ORIGINAL ARTICLE
UDC: 616-036.22:[616.8-082::614.2
https://doi.org/10.2298/VSP180422184V

Risk factors for healthcare associated infections and in-hospital mortality in a neurological intensive care unit in a tertiary hospital in Belgrade, Serbia: A prospective cohort study

Faktori rizika od nastanka bolničkih infekcija i smrtnog ishoda u neurološkoj jedinici intenzivnog lečenja u tercijarnoj bolnici u Beogradu, Srbija: prospektivna kohortna studija

Stefan Vidaković*, Ranko Raičević*†, Marija Grunauer†, Viktor Pasovski†, Vesna Šuljagić*‡

University of Defence, *Faculty of Medicine of the Military Medical Academy, Belgrade, Serbia; Military Medical Academy, †Clinic for Neurology, ‡Department for Prevention and Control of Nosocomial Infections, Belgrade, Serbia

Abstract

Background/Aim. Patients in a neurologic intensive care unit (ICU) are especially susceptible to healthcare-associated infections (HAIs). HAIs are cause of significant morbidity and mortality. Aim of this study was to assess the incidence of HAIs, to identify significant risk factors (RFs) and causative microorganisms for HAIs and to identify RFs for in-hospital mortality in a neurological ICU. **Methods.** A prospective cohort study was conducted in the six-bed ICU of the Clinic for Neurology, Military Medical Academy in Belgrade from January 1, 2014 to December 31, 2016. Active surveillance on HAIs was performed by the hospital infection control team, using methodologies of the European Centre for Disease Prevention and Control and the National Healthcare Safety Network/Centres for Disease Prevention and Control. **Results.** One hundred forty eight patients with a total of 2,708 patient-days were enrolled. There were 49 HAIs in 39 patients during the study period. The incidence and incidence density of HAIs were 26.3% and 18.1 per 1000 patient-days, respectively. The most frequent HAIs were urinary tract infections (15.5%), pneumonia (10.1%) and bloodstream infections (4%). RFs independently associated with HAIs in the neurological ICU were: urinary catheter [risk ratio (RR): 5.6; 95% confidence interval (CI): 1.153–27.632], urinary catheter-days (RR: 1.1; 95% CI: 1.057–1.188), central-line days (RR: 1.1; 95% CI: 1.010–1.150), and mechanical ventilation (RR: 0.3; 95% CI: 0.079–0.859). The most common microorganism was *Klebsiella* spp. RFs independently associated with in-hospital mortality in the neurological ICU were: mechanical ventilation (RR: 6.5; 95% CI: 2.868–14.116), Glasgow Coma Score (RR: 2.7; 95% CI: 1.135–6,396), and age (RR: 1.03; 95% CI: 1.005–1.055). **Conclusion.** Usage of invasive procedures during ICU hospitalization carries significant risk for development of HAIs. HAIs in ICU setting are most often caused by Gram-negative bacteria with substantial antimicrobial resistance. These results stress the importance of infection prevention.

Key words:
cross infection; neurology; critical care; risk factors; monitoring, physiologic; drug, resistance microbial.

Apstrakt

Uvod/Cilj. Bolesnici u neurološkim jedinicama intenzivnog lečenja (JIL) su u posebnom riziku od nastanka bolničkih infekcija (BI). BI uzrokuju značajan morbiditet i mortalitet. Cilj ovog istraživanja bio je da se utvrdi incidencija BI, identifikuju faktori rizika (FR) i uzročnici BI, kao i da se ustanove FR za smrtni ishod u neurološkoj JIL. **Metode.** U šestokrevetnoj JIL Klinike za neurologiju Vojnomedicinske akademije u Beogradu sprovedena je prospektivna kohortna studija od januara 2014. godine do decembra 2016. godine. **Rezultati.** U studiju je bilo uključeno 148 bolesnika praćenih tokom 2 708 bolesnik-dana. Registrovano je ukupno 49 BI kod 39 bolesnika. Incidencija BI bila je 26,3%, a gustina incidencije 18.1 na 1000 bolesnik-dana. Najčešće BI bile su: infekcije mokraćnog sistema (15,5%), pneumonija (10,1%) i sepsa (4%). FR povezani sa nastankom BI u neurološkoj JIL bili su primena urinarnog katetera [*risk ratio* (RR): 5,6; 95% *confidence interval* (CI): 1,153–27,632), dani primene urinarnog katetera (RR: 1,1; 95% CI: 1,057–1,188), dani primene centralnog vaskularnog katetera (RR: 1,1; 95% CI: 1,010–1,150) i primena mehaničke ventilacije (RR: 0,3;

