

Nosocomial infection rates of three-years in neurological intensive care unit and relationship to mortality

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ABSTRACT

Aim: The risk of developing nosocomial infections (NI) is higher in intensive care units (ICU). Recognition and treatment of NI is important in reducing mortality and morbidity. The aim of this study was to investigate the clinical and demographic characteristics, rates of mortality and nosocomial infection, agents of infection and antibiotic resistance rates of patients the neurological ICU.

Material and Method: The study was carried out between the dates of 01/06/2015 and 01/06/2018 in Neurological ICU. Data of all patients aged were retrospectively analyzed in accordance with the National Nosocomial Infections Surveillance System. SPSS 23 software was used for statistical analysis.

Results: Throughout the 3-year period, a total of 641 patients were followed up in the Neurological ICU and the most common diagnosis was ischemic cerebrovascular disease. It was found that 641 NIs developed in 55 patients in 5334 days of hospitalization in three years and the mortality rate was significantly higher in those with a NI (83.6%) compared to patients without a NI. The rate of NI the mean rate in three years was 9.98% and the most common NI was device-associated infections. In the 3-year period, the most common pathogen was *A. baumannii* which was susceptible to colistin in 100% of the cases, and resistant to imipenem in 96% of the cases.

Conclusions: The use of invasive tools should be reduced in order to reduce nosocomial infection and mortality rates in the ICU. Each ICU should monitor its own nosocomial infection agents and resistance rates and develop a rational antibiotic use.

Keywords: Nosocomial infection, antibiotic resistance, mortality, neurological intensive care unit

INTRODUCTION

The presence of a neurological intensive care unit (ICU) in tertiary hospitals which are reference centers in the organization of contemporary health systems has become a necessity (1). In our country, the rate of presence of a neurological ICU in centers older than 10 years is 90% (2). Status epilepticus, acute stroke, infectious or inflammatory diseases of the central nervous system, primary neurological diseases such as peripheral nervous system disorders, neuromuscular junction or muscle diseases, anoxic ischemic encephalopathy, fat embolism, hyper/hypo-glycemia and secondary neurological diseases such as encephalopathies associated with nutritional insufficiency and organ failure and hypertensive encephalopathy should be followed up in a neurological intensive care unit (3,4). Severe clinical course, old age, weak immune system, multiple drug use, risk of developing metabolic disorders and the frequency of invasive ICU procedures lead to an increase in the incidence of infections in

patients in Neurological ICU's. Nosocomial infection (NI) which develops after hospital admission and is not in the incubation period at the time of admission or that might develop after discharge is defined as infections acquired within 48-72 hours after admission and 10 days after discharge or 30-90 postoperative days after discharge (5). It was reported that 5-10% of the hospitalized patients and 20-25% of the ICU patients have a NI. Ventilator-associated infections, catheter infections and urinary tract infections are among the most common infections in a neurological ICU (6-8). It was shown that NI can be significantly reduced by careful infection control planning (9). Currently, the need for ICUs has been increased in parallel with the increase in elderly population, improvement in diagnosis and treatment processes and higher health expenditures. In ICU patients, recognition of infection agents and treatment of these infections play an important role in the prognosis of primary disease as well as in

duration of hospital stay. Detection of the most common infectious agents in hospitals through surveillance studies provides an appropriate and successful treatment plan. In addition, it is important to determine the common infectious agents in order to obtain a successful empirical treatment planning. However, there is limited data on the incidence, factors and effective antibiotherapy approaches with respect to NIs acquired in Neurological ICUs.

The aim of this study was to determine rates of NI rates and mortality, agents of NI and their antibiotic resistance, and to contribute to take control measures for NIs and to plan empirical treatment and reduce the rates of NI.

MATERIAL AND METHOD

The data of all patients followed up in the tertiary level neurological ICU of The Hospital of School of Medicine, University of Atatürk, between 01/06/2015 and 01/06/2018 were analysed retrospectively. The study was carried out with the permission of Ethics Board of Atatürk University, Faculty of Medicine (Permission granted/decision no: 05/21-07.06.2018). The trial was conducted in accordance with the Helsinki Declaration principles.

