4.72
Coagulase-negative *Staphylococci*	4	3.15
Enterococcus faecalis	3	2.36

Table 3. Main characteristics of patients in neurological intensive care unit

Variable	Patients with HIs (n = 89) n (%)	Patients without HIs (n = 448) n (%)	p
Age, $\bar{x}$ ±SD	71.9 ± 12.1	72.0 ± 11.4	0.807
≥ 65 years of age	70 (78.7%)	332 (74.1%)	0.367
Male	41 (46.1%)	186 (41.5%)	0.427
Previous stay in other dept.	24 (27%)	56 (12.5%)	<0.001*
Emergency admission	81 (91%)	420 (93.8%)	0.345
Infection at Admission	16 (18%)	22 (4.9%)	<0.001*
Injury	2 (2.2%)	6 (1.3%)	0.625
Diabetes mellitus	25 (28.1%)	110 (24,6%)	0,482
Cancer	3 (3.4%)	12 (2.7%)	0.724
Other co-morbidites**	73 (82%)	254 (56.7%)	<0.001*
Surgical intervention	8 (9%)	8 (1.8%)	0.002*
Central venous catheter	1 (1.1%)	2 (0.4%)	0.42
Peripheral venous catheter	86 (96.6%)	444 (99.1%)	0.093
Urinary catheter	87 (97.8%)	402 (89.7%)	0.015*
Urinary catheter ≥ 7 days	78 (87.6%)	214 (47.8%)	<0.001*
Artificial ventilation	1 (1.1%)	0 (0%)	0.166
Intubation	12 (13.5%)	10 (2.2%)	<0.001*
Glasgow Coma Scale score ≤ 9	56 (62.9%)	180 (40.2%)	<0.001*
Duration of hospital stay (days), $\bar{x}$ ± SD	18.8 ± 8.9	10.9 ± 7.4	<0.001*

*statistically significant
**chronic heart disease, chronic obstructive lung disease, hypertension, chronic hepatic and renal disease

Table 4. Risk factors for hospital infections in neurological intensive care unit (multivariate analysis)

Variable	B	p	OR	95% CI
Previous stay in other dept.	0.645	0.073	1.9	0.9
Infection at Admission	0.763	0.097	2.1	0.9 – 5.3
Other comorbidities**	1.365	<0.001*	3.9	1.9 – 7.9
Surgical intervention	1.731	0.008*	5.6	1.5 – 20.4
Urinary catheter ≥ 7 days	1.345	<0.001*	3.8	1.8 – 8.2
Intubation	0.825	0.148	2.3	0.7 – 6.9
Glasgow Coma Scale score ≤ 9	1.321	<0.001*	3.7	2 – 6.9
Duration of hospital stay	0.114	<0.001*	1.1	1.1 – 1.2

*statistically significant
**chronic heart disease, chronic obstructive lung disease, hypertension, chronic hepatic and renal disease
B - Coefficient of logistic regression analysis;
OR - Odds Ratio

hospital stay. On the other hand, in a study conducted at a neurological ICU in Germany, Zolldann *et al*. [19] reported an HI incidence rate of 21.0% and density of 24.8 per 1,000 patient-days of hospital stay. An earlier study conducted in the same country [20] reported somewhat higher values with a incidence rate of 24.2 and density of 25.0. High incidence rates of HIs are a common problem in many ICUs, primarily caused by the presence of severe conditions in patients. Longer life span and hospitalization of increasingly older patients whose immune systems are weak, utilization of a number of medical procedures (both diagnostic and therapeutic), and disregard of basic hygiene measures in daily work are frequently indicated as important factors that influence the increase of rates in hospital infections in ICUs [21]. Numerous examples from developed countries suggest that epidemiological surveillance of HIs and appropriate preventive measures, as well as training of health-care professionals make it possible to decrease the incidence of HIs.

In our study, the most frequent anatomical sites of HIs were urinary tract, blood, and skin and soft tissues, comprising approximately 95% of all recorded HIs. Other authors rank HIs differently in regard to anatomical sites. Dettenkofer *et al*. indicated that pneumonia, urinary tract infections, and blood infections are most commonly found in a neurological ICU [20]. Authors of a recent study conducted in Turkey suggest similar results [22]. One explanation for the small number of patients with hospital pneumonia recorded in this study may be found in the fact this department lacked technical capabilities for mechanical ventilation, widely considered an important risk factor for these infections. The patients in need of this medical procedure were transferred to another, appropriately equipped, ICU.

Our data indicate a major presence of urinary tract infections (73.27%), which could be expected given the state of consciousness in these patients caused by underlying disease, the presence of muscle weakness, and the older age of the patients, all of which necessitate urinary catheterization. The proportion of these infections in similar studies conducted in the world is smaller and ranges from 36.6% to 42.9% [19, 22], although urinary tract infections do not represent the most common HIs found in hospitals worldwide [23]. One of the important factors for the high incidence of urinary tract infections in our hospitals is the lack of national guidelines and measures to control these infections. Other countries with limited resources also have similar problems [24].