Correspondence to: Stefan Vidaković, University of Defence, Faculty of Medicine of the Military Medical Academy, Crnotravska 17, 11 000 Belgrade, Serbia. E-mail: vidakovic92@live.com

95% CI: 0,079–0,859). Najčešće registrovani uzročnik BI bila je *Klebsiella* spp. FR povezani sa smrtnim ishodom u neurološkoj JIL su bili: mehanička ventilacija (RR: 6,5; 95% CI: 2,868–14,116), Glasgov koma skor (RR: 2,7; 95% CI: 1,135 – 6,396) i starost bolesnika (RR: 1,03; 95% CI: 1,005–1,055). **Zaključak.** Upotreba invazivnih pomagala tokom boravka u neurološkoj JIL nosi značajan rizik od nastanka BI. U neurološkoj JIL BI su najčešće uzrokovane Gram negativnim bakterijama, koje ispoljavaju učestalu rezistenciju na antibiotike. Ovi rezultati naglašavaju značaj prevencije BI.

Ključne reči:
infekcija, intrahospitalna; neurologija; intenzivna nega; faktori rizika; fiziološke funkcije, praćenje; lekovi, rezistencija mikroorganizama.

Introduction

Healthcare associated infections (HAIs) are the cause of significant morbidity and mortality. This is especially important in intensive care units (ICUs) because of severe pathology and multitude of invasive diagnostic and therapeutic procedures [1]. Additionally, an infection risk increases with the length of stay in ICUs [2].

Patients in neurological ICUs are prone to HAIs because of underlying disease nature which is characterized by various disorders of consciousness, diminished protective reflexes, muscle weakness, concomitant immunosuppression, etc. These patients are often bedridden and immobilized, with indwelling central vascular catheter (CVC) and urinary catheter (UC), frequently requiring mechanical ventilation (MV) for extended period of time [3, 4]. They often receive intensive prolonged empirical antimicrobial therapy that could be potent driver of colonisation and infection by multidrug-resistant bacteria and *Clostridium difficile*. The surveillance on HAIs in this type of ICUs is widely accepted as control and prevention method and it can be valuable tool in risk factors (RF) identification and mortality and morbidity reduction [5].

Vincent et al. [2] found that there is a substantial international difference in infection prevalence, type of microorganisms and mortality. The most common microorganisms that cause HAIs in a neurological ICU are: coagulase-negative *streptococci*, *Escherichia coli, Staphylococcus aureus and Klebsiella* spp. [6].

The aim of this study was to assess the incidence of HAIs, to identify their significant RFs and causative microorganisms. We also wanted to identify RFs for in-hospital mortality in a neurological ICU.

Methods

This prospective cohort study was conducted in the six-bed ICU of the Clinic for Neurology at the Military Medical Academy (MMA) in Belgrade, 1,146-bed tertiary healthcare center, teaching hospital of the Faculty of Medicine of the University of Defence, Belgrade, Serbia. This neurological ICU was founded in 2013. A total of 148 patients hospitalized in the ICU for more than 24h from January 2014 to December 2016 were enrolled in this study. The patients whose length of stay was less than 24h or who died within the first 24h of admission into the ICU were excluded from the study. Active surveillance on HAIs was performed by the hospital infection control team, using methodologies of the European Centre for Disease Prevention and Control (ECDC) [7] and the National Healthcare Safety Network/Centres for Disease Prevention and Control (NHSN/CDC) [8]. Standardized form for data collection was used.