Demographic and clinical characteristics and status of discharge or death of the patients were recorded. The number and rates of nosocomial infections, number of inpatient days, number and rate of device-associated infections (DAI), number of days/rate of use of mechanical ventilator (MV), urinary catheter (UC), central venous catheter (CVC); rates of catheter associated urinary tract infection (CAUTI), ventilator-associated pneumonia (VAP), CVC-associated blood circulation infection (BCI), isolated microorganisms, antibiotic resistance rates and hand hygiene compliance rates were analyzed in light of the data obtained from the daily follow-up visits of infection control nurses, consultations of infection control physicians and daily visits of responsible physicians in the ICU in accordance with National Nosocomial Infections Surveillance System.

The NI rate was calculated using the formula of “NI rate=total number of nosocomial infections/number of inpatients x 100”. The device-associated NI rate was calculated using the formula of “Device-associated NI rate=device-associated NI number/days of invasive device x1000”.

Statistical Method

D’Agostino Pearson test was used to determine whether the parameters were normally distributed. The nominal data were compared using the chi-square test. The intergroup comparisons of the normally distributed data were performed using the independent t-test. The results were accepted significant when the two-way p-values were found below 0.05. All statistical calculations were performed using SPSS 23 software.

RESULTS

In this study, NI was detected in 55 of 641 patients who were followed up in the ICU throughout the three-year period between dates stated above. Of the patients with and without NIs, 56.8% and 60% were females, respectively. There was no statistically significant difference between the genders. The mean age was 71.5 (± 8.0) and 76.9 (± 8.3) years, respectively, and there was no statistically significant difference in age between the groups with and without NI. In both groups, patients were most frequently admitted for ischemic stroke, hemorrhagic stroke, epilepsy and other diagnoses, and the most common comorbidities were hypertension and diabetes mellitus. The 3-year mortality rates were higher in patients with NI with a statistically significant difference between the two groups (Table 1). It was determined that a total of 64 NIs were developed in 55 patients (including more than one NI episode in a single patient) and all patients who had multiple NIs died. The rate of NI was 10.53% in the year of 2015, 12.03% in 2016 and 6.81% in 2017 (Table 2).

Table 1. Demographic and clinical characteristics of patients

	Not NI (n=586)	NI (n=55)	p
Gender n (%)			
Female	331 (56.8)	33 (60)	0.091
Male	255 (43.2)	22 (40)	
Age, year (Mean \pm SD)	71.5 \pm 8.0	76.9 \pm 8.3	0.072
Mortality n (%)	282 (48.1)	46 (83.6)	<0.001
Diagnoses n (%)			
Ischemic stroke	414 (70.7)	41 (74.6)	0.882
Hemorrhagic stroke	69 (11.8)	11 (20)	
Epilepsy	34 (5.8)	2 (3.6)	
GBS	19 (3.2)	1 (1.8)	
ALS	9 (1.5)		
Muscle disease*	9 (1.5)		
Others**	32 (5.5)		
Additional disease n (%)			
Hypertension	312 (53.2)	36 (65.5)	0.648
Diabetes mellitus	133 (22.7)	15 (27.3)	
Atrial fibrillation	113 (19.3)	15 (27.3)	
CAD	76 (13)	11 (20)	
CHD	73 (12.5)	9 (16.3)	
COPD	59 (10.1)	3 (5.5)	
Malignancy	24 (4.1)	7 (12.7)	
CRF	21 (3.6)	5 (9.1)	

GBS: Guillain barre syndrome, ALS: Amyotrofik lateral skleroz *Myasteni gravis, primary muscle disease** Dementia, parkinson, subarachnoid hemorrhage, encephalitis. CAD: Coronary artery disease, COPD: Chronic obstructive pulmonary disease, CHF: Congestive heart failure, CRF: Chronic renal failure.

