The Risk Factors for Infections Acquired by Cerebral Hemorrhage and Cerebral Infarct Patients in a Neurology Intensive Care Unit in Turkey

Gul Ruhsar Yilmaz*, Mustafa Aydin Cevik, F. Sebnem Erdinc, Serap Ucler1 and Necla Tulek

Infectious Diseases and Clinical Microbiology Department and
1Neurology Department, Ankara Training and Research Hospital, Ankara, Turkey

Original Article

SUMMARY: Few studies have investigated the risk factors for nosocomial infections developed in neurology intensive care units (ICUs). In this study, the risk factors for ICU-acquired infections in patients with cerebral hemorrhage and cerebral infarct who were treated for more than 24 h at the Ankara Training and Research Hospital were prospectively evaluated over a study period of 14 months. Of 171 patients included in the study, 71 (41.5%) were found to have acquired 163 infections in the ICU unit throughout 1,867 patient days. The rate of infection per 100 patients admitted was 95.3, and per 1,000 patient days, 87.3. The most common nosocomial infections were urinary tract infection (42.9%), pneumonia (27%) and primary bacteremia (19%). Multivariate logistic regression analysis revealed age ≥ 70 (P < 0.05), the presence of a central venous catheter (P = 0.004), and parenteral nutrition (P = 0.02) as ICU-acquired infection risk factors. The presence of infection on admission was identified as a factor decreasing the risk of ICU-acquired infection (P < 0.001). The high infection rates found in this study may be due to lack of full compliance to infection control measures. In conclusion, each type of ICU has its own epidemiological findings for nosocomial infections and thus needs to determine the risk factors using periodical surveillance studies to guide control measures.

INTRODUCTION

Nosocomial infections are common among hospitalized patients, and even more so in intensive care units (ICUs) (1). For patients receiving intensive care, there are particular risk factors for acquiring one or more nosocomial infections (1). However, the literature reveals only a few studies evaluating the nosocomial infection risk factors in neurology ICUs (2,3). A few studies have investigated the risk factors for pneumonia in patients with acute ischemic stroke in neurology ICUs.

One of our studies emphasizing the increased mortality rate associated with nosocomial infections in neurology ICUs was recently published (4). The present study was designed as a part of the previously published study to evaluate the risk factors for neurology ICU-acquired infection(s) in patients with cerebral hemorrhage and cerebral infarct who received treatment for longer than 24 h.

PATIENTS AND METHODS

Setting and study period: An observational prospective study was conducted in the six-bed neurology ICU of the 500-bed Ankara Training and Research Hospital, Turkey. The study period was between March 15, 1999 and May 15, 2000.

The neurology ICU at the Ankara Training and Research Hospital is an open unit. The physician:patient ratio is 1:3, and the nurse:patient ratio is 1:2 during the day shift (8 h). Both the physician:patient and nurse:patient ratios are 1:6 at other times. Care is provided primarily by neurologists. In addition, daily visits are performed by an infectious diseases and clinical microbiology specialist. When required, consultation is available from other departments.

Definition of infection: The presence and absence of infection and its type were documented in light of the standard definitions (5,6). The standard definitions of the Centers for Disease Control and Prevention were used in the determination of nosocomial infections (5). Infections were classified as follows (5,6).

(i) Presence of infection on admission: an infection present on admission to the ICU or manifested within 48 h of admission to the ICU (community-acquired infection or a nosocomial infection deemed to be related to the prior admission to the same or another hospital).

(ii) ICU-acquired infection: an infection not present or incubating on admission to the ICU and occurring at least 48 h after admission to the ICU and on a different site and with different microorganisms from the primary infection.

ICU-acquired infection rates: To calculate the ICU-acquired infection rates, the number of patients and total
number of patient days in the ICU were recorded. These were calculated by dividing the total number of ICU-acquired infections by the total number of ICU patients (×100) and patient days (×1,000), respectively.