The data related to patients [age, gender, Glasgow coma score (GCS) on admission, primary diagnosis, the presence of underlying diabetes mellitus, neoplasms, presence of infections on admission] and those related to healthcare (CVC and central line days, MV and ventilator-days, UC and urinary catheter days, clinical outcome) and length of ICU stay were registered. The results of microbiological analysis and antimicrobial resistance were recorded on daily basis.

Only infections registered after 48h of admission were considered as HAIs. All HAIs were classified into following groups: urinary tract infection (UTI), pneumonia, bloodstream infection (BSI) and infection caused by *Clostridium difficile* (CDI). Microbiological analyses of the samples gathered from the patients with HAIs were performed in the Institute of Microbiology at the Military Medical Academy.

Incidence and incidence density were calculated as the number of HAIs *per* 100 patients and 1,000 patient/days or on 1,000 device/days (for specific devices associated with infection). The device utilization rate (DUR) was also calculated. DUR was determined using following formula:

$$\text{DUR} = \text{Number of device days} / \text{Number of patient days} * 100$$

Incidence rate of CDI was defined as the number of HAI CDI caused by *per* 10,000 patient-days. The in-hospital mortality rate was defined as the number of deaths per 100 patients.

Statistical analysis of data was performed using the SPSS software package (SPSS, Chicago, IL, USA, version 18.00). The results are expressed as mean ± standard deviation (SD) or as the proportion of the total number of patients. Testing for significant differences was conducted by the χ^2 test for categorical variables and the Student's *t*-test for continuous variables. The factors were considered to be significant at a *p*-value of ≤ 0.05. All *p*-values were two-tailed. RFs independently associated with HAIs and in-hospital mortality (poor clinical outcome) were identified by multivariate logistic regression analysis (MLRA) of variables selected by univariate logistic regression analysis (ULRA) with a limit for entering and removing variables of 0.05.

Results

During the 48-month study period, 148 patients with a total of 2,708 patient-days and mean length of ICU stay of

18.3 days (range, 3 to 97 days) were enrolled. The mean age of the patient population was 70.2 years (range, 15 to 94 years). Twenty-two or 14.9% of the patients had cerebral hemorrhage, 94 or 63.5% had ischemia, while other diagnoses (epilepsy, Parkinson's disease, multiple sclerosis, CNS tumors, polyneuropathies, traumas) accounted for 32 or 21.6% of all treated patients.

There were 49 HAIs in 39 patients during the study period. Thirty one patients (20.9%) had one, 6 patients (4%) had two and 2 patients (1.3%) had 3 infections during their stay in the neurological ICU. The incidence and incidence density of HAIs were 26.3 % and 18.1 *per* 1,000 patient-days, respectively.

UTIs (23 or 15.5%) were the most frequent HAIs. Incidence density was 0.8 UTIs per 1,000 patient-days. There were 10.4 UTIs *per* 1,000 catheter-days. Pneumonia (15 or 10.1%) was the second most common type of HAIs with incidence density of 5.5 *per* 1,000 patient-days. There were 12.3 ventilation associated pneumonias (VAPs) *per* 1,000 ventilator-days.

BSI (6 or 4%) had incidence density of 2.2 per 1,000 patient-days.

The DUR values were 81.3, 35.7 and 17.8 for UV, MV and CVC, respectively.

Risk factors for healthcare-associated infections acquisition

Demographic and clinical characteristics in the group with and the group without HAIs according to ULRA are shown in Table 1. According to ULRA, several characteristics were more frequent in the group with than in the group without HAIs: lenght of ICU hospitalization, CVC, MV, central line-days, ventilator-days and urinary catheter-days.

MLRA identified 4 RFs independently associated with HAIs in the neurological ICU: UC [risk ratio (RR): 5.6; 95% confidence interval (CI): 1.153–27.632), urinary catheter-days (RR: 1.1; 95% CI: 1.057–1.188), central line-days (RR: 1.1; 95% CI: 1.010–1.150), MV (RR: 0.3; 95% CI: 0.079–0.859).

The total of 55 microorganisms was detected in 39 HAIs (Tables 2 and 3).

CDI incidence rate was 14.8 *per* 10,000 patient-days.