The spectrum of the most common causative agents of HIs shows significant differences among hospitals, depending on the type of study, patient population, and diagnostic techniques. Previous studies have indicated the dominant role of Gram-positive bacteria in the development of HIs in ICUs, but the latest studies show that Gram-negative bacteria have taken the lead [24]. According to data reported by the National Nosocomial Infections Surveillance System (NNIS), in 2003, Gram-negative bacteria were isolated in 71% of urinary tract infections, 65% cases of pneumonia, 34% of surgical site infections and 24% of blood infections [9]. Our results are highly consistent with the above, since the proportion of Gram-negative bacteria comes close to 90% of all isolates. The most commonly found in our study were *Enterobacter cloacae* (19.69%), *Klebsiella spp* (15.75%), *Proteus mirabilis* (12.60%), *Pseudomonas aeruginosa* (11.02%), and *Escherichia coli* (10.24%). An important feature of isolated agents is the existence of antimicrobial resistance, often against more than three groups of antibiotics (multiresistance), which is a major therapeutic problem. The causative agents of HIs are specific to each health-care facility, even to individual sections within them, and good knowledge of these agents plays an important role when choosing

specific prevention strategies and recommended empirical antibiotic therapy.

It is of paramount importance to determine the coma status of patients, and thus their disease severity, in neurological ICUs. GCS is one of the simplest and most widely used scoring systems for assessment of damage to the central nervous system, and is often a routine procedure [11,12]. GCS score below 9 indicates severe craniocerebral damage in patients. In these patients the local defense mechanisms of the respiratory tract (cough reflex, swallowing) are often impaired, which makes it easier for microorganisms to stick and bind to mucosal surfaces, thus leading to the development of HIs. Our research showed that in patients with GCS score ≤ 9, the risk of HI development is 3.7 times higher (95% CI = 2-6.9) than it is in patients with GCS score ≥ 9.

To date, diabetes has been a chronic disease most frequently associated with hospital infections. Some authors have concluded that diabetic patients bear greater risks of occurrence of HIs, while others have seen no such connection. The fact remains that diabetes and stress-induced hyperglycemia are known factors related to high risk for complications and death in many critically ill patients [25]. Our study did not mark diabetes as a risk factor for development of HIs; however, we found that the presence of other chronic diseases or conditions (chronic heart disease, chronic obstructive pulmonary disease, hypertension) increases the risk of HIs 3.9 times (95% CI = 1.9-7.9). Existing chronic diseases can significantly decrease the body's immune response and impair the function of protective reflexes (coughing), making the body more susceptible to the development of HIs.

The results obtained in this study confirm that the main risk factor for hospital urinary tract infections is urinary bladder catheterization longer than seven days (OR = 3.8; 95% CI = 1.8-8.2). The results obtained bear a high correlation with those of similar studies conducted in Serbia [26] and other countries, which indicate that the risk of urinary tract infections increases with the duration of catheter use [27,28,29]. Urinary catheter traumatizes and expands the urethra, thus interrupting the natural defense mechanisms against infection and blocking paraurethral gland ducts. A biofilm consisting of bacteria cells, their polysaccharide glycocalix, host proteins, salts, and fibrin from damaged uroepithelial cells exudate develops on the catheter. Biofilm bacteria are inaccessible to treatment, and a urine stream cannot wash them off, which paves the way for less virulent microorganisms to cause infections when a catheter is present. In addition, the catheter enables upward bacterial migration [30]. Therefore, it is recommended that urinary catheters should be removed after five days, when patients usually become stable [28].

The study did not include a large number of patients with surgery performed; however, having surgery within the last 30 days proved itself as a significant risk factor for development of HIs (OR = 5.6; 95% CI = 1.5-20.4). Even though the most commonly found postoperative infections were surgical site infections (3%-22%), urinary tract infections were also found quite frequently. The rate of urinary tract HIs following different surgical interventions varies in other studies, ranging from 30.7% after gynecological surgery, to 4.1% after colorectal surgery, and 1.2% after non-abdominal surgery [31,32]. Urinary bladder catheterization, a standard procedure performed in patient preparation for more extensive surgical procedures and operations in epidural or spinal anesthesia, is the most likely cause of such high rates of postoperative urinary tract infections [31,32]. The newly developed HI further complicates the patient's health, since it can be life threatening and compromise the outcome of surgery, prolong treatment, increase patient suffering, and increase medical costs [31,32].

Our study indicates that prolonged hospital stay is a risk factor for the development of HIs, which is the same result obtained in several prior studies [32,33]. It has been demonstrated that hospital stay itself poses approximately 17.6% risk of hospital infection development, with each night spent in hospital increasing the risk by an additional 0.5% [34]. Prolonged hospital stay due to underlying disease and present co-morbidities necessitates a number of medical procedures that increase the possibility of transferring HI pathogens.

Obtained results on HI incidence, characteristics, and risk factors contributing to their occurrence serve as a basis for the control program and prevention of these infections in the Serbian setting. Epidemiological surveillance represents the first stage in the battle against HIs, which helps to promptly set hospital priorities and take appropriate preventive measures. The Serbian national strategy to decrease incidence of hospital infections includes systematic implementation of preventive measures identified through studies such as this one. The preventive measures are guided and followed by national and hospital committees for the HIs, established according to Serbian legislation.

Conclusion

Urinary tract infections are the most common HIs in neurological ICUs, and Gram-negative bacteria play an important role in their etiology. Our study has shown that co-morbidities, surgical interventions, urinary catheterization longer than seven days, GCS score ≥ 9 and prolonged hospitalization are risk factors for development of HIs in patients staying in the neurological ICU. To obtain a more complete picture of the role of these risk factors and others in the development of HIs, further studies with larger samples are required since it is a well-known fact that each ICU has specific epidemiological factors for the development of HIs. Early identification of risk factors should help physicians to recognize high-risk patients and implement appropriate preventive measures in order to forestall their occurrence.

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