Formulas used for the calculation of the device utilization ratios and device-associated infection rates are as follows (7):

\[ \text{Device utilization ratio} (DU) = \frac{\text{Number of device-days}}{\text{Number of patient-days}} \]

Device-associated infection rates = Number of device-associated infections for a specific site/Number of device-days × 1,000.

**Score of severity of illness:** The Glasgow coma scale (GCS) score was used to determine the severity of illness (8).

**Risk factors:** The potential risk factors for infection were recorded on admission and during hospitalization. The ages, gender, diagnoses on admission, underlying diseases (diabetes mellitus, heart failure, chronic obstructive lung disease, cancer), GCS scores (on admission, no patients were on sedative treatment at the time the GCS score was calculated) (8), and infection on admission to the ICU were recorded and investigated as potential risk factors for ICU-acquired infection. Central venous catheter (CVC), urinary catheter, nasogastric catheter, intubation, mechanical ventilation (MV), parenteral nutrition, H₂ receptor antagonists use, steroid treatment, and length of ICU stay were also recorded and were investigated as potential risk factors for ICU-acquired infection.

**Statistical analysis:** The chi-square test was used in univariate analysis. Stepwise logistic regression analysis was undertaken to control the effects of confounding variables. All variables found to be significantly \(P < 0.05\) associated with ICU-acquired infection in the univariate analysis were entered into the multiple regression model. All the statistical analyses were performed through SPSS 9.0 software (license number 012560001-1918281).

RESULTS

Ninety (53%) of 171 patients enrolled in the study were male, and 81 (47%) were female. The age range of the patients was 20 to 96 years (mean age, 66.0 ± 14.1). Of 171 patients, 108 (63.1%) had cerebral infarct and 63 (36.8%) had cerebral hemorrhage.

In 71 (41.5%) of 171 patients, 163 ICU-acquired infections were detected in 1,867 patient days. The rate of infection per 100 patients admitted was 95.3, and for 1,000 patient days, 87.3. The rank and distribution of ICU-acquired infections was as follows: urinary tract infection (UTI) \(42.9\%\), pneumonia \(27\%\), and primary bloodstream infection (BSI) \(19\%\) ranked as the first three. The distribution and rates of infections acquired in the ICU are demonstrated in Table 1. The organisms isolated as the agents of ICU-acquired infections ranked as the first three. The distribution and rates of infections acquired in the ICU are demonstrated in Table 1. The organisms isolated as the agents of ICU-acquired infections were *Klebsiella pneumoniae* \(19.8\%\), *Enterococcus* spp. \(14.9\%\) and *Candida* spp. \(14.9\%\), ranking as the first three highest rates.

The ventilator-associated pneumonia rate was 53.4 per 1,000 ventilation days, the urinary catheter-associated urinary infection rate was 37.5 per 1,000 urinary catheter days and the central venous line-associated primary BSI rate was 35.3 per 1,000 central venous line days (Table 2).

The values of the variables studied as the potential risk factor for ICU-acquired infections, age ≥ 70 \(P < 0.05\), GCS ≤ 10 \(P < 0.05\), the presence of CVC \(P = 0.0001\), and parenteral nutrition \(P = 0.001\) were statistically significant for ICU-acquired infection(s) in the univariate analysis. However, the presence of infection on admission to the ICU \(P = 0.01\) was found to significantly decrease ICU-acquired infection risk. Age 60 or over, gender, and underlying disease, nasogastric catheter, MV, enteral nutrition, H₂ receptor antagonists and corticosteroid use were not defined as risk factors for ICU-acquired infection(s) in the univariate analysis. The variables studied as potential risk factors for ICU-acquired infections have been presented in Table 3. Since all of the patients were using a urinary catheter and peripheric venous catheter (PVC), urinary catheter and PVC could not be statistically evaluated as risk factors.