Table 1

Distribution of patients with and without HAIs according to demographic and clinical characteristics: results of univariate logistic regression analysis

Variable	Patients with HAIs (n = 39)	Patients without HAIs (n = 109)	*p* value
Male, n (%)	26 (66.7)	60 (55.0)	0.207
Age (years), mean ± SD	67.1 ± 18.9	71.4 ± 16.5	0.216
Primary diagnosis, n (%)			0.640
hemorrhage	4 (10.2)	18 (16.5)	
ischemia	26 (66.7)	68 (62.4)	
other	9 (23.1)	23 (21.1)	
Glasgow coma score, n (%)			0.659
3–9	10 (25.6)	32 (29.4)	
10–15	29 (74.4)	77 (70.6)	
Diabetes mellitus, n (%)	2 (5.1)	18 (16.5)	0.131
Neoplasm, n (%)	0 (0)	1 (0.9)	/
Infection at admission, n (%)	7 (17.9)	9 (8.3)	0.130
Survived, (%)	23 (59.0)	66 (60.6)	1.000
ICU hospitalization days, mean ± SD	32.5 ± 19.6	13.2 ± 11.9	< 0.001
CVC, n (%)	15 (38.5)	14 (12.8)	0.001
Central line days, mean ± SD	8.5 ± 14.7	1.4 ± 4.1	< 0.001
MV, n (%)	26 (66.7)	45 (41.3)	0.011
Ventilator days, mean ± SD	14.7 ± 21.3	3.6 ± 9.3	< 0.001
UC, n (%)	35 (89.7)	94 (86.2)	0.777
Urinary catheter days, mean ± SD	26.4 ± 17.6	10.8 ± 10.4	< 0.001

HAIs – healthcare associated infections ; ICU – intensive care unit; CVC – central vascular catheter; MV – mechanical ventilation; UC – urinary catheter.

Table 2

Distribution of microorganisms isolated from patients with HAIs

Microorganisms	Total n (%)	BSI n	Pneumonia n or n (%)	UTI n or n (%)	Diarrhea n or n (%)
Klebsiella spp.	11 (19.0)	1	3	7 (25.9)	0
Acinetobacter spp.	10 (17.2)	1	5 (25.0)	4	0
Enterococcus spp.	8 (13.8)	1	0	7 (25.9)	0
Proteus spp.	8 (13.8)	0	3	5	0
Pseudomonas aeruginosa	6 (10.3)	1	3	2	0
Clostridium difficile	4 (6.9)	0	0	0	4 (100)
Escherichia coli	3 (5.1)	0	1	2	0
Staphylococcus aureus	2 (3.4)	0	2	0	0
Coagulase negative *staphylococci*	2 (3.4)	2	0	0	0
Streptococcus spp.	1 (1.7)	0	1	0	0
Serratia spp.	1 (1.7)	1	0	0	0
Coryneform bacteria	1 (1.7)	0	1	0	0
Hemophilus spp.	1 (1.7)	0	1	0	0
Total	58 (100)	7	20	27	4

HAIs – healthcare associated infections; BSI – bloodstream infection; UTI – urinary tract infection.

Table 3

Antimicrobial resistance of isolated strains

Microorganism	n	AMR
Klebsiella spp.	11	11 to 3G (100%), 5 to CBP (45.4%)
Acinetobacter spp.	10	All to CBP (100%)
Enterococcus spp.	10	2 to vancomycin (20%)
Pseudomonas aeruginosa	6	4 to CBP (66.7%)
Proteus spp.	5	4 to 3G (80%), 3 to CBP (60%)
Clostridium difficile	4	–
Staphylococcus aureus	2	All were MRSA
Escherichia coli	2	–
Serratia marcescens	1	1 to 3G and CBP

AMR – antimicrobial resistance; 3G – third-generation cephalosporins; CBP – carbapenems; MRSA – methicillin resistant *Staphylococcus aureus.*

Risk factors for poor clinical outcome of treated patient

While overall mortality rate was 39.9%, mortality rate in patients with HAIs was 59%. Demographic and clinical characteristics in patients with poor *versus* patients with favourable clinical outcome according to ULRA are shown in Table 4.

