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The Relationship Between Mortality and Hospital-Acquired Infections in Patients Followed-up with Neurological Complaints in the Third Level Intensive Care Unit

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Abstract: We aimed to evaluate the demographic characteristics of patients with neurological complaints in Level III Intensive Care Unit (ICU) and hospital-acquired infection rate, isolated pathogen factors and regional distribution of them, relationship with invasive device use, and mortality rates. 176 patients who were followed up in ICU within 12 months were included in the study. The demographic information, analysis, culture results of the patients, consultation notes of the infection committee doctors, and nurse observation charts were examined and the patient's data were collected. 46 of the 176 patients died included in the present study. The mortality rate was determined at 26.13%. A total of 38 hospital-acquired infection (HAI) attacks were detected in 33 of all patients due to some of the patients having more than one attack. In addition, the rate of HAI was found at 21.59%. Central venous catheter-related bloodstream infections (CRBSI) in 2 patients (6.06%), mechanical ventilator independent pneumonia in 6 patients (18.1%), mechanical ventilator-associated pneumonia (VAP) or ventilator-associated tracheobronchitis (VAT) were detected in 11 patients (33.3%), and urinary tract infection (UTI) was found in 14 patients (42.4%). Whereas the mortality rate was found as 60.60% (20 of 33) in patients with HAI attack, this ratio was found as 18.18% (26 of 143) in patients without HAI attack. In patients who followed up with neurological complaints in the ICU, it was determined that having an HAI, recurrent HAI attacks, and ventilator-associated pneumonia (VAP) or ventilator-associated tracheobronchitis (VAT) increased mortality. By knowing infection surveillance data in ICUs, effective empirical treatment can be provided until the exact HAI pathogen is known. Understanding and effectively treating HAI data in ICU affects the prognosis, cost, and mortality rate of primary neurological disease by lowering HAI rates.

Keywords: Neurology Intensive Care Unit, Hospital-Acquired Infection, Infection Control, Mortality.

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1. Introduction

Infections occurring up to 1 year in case of permanent device use are hospital-acquired infections (HAI), which occur not in the incubation period before applying to a hospital but in 48-72 hours after applying to a hospital, and despite the development in the hospital in the first 10 days after hospital discharge, and 30-90 days after surgery (1). Intensive care units (ICU) are among the most common HAI areas compared to other units, services of the hospital. While only 5-10% of all hospitalized patients are treated in ICUs, 25% of all nosocomial infections are found, and the prevalence of nosocomial infections in ICUs is 5-10 times higher than general hospital wards (2).

Patients hospitalized in neurological intensive care units are the most common patients with cerebrovascular disease. These patients could be need intubation due to cerebral edema, and if they are not fed, they may need to be fed with a nasogastric tube. The patient's changes of the are followed by regular blood tests, close consciousness monitoring and clinical examination due to invasive procedure increases, whiches increases hospital-acquired infection rates. Prolonged hospitalization, clinical severity of primary disease (decrease in consciousness caused by the disease, difficulty in swallowing), multi-organ failure, decreased immune respond resistance, presence of comorbid disease, presence of metabolic disorder, increased invasive interventions (urinary catheter, central venous catheter, mechanical ventilation applications), increased antibiotic use and resistance, non-compliance with hygiene conditions, and advanced age can be considered as the reasons for more frequently development of HAI in ICUs (3-5). HAIs prolong hospital stay, increase mortality, impair quality of life, cause loss of labor, and synonym hospital costs (2, 6). In this study, we evaluated the demographic characteristics of patients who were followed up in our intensive care unit with neurological complaints, pathogenic factors, and regional distribution of HAI, the relationship between invasive device use, mortality, and HAI-related mortality rates.

2. Material and Methods

Among the neurology patients hospitalized in the neuro ICU between August 2018 and August 2019, 176 were included in the study. Patient data were scanned retrospectively between these dates, and the data of the patients were collected using the analysis of the patients, culture results, consultation notes of the infection committee doctors, and nurse observation charts. Patients between 17-90 years old were included in the study (patients under 16 years of age were not followed up in adult intensive care units). Patients who were positive infection on the day of admission to the intensive care unit and patients who died within the first 2 days (48-72 hours after applying to a hospital) after their arrival or were discharged from the intensive care unit were excluded from the study. HAI diagnosis was established according to the 'Disease control and prevention center criteria (7). In addition to the culture samples studied, patients' fever follow-up in the nurse registration forms and daily progress held by intensive care physicians, clinical examination findings, and general conditions of the patients were taken into consideration. While calculating the infection rate, 'the rate of infection=the number of patients detected with infection and hospitalized in the ICU/ the total number of patients hospitalized in the ICU x100' formula is used. The ICU's infection rate was calculated by 'the number of infections detected in the intensive care unit/the number of infections detected in the entire hospital x100.' Other calculations were as listed: VAP rate=VAP number/total ventilator day x1000, catheter-related urinary system infection rate=catheter-related urinary system infection number/urinary system catheter day x1000 and central venous catheter-related bloodstream infection (CRBSI) rate=central venous catheter-associated number of bloodstream infections/central venous catheter day x1000 (8).