Table 2. Distribution of NI rates and mortality rates by years

	2015	2016	2017	Total
Number of patients (n)	209	241	191	641
Number of NI patients (n)	22	29	13	64
NI patients rate (%)	10.53	12.03	6.81	9.98
Number of patients with NI (n)	15	27	13	55
Mortality n (%)	12 (80)	23 (85.1)	11 (84.6)	46 (83.6)

NI: Nosocomial Infection, NI rate=Nosocomial Infectionrate/Number of inpatients x 100

DAIs were the most common in each of the three years and in the of three years total. The at total of three years, catheter associated urinary tract infection (CAUTI) was the most common, VAP was the second, and laboratory proven BCI was the third. Considering the distribution by years, it was found that the most frequent CAUTI in 2015, CAUTI and VAP in 2016, and VAP in 2017. During these three years, it was seen that the use of mechanical ventilators, urinary catheters and central venous catheters increased. In the three years data, the rate of DAIs was highest in VAP (Table 3).

In the three-year period, 75 pathogenic microorganisms were isolated and the most common pathogenic agent was gram-negative bacteria (94.7%). In 2016 and 2017, all of the agents consisted of gram-negative bacteria. While *Escherichia coli* (*E. coli*) was the most common causative agent in the year 2015, *Acinetobacter baumannii* (*A. baumannii*) was the most common causative agent in 2016 and 2017, and the total three-year period (Table 4).

Table 3. Distribution of NI regions over the years and NI rates

	2015 (n=22)	2016 (n=29)	2017 (n=13)	Total (n=64)
Device-associated infection n (%)	14 (63.6)	20 (68.9)	10 (76.9)	44 (68.7)
VAP	3	9	5	17
CVC related BCI	-	2	2	4
CAUTI	11	9	3	23
Non instrument-associated infection n (%)	8 (36.4)	9 (31.1)	3 (23.1)	20 (31.3)
Proven by laboratory BCI	8	5	3	16
Clinically defined pneumonia	-	1	-	1
Pneumonia specific laboratory findings	-	2	-	2
Skin and soft tissue infection	-	1	-	1
Patient day/ Number of patients	1527/209	1947/241	1860/191	5334/641
MV used days n (%)	831 (54)	1251 (64)	1452 (78)	3534 (66)
VAP rate	3.61	7.19	3.44	4.81
UC used days n (%)	1523 (99.7)	1946 (100)	1858 (100)	5327 (100)
CAUTI rate	7.22	4.62	1.61	4.32
CVC used days n (%)	164 (10.7)	528 (27.1)	703 (37.8)	1395 (26.2)
CVC-associated BCI rate	-	3.79	2.84	2.87

Instrument associated infection rate: Number of device-associated infections /Number of invasive instrument days x1000 NI: Nosocomial infection, BCI: Blood circulation infection, VAP: Ventilator associated pneumonia, CVC: Central venous catheter, UTI: Urinary tract infection, MV: Mechanical ventilation, UC: Urinary catheter, CAUTI: Catheter associated urinary tract infection.

For the distribution of pathogen microorganisms by infection sites, the most common causative agent for CAUTI was found to be *E. coli*, *A. baumannii* for VAP and *Klebsiella pneumoniae* (*K. pneumoniae*) for CVC-associated BCI (Table 4) in the three-year period.

In our study, while *A. baumannii*, *E. coli*, *K. pneumoniae* were resistant to most antibiotics, *A. baumannii* and *K. pneumoniae* were 100% sensitive to colistin. The rates of resistance to various antibiotics for all three pathogens are shown in Table 5.