RFs independently associated with in-hospital mortality in the neurological ICU were: MV (RR: 6.5; 95% CI: 2.868–14.116), GCS (RR: 2.7; 95% CI: 1.135–6,396), and age (RR: 1.03; 95% CI: 1.005–1.055).

Increasing morbidity and mortality associated with HAIs in the neurologic ICU is a topic of serious concern today. A few studies addressed these issues during first two decade of 21st century. A comparative review of our results and those of these studies is given in Table 5.

Table 4

Distribution of survived patients and died patients according to their demographic and clinical characteristics: results of univariate logistic regression analysis

Characteristics	Survived patients (n = 89) n (%)	Died patients (n = 59) n (%)	*p*
Male	59 (68.6)	27 (31.4)	0.021
Age (years)			
< 65	33 (37.1)	11 (18.6)	0.018
≥ 65	56 (62.9)	48 (81.4)	
Primary diagnosis			
hemorrhage	11 (12.4)	11 (18.6)	
ischemia	54 (60.7)	40 (67.8)	0.124
other	24 (27.0)	8 (13.6)	
Glasgow coma score			
3–8	16 (18.0)	22 (37.3)	0.01
9–15	73 (82.0)	37 (62.7)	
Diabetes mellitus	9 (10.1)	11 (18.6)	0.215
Neoplasm	1(1.1)	0 (0)	/
Infection at admission	13 (14.6)	3 (5.1)	0.120
HAIs	23 (25.8)	16 (27.1)	1.000
Duration of hospitalization in ICU, mean ± SD	18.3 ± 16.6	19.3 ± 15.6	0.004
CVC	18 (20.2)	11 (18.6)	0.979
MV	29 (32.6)	42 (71.2)	0.000
UC	79 (88.8)	50 (84.7)	0.642

CVC – central vascular catheter; MV – mechanical ventilation; UC – urinary catheter; HAIs – healthcare-associated infections; ICU – intensive care unit.

Table 5

Results from current and other relevant studies (mean values)

Parameters	Current study	Zolldan et al. [9] study	Tekin et al. [6] study	Dettenkofer et al. [4] study	Djordjevic et al. [13] study
Patients (n)	148	338	11772	505	537
Patient days (n)	2,708	2,867	133,992	4,873	6,549
Length of stay (days)	18.3	8.5	34.3	9.6	–
Incidence (%)					
UTI	15.3	36.6	32.0	8.7	13.78
pneumonia	10.1	29.6	25.1	11.7	0.74
bloodstream infection	4	15.5	17.2	1.4	2.05
VAP (*per* 1000 days of MV)	12.3	12.8	–	20.4	–
Overall incidence (incidence density) (%)	26.3 (18.1)	21.0 (24.8)	3.7 (3.2)	24.2 (25.0)	18.81 (15.42)
Device use rate (%)					
UC	81.3	92	–	86	–
CVC	17.8	69	–	75	–
MV	35.7	57	–	22	–
Dominant microorganism	*Klebsiella* spp.	*Escherichia coli*	*Coagulase negative staphylococci*	*Acinetobacter* spp.	*Enterobacter cloacae*
In-hospital mortality rate (%)	39.9	–	–	–	–

UTI – urinary tract infection; VAP – ventilation associated pneumonia; UC – urinary catheter; CVC – central vascular catheter; **MV – mechanical ventilation.**

Discussion

Tekin et al. [6] found that during fourteen year surveillance of patients who had cerebrovascular diseases and epilepsy, treated in the Clinic for Neurology in southeast of Turkey, overall incidence of HAIs was 3.7% (range 1.0–7.7) and overall incidence density was 3.2 (range 0.8–7.2). The rates reported in studies conducted in patients in neurological ICUs were higher. Dettenkofer et al. [4] reported that the incidence was 24.2% and incidence density was 25.0 *per* 1,000 patient days. Zolldann et al. [9] found overall incidence and incidence density as 18.5% and 25.0 respectively, while Abdulhasan et al. [10] presented results acquired during 6-year surveillance study with 227 HAIs that were identified for a rate of 10.9/1000 ICU days. Highest incidence rate were registered for subdural hematoma and intracerebral/intraventricular hemorrhage, 21.3 and 21.1 *per* 1,000 patient days, respectively. In the present study, overall incidence was 26.3% and incidence density was 18.1 *per* 1,000 patient-days.