Blood, tracheal aspirate, wound site, urine, catheter examinations were taken from every patient with a fever of 38 °C and above. If the patients with catheters have symptoms, catheter tip culture, hematological, biochemical tests and, if required, radiological examinations were performed. Peripheral blood samples were sown in blood culture bottles, eosin methylene blue agar, and bloody agar. The presence of the signal was evaluated by monitoring the culture bottles daily for up to 7 days in terms of reproduction. Wound site, discharge, sputum, and catheter samples were evaluated for the presence of leukocytes. It was defined according to the colony and Gram-staining characteristics of breeding pathogens. In addition to the standard medium, culture samples taken were planted in special nutrients such as motion medium, indole medium, Christensen urea agar, and examined according to gram staining feature, colony characteristics, gram staining properties, coagulase, catalase, pyrrolidinyl arylamidase, esculin hydrolysis. Additional properties such as reproduction in 6.5% sodium chloride, oxidase test were also examined. Tracheal aspirates were taken by aspiration after giving physiological serum with a deep aspiration of the endotracheal tube, following the disinfection rules with sterile catheters. Since this study was retrospective, no consent was obtained from patients. Local ethics committee approval was received (KAEK 2019/16-155). The current study was followed by Helsinky critiques.

2.1. Statistical Analysis

SPSS 20.0 package program was used to evaluate patient data. Frequency, calculations of percentage distribution, and descriptive statistical evaluation were made using the package program. The Mann-Whitney Test, one of the non-parametric tests, was used to analyze the number of deaths in patients with and

without HAI. Kruskal Wallis test, one of the non-parametric tests, was used to analyze death by infection region among those who had HAI, and Mann-Whitney test was used in paired comparisons. SPSS package program was used for all statistical analyzes.

3. Results

176 patients who were hospitalized in ICU for one year were included in the study. The mean age was 66.25±13.66 years (age range 17-90). The patients were female 51.7% (n=91) and were male 48.3% (n=85). The patients were ischemic stroke 67.6% (n=119), were epilepsy 11.3% (n=20), were dementia 6.8% (n= 12), were hemorrhagic stroke 5.6% (n=10), were Parkinson's disease (PD) 5.1% (n=9), subarachnoid hemorrhage (SAH) 1.7% (n=3), Guillain Barre syndrome (GBS) 1.1% (n=2), and amyotrophic lateral sclerosis (ALS) 0.5% (n=1). According to the patients' medical history, the patients were hypertension 27.8% (n=49), diabetes mellitus 18.1% (n=32), chronic heart failure 11.9% (n=21), chronic obstructive pulmonary disease (COPD) 2.2% (n=4), 3 malignant brain tumors (1.7%), chronic kidney failure (CKF) 1.7% (n=3), lung adenocarcinoma 0.5% (n=1), malignant skin tumor 0.5% (n=1), shunt operation 0.5% (n=1), gastric adenocarcinoma 0.5% (n=1), 1 operated larynx malignancy 0.5% (n=1) (Table 1).

Table 1: Demographic Characteristics of Patients in A One-Year Period in The Neuro-ICU.