Table 4. Distribution of NI-causing microorganisms isolated by region and years

NI Location	2015 n=22	2016 n=36	2017 n=17	Total n=75
VAP n (%)	3 (13.6)	12 (33.4)	7 (41.2)	22 (29.3)
<i>Acinetobacter baumannii</i>	2 (9.1)	9 (25)	7 (41.2)	18 (24)
<i>Pseudomonas aeruginosa</i>	1 (4.5)	-	-	1 (1.3)
<i>Klebsiella pneumoniae</i>	-	2 (5.6)	-	2 (2.7)
<i>Escherichia coli</i>	-	1 (2.8)	-	1 (1.3)
CAUTI n (%)	11 (50)	11 (30.6)	5 (29.4)	27 (36)
<i>Acinetobacter baumannii</i>	2 (9.1)	1 (2.8)	3 (17.6)	6 (8)
<i>Pseudomonas aeruginosa</i>	1 (4.5)	2 (5.6)	1 (5.9)	4 (5.3)
<i>Klebsiella pneumoniae</i>	1 (4.5)	3 (8.3)	-	4 (5.3)
<i>Escherichia coli</i>	5 (22.7)	5 (18.9)	1 (5.9)	11 (14.7)
<i>Enterococcus</i> spp.	1 (4.5)	-	-	1 (1.3)
Proven by laboratory BCI n (%)	8 (36.4)	5 (13.9)	3 (17.6)	16 (21.3)
<i>Acinetobacter baumannii</i>	1 (4.5)	2 (5.6)	1 (5.9)	4 (5.3)
<i>Pseudomonas aeruginosa</i>	1 (4.5)	-	-	1 (1.3)
<i>Klebsiella pneumoniae</i>	-	1 (2.8)	2 (11.8)	3 (4)
<i>Escherichia coli</i>	2 (9.1)	1 (2.8)	-	3 (4)
<i>Enterococcus</i> spp.	1 (4.5)	-	-	1 (1.3)
<i>Staphylococcus aureus</i>	1 (4.5)	-	-	1 (1.3)
<i>Enterobacter</i> spp	1 (4.5)	-	-	1 (1.3)
<i>Acinetobacter lwoffii</i>	-	1 (2.8)	-	1 (1.3)
<i>Candida tropicalis</i>	1 (4.5)	-	-	1 (1.3)
CVC-associated BIC n (%)	-	2 (5.6)	2 (11.8)	4 (5.3)
<i>Acinetobacter baumannii</i>	-	-	1 (5.9)	1 (1.3)
<i>Klebsiella pneumoniae</i>	-	2 (5.6)	1 (5.9)	3 (4)
Skin and soft tissue infection n (%)	-	2 (5.6)	-	2 (2.7)
<i>Acinetobacter baumannii</i>	-	1 (2.8)	-	1 (1.3)
<i>Enterobacter aerogenes</i>	-	1 (2.8)	-	1 (1.3)
Clinically defined pneumonia n (%)	-	1 (2.8)	-	1 (1.3)
<i>Escherichia coli</i>	-	1 (2.8)	-	1 (1.3)
Pneumonia specific laboratory findings n (%)	-	3 (8.3)	-	3 (4)
<i>Acinetobacter baumannii</i>	-	3 (8.3)	-	3 (4)

NI: Nosocomial infection, BCI: Blood circulation infection, VAP: Ventilator associated pneumonia, CVC:Central venous catheter, UTI: Urinary tract infection, MV: Mechanical ventilation, UC: Urinary catheter, CAUTI: Catheter associated urinary tract infection.

Table 5. Antibiotic resistance rates of *A. baumannii*, *E. coli*, and *K. pneumoniae* in three years.

	<i>A. baumannii</i> n (%)	<i>E. coli</i> n (%)	<i>K. pneumoniae</i> n (%)
Antibiotic			
Amikacin	13 (73%)	5 (42%)	4 (50%)
Ampicillin	7 (100%)	9 (75%)	3 (100%)
Ampicillin-sulbactam	5 (100)	7 (78%)	2 (100%)
Gentamicin	10 (42%)	3 (19%)	6 (60%)
Ertapenem	7 (100%)	-	-
Aztreonam	6 (100%)	-	6 (100%)
Imipenem	22 (96%)	2 (17%)	8 (80%)
Colistin	0	-	0
Levofloxacin	14 (100%)	-	7 (100%)
Meropenem	33 (100%)	4 (36%)	8 (100%)
Netilmicin	3 (60%)	1 (100%)	2 (50%)
Piperacillin	10 (100%)	4 (100%)	4 (100%)
Piperacillin-tazobactam	18 (95%)	5 (84%)	7 (87%)
Ceftazidime	4 (100%)	-	1 (100%)
Seftriakson	1 (100%)	-	1 (100%)
Ciprofloxacin	3 (100%)	-	1 (100%)
Cefepim	3 (100%)	1 (100%)	2 (100%)
Tigeksilin	1 (25%)	-	-

DISCUSSION

Infections acquired in ICUs cause a significant increase in morbidity, mortality and treatment costs (10). Neurological ICUs poses additional risk factors due to elderly patient population, immobility due to mental and motor regression and debilitation of the patients and long hospitalizations besides the increased risk of NI which is common in all ICUs. The cases followed up consisted of elderly patients. The mean age of patients with a NI was 76.9 (± 8.3) years, whereas the mean age of those had no NI was 71.5 (± 8.3) years with no statistically significant difference between the groups. The patients with and without NIs were most frequently treated for the diagnosis of ischemic cerebrovascular disease.