DUR was calculated as ratio of devices-days to patients-days for each location type. These data may serve as marker of severity of illness of patients or measure of use invasive devices which constitute extrinsic RF for HAIs [11].

The most relevant database documenting HAIs in ICUs is provided by the NHSN in the United States (US). Pooled data of the surveillance activities in participating US hospitals are published annually. In 2011, US neurological ICUs reported pooled mean urinary catheter-associated UTI rates of 3.4 (21 ICUs, 116 catheter-associated UTI, 34,422 urinary catheter-days) and pooled mean urinary catheter DUR of 0.66 (21 ICUs, 34,422 urinary catheter-days, 48,549 patients-days) [12]. In our neurological ICU, we recorded 10.4 UTI *per* 1,000 catheter-days and DUR for urinary catheters was 0.81. MLRA confirm that use of UC (RR: 5.6; 95% CI: 1.153–27.632) and duration of urinary catheterization (RR: 1.1; 95% CI: 1.057–1.188) were independent RFs for HAIs. These data bear high correlation with those of similar studies conducted in Serbia [13].

VAP refers to hospital-associated pneumonias (HAP) that develops among patients on MV and presents more than 48 hours after endotracheal intubation [14]. Our results also show significant incidence of VAP (incidence density was 12.3) which corresponds with results published by Zolldan et al. [9]. Also, we found that patients with HAIs more often had presence of MV and higher number of ventilator-days ($p = 0.011$ and $p < 0.001$, respectively). In 2011, the US neurological ICUs reported pooled mean VAP of 3.6 (19 ICUs, 64 VAPs, 17,656 ventilator-days) and pooled mean ventilator DUR of 0.36 (19 ICUs, 17,656 ventilator-days, 48,822 patient days) [12]. Our results showed the same ventilator DUR as in theUS neurological ICUs, but rate of VAP was far higher.

We detected low incidence of BSI (4%) in our study, but patients with HAIs more often had presence of CVC and higher number of central line-days than patients without HAIs ($p = 0.011$ and $p < 0.001$, respectively). Some underreporting cannot be ruled out, because blood cultures were missed in few cases of febrile episodes in patients with CVC in place.

According to data for 2014, the ECDC reported the relative contribution of Gram-negative bacteria as a cause of HAIs in ICUs in European hospitals, with higher proportions of HAIs caused by *Klebsiella* spp. and *Acinetobacter* spp. in some countries [15]. The results of our study conducted in the neurological ICU confirmed that the most commonly cause of HAIs was *Klebsiella* spp., followed by *Acinetobacter* spp.,

Proteus spp. and *Enterococcus* spp. Dettenkofer et al. [4] also reported isolation of *Acinetobacter* spp. as most common cause of HAIs in neurological ICU patients, especially as the cause of pneumonia (22.4%). *Acinetobacter* spp. was the most frequent cause of pneumonia (25%) in our patients, too.

In their study, Zolldan et al. [9] found that UTIs were predominately caused by *Escherichia coli* (33.3%) and *Enterococcus* spp. (33.3%), while UTIs in our patients were caused by *Klebsiella* spp. (25.7%) and *Entercoccus* spp. (25.7%).

During 2014 in European ICUs resistance to third generation cephalosporins was reported in 44% of *Klebsiella* spp. isolates; carbapenem resistance was reported in 8% of *Klebsiella* spp. isolates, in 28% of *Pseudomonas aeruginosa* isolates and 64% of *Acinetobacter* spp. isolates [15]. Significantly high resistance to third generation cephalosporins for *Enterobacteriaceae* isolates in our study gives us limited treatment options for Gram-negative bacterial infections and making carbapenems as the treatment of choice. High percentages of resistance to carbapenems of Gram-negative bacteria reflect challenges for treatment of our neurological ICU patients.