Sex	
Female	91 (51.7%)
Male	85 (48.3%)
Medical Diagnosis	
Ischemic stroke	119 (67.6%)
Epilepsy	20 (11.3%)
Dementia	12 (6.8%)
Hemorrhagic stroke	10 (5.6%)
Parkinson's disease	9 (5.1%)
Guillain Barre Syndrome	2 (1.1%)
Subarachnoid hemorrhage	3 (1.7%)
Motor Neuron Disease	1 (0.5%)
Concomitant diseases	
Hypertension	49 (27.8%)
Diabetes mellitus	32 (18.1%)
Congestive heart failure	21 (11.9%)
COPD	4 (2.2%)
Chronic renal failure	3 (1.7%)
Malignant Brain Tumor	3 (1.7%)
Lung Cancer	1 (0.5%)
Malignant Skin Tumor	1 (0.5%)
Previous Shunt Operation	1 (0.5%)
Gastric Cancer	1 (0.5%)
Opere Larynx Cancer	1 (0.5%)

The HAI developed in 33 (18.75%) of all patients included in the study. A total of 38 HAI attacks were detected in 33 patients diagnosed with HAI. The HAI rate was calculated as 21.59%. 1 episode in 29 patients (76.31%), 2 episodes in 3 patients (7.89%), 3 HAI episodes in 1 patient (2.63%) were observed. 17 were female (51.5%) and 16 were male (48.5%) of the 33 patients with HAI. HAI was detected in 20 patients with ischemic strokes (60.60%), 5 hemorrhagic strokes (15.15%), 3 epilepsy (9.09%), 2 Parkinson's disease PD (6.06%), 1 Subarachnoid hemorrhage SAH (3.03%), 1 Guillain-Barré syndrome GBS (3.03%), 1 Amyotrophe Lateralsklerose ALS (3.03%) (Table 2).

Table 2: Demographic Characteristics of Patients with a Hospital-Acquired Infection in The Neuro-ICU For A Year.

Total Number of Patients	**n=33**
Sex	
Female	17 (51.5%)
Male	16 (48.5%)
Medical Diagnosis	
Ischemic stroke	20 (60.6%)
Hemorrhagic stroke	5 (15.15%)
Epilepsy	3(9.09%)
Parkinson's Disease	2(6.06%)
Guillain Barre Syndrome	1(3.03%)
Subarachnoid hemorrhage	1(3.03%)
ALS	1(3.03%)

46 of the patients who were hospitalized in the neuro ICU died. The mortality rate was found as 60.60% (20 of 33) in patients with HAI attack, and this ratio was found as 18.18% (26 of 143) in patients without HAI attack (p=0.024) (Table 3).

Table 3: Mortality Rates of Hospital-Acquired Infections in The Neuro-ICU For One Year.

Total Inpatient	176
Patient not having a hospital-acquired infection	143
Patient having hospital-acquired infection	33
Total deceased patient	46 (26.1%)
Decased patients who did not have a hospital-acquired infection	26 (18.1%)
Deceased patients who had a hospital-acquired infection	20 (60.6%)
Deceased patient who had pneumonia as a hospital-acquired infection	14 (70%)
Deceased patients who had UTI as a hospital-acquired infection	6 (30%)

14 of the deceased HAI patients were pneumonia (70%) and 6 of them were patients with UTIs (30%). All of the 4 patients (100%) who had more than one HAI attack were patients with pneumonia, and all of these patients died. Distribution of patients with HAI according to localization was 17 pneumonia (51.5%), 14 urinary tract infections (42.4%), and 2 central venous catheter-related bloodstream infections (p=0.018, p=0.024) (Table 4).

Table 4: Regional Percentage Distribution of Hospital-Acquired Infections in The Neuro-ICU For A Year.

Pneumonia	17 (51.5%)
Mechanical ventilator-associated lung infection	11 (64.7%)
Mechanical ventilator unrelated pneumonia	6 (35.3%)
Urinary system infection	14 (42.4%)
Bloodstream infection	2 (6.06%)
Central venous catheter-associated bloodstream infection	2 (6.06%)

The total hospitalization day of the ICU was calculated as 837 days. The day of hospitalization in the total ventilator in the intensive care unit was 309 days, the ventilated patient follow-up rate was 36.9%, and the VAP rate was calculated as 19.2%. Total central venous catheter use day was calculated as 202, and the catheter-related bloodstream infection rate was calculated as 4.9% (Table 5).

Table 5: The Use of Mechanical Ventilators, Urinary Catheters and Central Venous Catheters ın The Neuro-ICU For One Year and Associated Infection Rates.