In the literature, different results were obtained regarding the rate of NI which was reported to be 5-10% in the overall hospital wards and 20-25% in the ICUs (11,12). The rate of NI developed in the ICUs varies between 5.3 and 56.1% in Turkey. A study performed in a reanimation unit reported the frequency of NI as 53.5% (13). Another study conducted in an ICU revealed that 17% of patients had NI (14). In our study, the 3-year NI rate was found to be 9.98% although it varied from year to year.

Various causes of NI have been reported in the literature. In addition to the studies reporting urinary tract infection as the most common cause of NI, pneumonia has also been reported as the most common cause in some other studies (15-18). In another study conducted in the Neurology ICU, the rates of urinary tract infection

were found to be high, and 95% of the infections were reported to be associated with urinary catheters (19). Again, in the same study, it was observed that the most common cause of UTI was *E. coli* and the second was *K. pneumoniae*. In our study, we determined that the most common cause of NI in 2015 and 2016 was CAUTI, *E. coli* was the most common cause of CAUTI, and *A. baumannii* was the second. In 2017, the most common causative agent was *A. baumannii*. All of the factors were associated with the use of UC.

Vincent et al. (17) reported that the most common cause of NI was pneumonia with a rate of 46.9%. In a different study conducted in intensive care units, it was reported that pneumonia was the most common, followed by UTI, bacteremia, sepsis and catheter infections (18). In our study in three years, nosocomial pneumonia (VAP (n=17) + specific laboratory findings pneumonia (n=2) + clinically defined pneumonia (n=1)) was in the second place along with BCI (laboratory proven BCI (n=16) +CVC- associated BCI (n=4)) (Tablo 3). VAP was the most common among cases of pneumonia in a total of three years and each year. In 2015 and 2017, all pneumonia were VAP. Other rare types of pneumonia were observed only in 2016. Eren et al. (19) reported most frequently isolated that *A. baumannii* and *P. aeruginosa* were in VAP in the ICU. In our study, *A. baumannii* was the most frequently isolated pathogen in VAP.

In the study of Saltoğlu et al. (20), bacteremia rate among NIs was found to be 20.5 %. In our study, BCI (Laboratory-proven BCI+CVC- associated BCI) second among NIs in three years (Table 3). A previous study was determined that the most common causative agents of BCI were *Staphylococcus aureus* and coagulase-negative staphylococci (21). In our study, *A. baumannii* was found to be the most common cause of BCI. BCI is mostly associated with CVC and they can lead to severe sepsis. According to our findings, the most common laboratory-induced BCI was identified among bloodstream infections. While CVC- associated BCI was not seen in 2015, it was observed that it increased in 2016 and 2017. We thought that this situation might be due to the increase in CVC usage rates. In our study, the most common cause of CVC associated BCI was *K. pneumoniae*.

Skin and soft tissue infections are common in ICUs with long hospitalization periods, and *A. baumannii* and *S. aureus* are frequently isolated agents (19,22). Skin and soft tissue infections were detected in our neurology intensive care unit only in 2016, and the isolated agents were *A. baumannii* and *Enterobacter aerogenes*. Skin and soft tissue infections were not observed in 2015 and 2017.

In 2006, Üstün et al. (23) found that 83% of NI in neurology ICU was DAI. In our study, the rate of DAI among NI was in the first place with 68.7%. In DAI, CAUTI was the most common, followed by VAP and CVC- associated BCI. The high rate of DAI indicates the necessity of determining invasive procedure indications well, removing invasive devices as early as possible, and taking simple infection control measures such as hand hygiene.