The variables that were determined as statistically significant risk factors for ICU-acquired infections in univariate analysis were also studied through stepwise logistic regression analysis. The analysis revealed that age ≥ 70 \(P < 0.05\), the presence of CVC \(P = 0.004\), and parenteral nutrition \(P = 0.02\) were statistically significant and independent risk factors for ICU-acquired infection(s). The presence of infection on admission was determined as an independent factor that significantly decreased ICU-acquired infection \(P < 0.001\) (Table 4). Sixty patients had infection on admission day. Of these patients, 38 had pneumonia. Twenty-seven of them were treated with sulbactam/ampicillin alone or combined with quinolone, whereas 11 of them were treated with second or third generation cephalosporin alone or combined with quinolone or macrolide. Eight patients with UTI were given quinolone while 10 with nosocomial pneumonia or clinical sepsis were started on meropenem. Vancomycin plus metronidazole and aztreonam combination was given to one patient with dural sinus thrombosis. One patient with nosocomial UTI and two patients with pneumonia died before antibiotic therapy. The admission diagnosis of these three patients was cerebral infarct.

When age, hospitalization time, and GCS were studied as continuous variables, the mean hospitalization time of the patients who acquired infection in the ICU was significantly higher than that of the patients who did not acquire infection in the ICU. The age and GCSs of the two groups were not significantly different. The continuous variables studied for the ICU-acquired infections have been presented in Table 5.
Table 3. Nosocomial infection risk factors in neurology ICU (univariate analysis)

<table>
<thead>
<tr>
<th>Risk factor (n)</th>
<th>ICU-acquired nosocomial infection (%)</th>
<th>P</th>
<th>Relative risk</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>&gt; 0.05</td>
<td>1.38</td>
<td>0.67-2.83</td>
<td></td>
</tr>
<tr>
<td>&lt; 60 (42)</td>
<td>15 (35.7)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 60 (129)</td>
<td>56 (43.4)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>≤ 70 (102)</td>
<td>&lt; 0.05</td>
<td>2.08</td>
<td>1.12-3.90</td>
</tr>
<tr>
<td>≥ 70 (69)</td>
<td>36 (52.1)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td>&gt; 0.05</td>
<td>0.80</td>
<td>0.48-1.61</td>
<td></td>
</tr>
<tr>
<td>Female (81)</td>
<td>35 (43.2)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male (90)</td>
<td>36 (40.0)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glargosoma scale ≤ 10 (113)</td>
<td>53 (46.9)</td>
<td>&lt; 0.05</td>
<td>0.51</td>
<td>0.26-0.99</td>
</tr>
<tr>
<td>&gt; 10 (58)</td>
<td>18 (31.0)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Underlying disease</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart failure (53)</td>
<td>26 (49.1)</td>
<td>&gt; 0.05</td>
<td>1.56</td>
<td>0.81-3.00</td>
</tr>
<tr>
<td>Diabetes mellitus (28)</td>
<td>14 (50.0)</td>
<td>&gt; 0.05</td>
<td>1.51</td>
<td>0.67-3.40</td>
</tr>
<tr>
<td>Underlying 2 or more diseases (107)</td>
<td>47 (43.9)</td>
<td>&gt; 0.05</td>
<td>1.31</td>
<td>0.69-2.46</td>
</tr>
<tr>
<td>Presence of infection on admission</td>
<td>17 (28.3)</td>
<td>0.01</td>
<td>0.42</td>
<td>0.21-0.81</td>
</tr>
<tr>
<td>Nasogastric catheter</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Steroid use (98)</td>
<td>43 (43.9)</td>
<td>&gt; 0.05</td>
<td>1.26</td>
<td>0.68-2.33</td>
</tr>
<tr>
<td>Central venous catheter (19)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mechanical ventilation (26)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parenteral nutrition (93)</td>
<td>49 (52.7)</td>
<td>0.0001</td>
<td>2.83</td>
<td>1.48-5.37</td>
</tr>
<tr>
<td>Enteral nutrition (8)</td>
<td>5 (62.5)</td>
<td>&gt; 0.05</td>
<td>2.45</td>
<td>0.56-10.60</td>
</tr>
<tr>
<td>Use of H2 receptor antagonists (105)</td>
<td>45 (42.9)</td>
<td>&gt; 0.05</td>
<td>1.15</td>
<td>0.62-2.16</td>
</tr>
</tbody>
</table>

1) It has been compared with the infection rates in the patient group without the parameter studied.
2) The relative risk for ICU-acquired infection was 0.42 times lower.