CDI is a major cause of nosocomial illness worldwide. The disease occurrence in the US has doubled during 2001–2010 [16]. Increased ward-level prescriptions for antimicrobial drugs have have been shown to increase CDI in hospitalized patients [17]. We identified CDI incidence rate of 14.8 *per* 10,000 patients-day during study period. According to data from North America and Europe, registered incidence rate in ICUs varied from 8.7 [18] to 53.9 [19] cases *per* 10,000 patient-days.

A recently published study, in which results of two large studies (the SOAP – Sepsis Occurrence in Acutely ill Patients and the ICON – Intensive Care Over Nations) were compared, showed that overall mortality rate in all ICUs involved decreased over time from 18.5% to 16.8%, although diseases severity increased [20]. Colpan et al. [21] conducted prospective study in three surgical and one medical ICUs and found overall mortality rate of 46.7%, significantly higher in patients with HAIs than in patients without HAIs ($p < 0.001$). Another study from Turkey, that specifically followed neurological ICU patients, found that overall mortality rate was 60% with higher mortality rate in patients with than in patients without HAIs [3]. In our ICU, overall in-hospital mortality rate was 39.9% and was similar in patients with and those without HAIs (59.0% vs 60.6%, respectively). Compared to the Turkey study we registered lower ICU mortality rate, but compared with those in ICUs involved in the SOAP and ICON studies, it is significantly higher. This may be explained by the fact that patients in neurological ICUs are especially severe and prone to complications and thus should be evaluated independently.

Cevik et al. [3] have shown that HAIs, MV, two or more underlying diseases and low GCS, as independent factors increase mortality in the neurologic ICU. Colpan et al. [21], on the other hand, have found that HAIs, mean age, mean Acute Physiology and Chronic Health Evaluation (APACHE II) score, MV, and stay in the medical/surgical ICU, enteric nutrition, tracheostomy and use of steroid or chemotherapy are independent RFs for in-hospital mortality. Our study confirmed MV, age and low GCS (3–8) as independent RFs for in-hospital mortality.

There are several limitations of our study. The main limitation is that it was performed at the single ICU of tertiary healthcare centre. Second limitation is the possibility of confounding variables that were not examined in our study. Some parameters were not included, e.g. existence of different underlying diseases (we analyzed only diabetes mellitus) enteric nutrition, steroid therapy, localization of ischemic/haemorrhagic lesions and analyzing these factors could enhance the relevance of our results. Lastly, we did not include appropriateness of antimicrobial therapy in analysis of in-hospital mortality.

The strength of our study is that it was prospective and could be generalized to all neurologic ICU patients.

Conclusion

The results of this study can be used to guide local prevention efforts in patient care areas that are shown to have highest incidence of invasive devices-associated HAIs and high DUR. Further studies involving burden of HAIs caused by Gram-negative carbapenem resistant bacteria in neurological ICUs and their antibiotic treatment are needed.

REFERENCES

1. *Daschner FD, Frey P, Wolff G, Baumann PC, Suter P.* Nosocomial infections in intensive care wards: a multicenter prospective study. Intensive Care Med 1982; 8(1): 5–9.
2. *Vincent JL, Rello J, Marshall J, Silva E, Anzueto A, Martin CD,* et al. EPIC II Group of Investigators. International study of the prevalence and outcomes of infection in intensive care units. JAMA 2009; 302(21): 2323–9.
3. *Cevik MA, Yilmaz GR, Erdinc FS, Ucler S, Tulek NE.* Relationship between nosocomial infection and mortality in a neurology intensive care unit in Turkey. J Hosp Infect 2005; 59(4): 324–30.
4. *Dettenkofer M, Ebner W, Els T, Babikir R, Lucking C, Pelz K,* et al. Surveillance of nosocomial infections in a neurology intensive care unit. J Neurol. 2001; 248(11): 959–64.
5. *Coello R, Gastmeier P, de Boer AS.* Surveillance of hospital-acquired infection in England, Germany, and The Netherlands: will international comparison of rates be possible? Infect Control Hosp Epidemiol 2001; 22(6): 393–7.
6. *Tekin R, Dal T, Çevik MU.* Fourteen Year Surveillance of Nosocomial Infections in Neurology Unit. J Bacteriol Parasitol 2012; 3(7): 3–5.
7. *European Centre for Disease Prevention and Control.* European Surveillance of Healthcare-Associated Infections in Intensive Care Units– HAI-Net ICU protocol, version 1.01. 2010. Available from: https://ecdc.europa.eu/.../european-surveillance-healthcare-associa...
8. *Horan TC, Andrus M, Dudeck MA.* CDC/NHSN surveillance definition of health care-associated infection and criteria for specific types of infections in the acute care setting. Am J Infect Control 2008; 36(5): 309–32.