	Day	**%**
Mechanical ventilator usage	309	36.9
Ventilator-associated pneumonia rate	-	19.2
Central venous catheter usage	202	24.13
Central venous catheter-associated bloodstream infection rate	-	4.9

22 HAI attacks were detected in 17 patients with pneumonia. 11 of these patients were defined as VAP or ventilator-associated tracheobronchitis (VAT) (64.7%), and 6 of these were ventilator-unrelated pneumonia (35.3%). When looking at the distribution factors of 16 HAI attacks of 11 patients diagnosed with VAP-VAT, there were 5 HAI attacks of *Acinetobacter baumannii*, 4 HAI attacks of *Pseudomonas aeruginosa*, 3 HAI attacks of *Escherichia coli*, 2 HAI attacks of methicillin -resistant *Staphylococcus aureus*, 2 HAI attacks of *Klebsiella pneumonia*. In the distribution factors of 6 HAI attacks of patients suffered from mechanical unrelated ventilator pneumonia, it was observed that 2 HAI attacks of methicillin-resistant *Staphylococcus aureus*, 1 HAI attack of *Acinetobacter baumannii*, 1 HAI attack of *Pseudomonas aeruginosa*, 1 HAI attack of Klebsiella Pneumonia, and 1 HAI attack of *Burkholderia cepacia* (Table 6).

Table 6: The Factors of The Hospital-Acquired Pneumonia in The Neuro-ICU For A Year and The Percentage Distribution of These Factors.

Ventilator-associated	**11(64.7%)**
Acinetobacter Baumannii	5 (45.4%)
Pseudomonas aeruginos	4 (36.3%)
E. coli	3 (27.2%)
Meticillin-resistant Staphylococcus Aureus	2 (18.1%)
Klebsiella pneumoniae	2 (18.1%)
Ventilator unrelated	**6 (35.6%)**
Meticillin-sensitive staphylococcus	2 (33.3%)
Acinetobacter	1 (16.6%)
Pseudomonas aeruginosa	1 (16.6%)
Klebsiella pneumoniae	1 (16.6%)
Burkholderia cepacia	1 (16.6%)

In our intensive care unit, 12 different types of pathogens causing HAI were detected. The most frequently isolated microorganism was *Acinetobacter baumannii*. The distribution areas of these microorganisms are given in Table 5 and Table 6.
Urinary catheters were used in all (100%) of 14 HAI patients with UTI. The distribution factors in patients with UTI was *Escherichia coli* in 4 patients (28.5%), *Klebsiella* in 3 patients (21.4%), and *Candida spp*. in 2 patients (7.1%), *Candida glabrata* in 1 patient (7.1%), *Enterococcus faecali* in 1 patient (7.1%), methicillin-resistant coagulase-negative staphylococci in 1 patient (7.1%), and pseudomonas in 1 patient (7.1%), and *Enterococcus faecali* in 1 patient (7.1%) (Table 7).

Table 7: The Factors of The Hospital-Acquired Urinary System Infections in The Neuro-ICU For A Year and The Percentage Distribution of These Factors.

Escherichia coli	4 (28.5%)
Klebsiella pneumonia	3 (21.4%)
Candida spp.	2 (14.2%)
Candida glabrata	1 (7.1%)
Enterococcus faecalis	1 (7.1%)
Coagulase negative staphylococcus	1 (7.1%)
Pseudomonas aeruginosa	1 (7.1%)
Enterococus faecium	1 (7.1%)

CRBSI was detected in 2 patients. Coagulase-negative *Staphylococcus aureus* was produced in the blood culture of 2 patients. Both patients with reproduction in blood culture were evaluated and treated as sepsis.

4. Discussion

In current study, the rate of HAI was found as 21.59%, the mortality rate of all patients was 26.13%, and the mortality rate of patients who suffered from HAI was found to be higher than patients without HAI (60.60%, 18.18%, respectively). It was observed that the development of HAI is an important factor that increases the mortality rate. In studies conducted in the literature, it was observed that suffering from HAI increases the mortality rate (2). The majority of patients in this study were stroke patients. In a meta-analysis examining the effect of post-stroke infection development on mortality rate, the mortality rate was 48% in stroke patients who developed an infection and 18% in stroke patients who did not develop infection (9).

Localization of infection and pathogens of HAIs seen in intensive care units may differ according to each other (10). In a study conducted by Eren et al. in our country, it was found that the most common HAI in the neurological ICU was UTI, with 71.88% over a period of one year (11). Again, in our country, in a study conducted by Şahin et al., it was stated that the most common HAI in the neuro ICU was pneumonia with 43.3% (12). In a multicenter study conducted with 6-year data abroad, it was found that 102 of 227 HAI attacks diagnosed in neuro ICUs were pneumonia and 78 of them were UTI attacks (13). In this study, the most common localization of HAI in the ICU and the number of HAI attacks were pneumonia as the lower respiratory tract infection, and patients who had HAI in the form of pneumonia had higher mortality. 14 of the 20 patients, who died with the diagnosis of HAI, were patients who had pneumonia (70%). Following in this study here, studies in the literature have shown that having pneumonia increases the risk of developing mortality (9, 14).