The frequency and distribution of microorganisms responsible for NI may vary in different clinics (24). A study reported that 64% of the bacteria isolated in ICU were gram-negative bacteria and 27% were gram-positive bacteria, among which *A. baumannii*, *S. aureus*, and *E. coli* were the most frequently isolated species (25). Gram-negative bacteria were reported to be most frequently isolated in 49.4% of the cases in another study conducted in the ICU between 2014-2015 years and *A. baumannii* was the most common among them, followed by *K. pneumoniae* and *E. coli*, in descending order (26). In the same study, 47.8% gram-positive bacteria, and 2.7% *Candida* species were detected. In another study, *A. baumannii* (69.83%) was the most frequently isolated agent from ICU (27). As reported in studies, gram-negative bacteria are reported to be dominant in the flora (23-27, 28). In our study, 95% of the isolated agents were gram-negative bacteria, 4% were gram-positive cocci and 1% were fungal infections. In 2016 and 2017, all of the microorganisms isolated were gram-negative bacteria. It was found that the most common agent of NI was *E. coli* in 2015 and *A. baumannii* in 2016 and 2017. In the 3-year period, the most common cause of NI was *A. baumannii* (%43,9), followed by *E. coli* (%21,3) and *K. pneumoniae* (%16), in descending order. Our results demonstrated that gram-negative bacilli were the most commonly isolated agents in a Neurological ICU and that they dominated the flora. It is of great importance to knowledge the alterations of the pathogenic microorganisms compared to previous years when planning empirical treatment for the NIs in the fight against NIs.

The development of antibiotic resistance is a common problem in ICUs. ICUs are places where antibiotic-resistant bacteria rapidly emerge and spread. Multiple and long-term antibiotic use increases the risk of colonization with resistant microorganisms in ICUs (29,30). *A. baumannii* has been reported to be more susceptible to imipenem and amikacin compared to other antibiotics (31). Colistin, among the antimicrobial agents has been demonstrated to be the most effective agent against the pathogens *P. aeruginosa* and *A. baumannii* (32-35). According to the three-year data including the years 2015, 2016, and 2017 in this present study, *A. baumannii* was 100% susceptible to colistin, 75% susceptible to tigecycline and 58% susceptible to gentamicin, whereas it was 96% resistant to imipenem and 100% resistant to

meropenem. *E. coli* was found to be 83% susceptible to imipenem, 81% to gentamicin and 64% to meropenem. *K. pneumoniae* was found to be 100% susceptible to colistin, whereas it was 80% resistant to imipenem and 100% resistant to meropenem. This present study revealed that gram-negative bacilli were most susceptible to colistin. The results of this present study demonstrated that the susceptibility of gram-negative bacilli to imipenem and meropenem was decreased compared to the previous studies. This demonstrates how much antibiotic resistance and susceptibility rates have changed over the years and we believe that detecting this change each year will play an important role in the planning of empirical treatment. Therefore, further resistance problems could be avoided with the development of more rational antibiotic administration strategies.

There are many factors affecting mortality in ICUs. In various studies, the mortality rate in ICU in our country has been reported at varying rates such as 24.5% and 61.5%. The mortality rate was found to be 60% in a study conducted in our country's neurology ICU between 1999-2000 (5). In our study, the mortality rate was found to be 51.2% which was consistent with the literature. The mortality rate of patients with NI was 83.6%, and without NI was 48.1%. The high mortality rates may be due to the fact that most of the patients accepted to the neurology ICU are admitted to the hospital with severe neurological diseases such as cerebral infarction and cerebral hemorrhage, and accompanying chronic diseases such as DM and coronary artery disease. In addition, patients followed up in the neurology ICU have additional risk factors such as elderly patient population, immobility, and debility. In this study, most of the patients who developed HE were hospitalized for severe diseases such as ischemic stroke and hemorrhagic stroke. In our study, the three-year mortality rate in neurology ICU was 48.1% in patients who did not develop HE, while this rate was 83.6% in patients with NI, and this difference was statistically significant. According to our results, we believe that NI prevention will decrease mortality rates.

CONCLUSION

In order to reduce NI and mortality in the ICU, it is necessary to reduce the use of invasive devices, increase training activities for infection control measures, and to implement a regular resistance tracking program. Recognition of NI, determination of pathogenic microorganisms and their antibiotic susceptibility are highly important for determining empirical treatment and reducing mortality and morbidity. Every center, like in our study, should determine the HE factors and resistance rates in its own intensive care units, and rational antibiotic use should be developed.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Ethics Board of Atatürk University, Faculty of Medicine (05/21-07.06.2018).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

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