9. *Zolldann D, Spitzer C, Häfner H, Waitschies B, Klein W, Sohr D*, et al. Surveillance of nosocomial infections in a neurologic intensive care unit. Infect Control Hosp Epidemiol 2005; 26(8): 726–31.
10. *Abulhasan YB, Rachel SP, Châtillon-Angle MO, Alabdulraheem N, Schiller I, Dendukuri N,* et al. Healthcare-associated infections in the neurological intensive care unit: Results of a 6-year surveillance study at a major tertiary care center. Am J Infect Control 2018; 46(6): 656–62.
11. *Jarvis WR, Edwards JR, Culver DH, Hughes JM, Horan T, Emori TG, et al.* Nosocomial infection rates in adult and pediatric intensive care units in the United States. National Nosocomial Infections Surveillance System. Am J Med 1991; 91(3B): 185S–191S.
12. *Dudeck MA, Horan TC, Peterson KD, Allen-Bridson K, Morrell GC, Pollock DA*, et al. National Healthcare Safety Network (NHSN) report, data summary for 2009, device-associated module. Am J Infect Control 2011; 39(5): 349–67.
13. *Djordjevic Z, Jankovic S, Gajovic O, Djonovic N, Folic N, Bukumiric Z.* Hospital infections in a neurological intensive care unit: Incidence, causative agents and risk factors. J Infect Dev Ctries 2012; 6(11): 798–805.
14. *Borgatta B, Rello J.* How to approach and treat VAP in ICU patients. BMC Infect Dis 2014; 14(1): 211.
15. *European Centre for Disease Prevention and Control.* Healthcare-associated infections acquired in intensive care units. In: ECDC. Annual epidemiological report for 2015. Stockholm: ECDC; 2017.
16. *Reveles KR, Lee GC, Boyd NK, Frei CR.* The rise in Clostridium difficile infection incidence among hospitalized adults in the United States: 2001–2010. Am J Infect Control 2014; 42(10): 1028–32.
17. *Brown K, Valenta K, Fisman D, Simor A, Daneman N.* Hospital ward antibiotic prescribing and the risks of Clostridium difficile infection. JAMA Intern Med 2015; 175(4): 626–33.
18. *Bouza E, Rodríguez-Créixems M, Alcalá L, Marín M, de Egea V, Braojos F*, et al. Is Clostridium difficile infection an increasingly common severe disease in adult intensive care units? A 10-year experience. J Crit Care 2015; 30(3): 543–9.
19. *Micek ST, Schramm G, Morrow L, Frazee E, Personett H, Doherty JA*, et al. Clostridium difficile infection: a multicenter study of epidemiology and outcomes in mechanically ventilated patients. Crit Care Med 2013; 41(8): 1968–75.
20. *Vincent J, Lefrant J, Kotfis K, Nanchal R, Martin-Loeches I,Wittebole X*, et al. Comparison of European ICU patients in 2012 (ICON) versus 2002 (SOAP). Intensive Care Med 2018; 44(3): 337–44.
21. *Colpan A, Akinci E, Erbay A, Balaban N, Bodur H.* Evaluation of risk factors for mortality in intensive care units: a prospective study from a referral hospital in Turkey. Am J Infect Control 2005; 33(1): 42–7.

Received on April 13, 2018.
Accepted on November 8, 2018.
Online First November, 2018