In this study, here all patients who had recurrent HAI also had VAP / VAT and all 4 patients (100%), who had recurrent HAI, died. It was seen that having a recurrent HAI attack increased the mortality rate (9,15). In this study, it was observed that the second most common cause of HAI was UTI after pneumonia in the ICU. All patients who had UTI attacks had urinary catheterization. UTI attacks were detected in 14 patients. 6 of the 20 patients who died with the diagnosis of HAI were patients with UTI (30%). Before the intervention to patients to reduce UTIs, UC should not be worn except for compulsory situations. Infection control measures such as hand washing, changing gloves and paying attention to isolation rules must be followed (16).

Thanks to the fact that ICUs are divided into branches so that the intensive care of neurology and neurosurgery became frequent, a recuperation in the prognosis of patients, who have been followed by physicians who have mastered the anatomy and physiology of the central nervous system, and a decrease in the cost of inpatient treatment are detected (17, 18). The introduction of new antibiotics every day, the rapid increase in the technology of medical devices and equipment used in intensive care units, the planned work of hospital infection committees, and regular training of employees provide the opportunity to survive in the intensive care units of many patients. There are advantages of the frequent presence of ICUs, and there are disadvantages such as the risk of developing HAI as well. Intensive care units are areas with a high risk of infection where changes in consciousness, dysphagia, and comorbidity are common, and patients with multiple organ damage and low immune resistance are treated. When one or more of these conditions coexist, colonization and pathogen transmission become easier. Long hospitalization, usage of the central and peripheral venous catheter, follow-up with endotracheal intubation, and urinary catheterization cause an increase in HAI (16, 19, 20). Early diagnosis of HAI, early initiation of treatment, determination of pathogen type and antibiotic susceptibility affects the prognosis of primary neurological disease, reduces mortality and morbidity rate, and reduces antibiotic resistance and cost of expense spent (20-22).

Acinetobacter baumannii was seen as the most frequently isolated pathogen in this study, and it was also the most common factor of pneumonia. In Ciraligil's study, which examined antimicrobial resistance in ICUs at the national level, it was emphasized that *Acinetobacter baumannii* infections are an important problem for ICUs (23). In current study, the most common factor of UTI was found to be *Escherichia coli*. In a study in which catheter-related UTIs were evaluated in ICUs, the most common pathogen was reported to be *Escherichia coli*.

5. Conclusion

The limitations of in current study are that it is a single-center study, the number of patients is limited, and that consciousness of patients' and disease severities, antibiotics, and resistance profiles given to the patients, pediatric patients are not included in the study.

Providing hand hygiene practice, trying to avoid insertion of a urinary catheter, if a urinary catheter is mandatory, compliance with hygiene conditions when inserting a urinary catheter, paying attention to sterilization while performing aspiration, receiving regular infection control training, increasing the number of health personnel per patient, paying attention to the isolation rules and regulating the conditions of the intensive care units are important to reduce HAI. (16, 19, 24, 25)

The infection rate and ratio of each intensive care unit should be calculated periodically, microorganisms seen in intensive care should be evaluated, and ICU-specific pathogen profiles should be determined frequently. To reduce the antibiotic resistance increasing day by day, unnecessary antimicrobial therapy should be avoided by periodically reviewing the resistance profiles of HAI

pathogens in ICUs. Knowing the factors of HAI specific for ICU increases the effectiveness of the empirical treatment to be started. In each ICU, HAI data should be regularly compared with the literature and included in surveillance studies. Prospective surveillance studies involving multicentre, broad patient participation, and pediatric and adult age groups are needed to reduce and control HAIs. In the present study, the indomethacin-induced gastric ulcer model in rats was used for the first time to investigate the gastroprotective effect of TQ. Additionally, the antioxidant effect of TQ was examined in ulcerative gastric tissues.

Conflict of Interests
None
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None
Author Contributions
Yardım A and Çelik H contributed to the conception and design of the study. Yardım A and Yeşildağ K contributed to the collection of the data and statistical analysis and evulation of the results. Yardım A and Doğan M contributed to the creating and writing of manuscript. Yardım A and Yıldız O contributed to revising the work and final approval of the version

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