DISCUSSION

Recently, specific neurological intensive care has gained in importance (9,10). However, information on the occurrence of nosocomial infections in the neurology ICUs is limited (3,8,11-14). The altered sensorium, incompetence of pharynx and larynx, muscle weakness requiring intubation and ventilation of the patients in neurology ICUs are some of the factors that lead to nosocomial infections (15). In addition, patients with severe brain injury appear to be at greater risk for nosocomial infection than other ICU patients (16-22).

Dettenkofer et al. have reported pneumonia, UTI and BSI as the most commonly encountered infections in neurology ICUs, whereas Khanna et al. have detected pneumonia, UTIs and sepsis as the most common (2,11). Schmutzhard et al., on the other hand, have ranked the regionally specific nosocomial infections as bacteremia, pneumonia, and UTI in neurology ICUs (10). In our study, the first three infection types in order of frequency were UTI, pneumonia and BSI.

The high incidence of nosocomial infection is a common problem in ICUs because of the severity of illness of the patients treated and the high number of medical devices used (11,23,24). The most important factor affecting device-associated infection rates is the device-use rates. The higher the device-use is, the significantly higher the device-associated infection rates are (25). Therefore, to interpret the device-associated infection rates, the rates of device-use must be known (26). Device-use, which is a measure of invasive practices of the unit and possibly a marker for severity of illness of patients, varies significantly depending on the type of ICU, leading to variations in device-associated infection rates in various ICU types (26). Device-associated, device-day infection rates were reported in only Dettenkofer et al.’s study of the few studies performed in neurology ICUs: 20.4 ventilator-associated pneumonias per 1,000 ventilator-days, 10.0 urinary catheter-associated UTIs per 1,000 urinary-catheter days and 1.9 central-line associated BSI per 1,000 central line days were reported (11). When the findings of the present study (ventilator-associated pneumonia rate was 53.4 per 1,000 ventilation days; urinary catheter-associated urinary infection rate was 37.5 per 1,000 urinary catheter days, and central venous line-associated primary BSI rate was 35.3 per 1,000 central venous line days) were compared, the device-associated, device day infection rates found in our study were higher.

Dettenkofer et al. have reported that pneumonia is the most prevalent infection (11). The authors have attributed the higher prevalence of pneumonia among the patients of the neurology ICU to most having suppressed levels of consciousness (11). Pneumonia is a frequent complication in neurological ICUs. This has also been reported in other studies (3,11,27). In our study, the ventilator utilization ratios (0.07) were lower than those in the study by Dettenkofer et al. (0.22) and the National Nosocomial Infections Surveillance (NNIS) data for medical ICUs (0.47) (11,28). However, the rate of ventilator-associated pneumonia was 53.4. The high infection rates found in this study may be due to a lack of full compliance to infection control measures and faulty device application and care practices by the neurology ICU where the study was conducted.

In addition, central line utilization ratios (0.21) were lower than those in the study by Dettenkofer et al. (0.75), and the NNIS data for medical ICUs (0.50) (11,28). The CVC associated infection rate was 35.3, which is considerably
higher than the findings in the study performed by Dettenkofer et al. (11). Urinary catheter utilization was higher (0.99) compared to other available data (0.86, Dettenkofer et al.; 0.69, NNIS medical ICUs) (11,28). In our study, the high urinary catheter infection (37.5) may be a result of high urinary catheter utilization.

In developing countries like Turkey, sources to take measures for infection control usually are not sufficiently allocated and, due to lack of nationally established policies, control measures remain limited (29). On the other hand, the variations in intrinsic risk factors of patients in various ICUs and the effects of these variations on nosocomial infection rates should also be taken into consideration. The factors of nosocomial infection risk for patients in neurology ICUs are different from those for patients in other ICUs. The studies on nosocomial infection risk factors in neurology ICUs are limited in number. In this study, the multivariate logistic regression analysis revealed that age 70 and over (P < 0.05), the presence of CVC (P = 0.004), and parenteral nutrition (P = 0.02) were risk factors for nosocomial infections. The presence of infection on admission was identified as a factor decreasing the risk of ICU-acquired infection (P < 0.001).

Unlike what was reported in some studies, advanced age was found to be a risk factor for nosocomial infections in ICUs in most of the published studies (1,30-32). Katzan et al. reported that the mean age of the acute stroke patients who developed pneumonia in ICUs was statistically higher than those who did not develop pneumonia (33). In our study, while in univariate analysis, age over 60 years did not indicate a significant difference for infection, patients aged 70 and over had a 2.17 times higher risk of infection. Thus, it can be said that older patients are more susceptible to nosocomial infections than younger ones and that poor nutrition and chronic debilitation are associated with reduced immune defense, explaining the increased risk of nosocomial infections in such patients (1,30-32).

Because it determines comatose status, GCS has been in use by neurology ICUs (14,34). Similarly, in the neurology clinic where this study was conducted, the use of scores obtained through GCS is a routine procedure. Thus, to determine the severity of disease, the GCS scores were used. However, the lack of use of APACHE II scores is a limitation of the present study for comparison among various studies. In earlier studies, CVC was reported to be a predisposing factor for nosocomial infection (1,35). In a study by Khamna et al. in neurology ICU, however, no correlation was detected between the presence of CVC and nosocomial infection (2). In our study, the presence of CVC was detected as a significantly independent risk factor for nosocomial infection as a result of uni and multivariate analyses (P = 0.004, relative risk, 7.93). A recent study which was conducted in our country and which involved a single-day point prevalence in 56 ICUs of 22 centers has shown the presence of CVC as a risk factor for nosocomial infection through uni and multivariate analyses (P = 0.014) (29).

Parenteral nutrition has been known to be one of the predisposing factors for nosocomial infections acquired in ICUs (1). In our study, parenteral nutrition was detected to be a risk factor for ICU-acquired infections among the patients with cerebral hemorrhage and infarct who were hospitalized in the neurology ICU in multivariate analysis. Another single-day prevalence study conducted in ICUs in Mexico detected the peripherally administered infusion of hyperosmolar solutions to present as a risk factor for ICU-acquired infections, which was shown through multivariate analysis (36).

Strikingly, the patients in our study, some of who had infections at the time of admission, had a relatively lower risk for ICU-acquired infections. This may be associated with the antibiotic treatment provided for these patients who applied with infections.

Some previous reports have emphasized the need for elucidating details of ICU-acquired infections in various neurology ICUs in order to develop preventive methods and prevent nosocomial infections in patients treated in neurology ICUs (11). This study was undertaken with the aim of contributing to the limited literature on nosocomial infections occurring in neurology ICUs with the data obtained in a tertiary hospital of Turkey, a developing country. At the time of the study, the hospital infection control committee and unit where the study was conducted had implemented no ongoing attempts at infection control. We believe that low nurse/patient and physician/patient ratios has led to the insufficient practice of universal precautions such as hand-washing and the use of gloves. The studies on this issue performed in our country and their results, which have been reported nationally and internationally, have demonstrated a problem of compliance to infection control precautions (37,38). Unfortunately, a shortage of health care personnel has persisted in our country. The primary issue to overcome seems to be education and lack of infection control.

In conclusion, each type of ICU has its own epidemiological findings for nosocomial infections and thus needs to determine the risk factors using periodical surveillance studies to guide control measures.

REFERENCES