Risk factors and cost of nosocomial infections in pediatric patients with traumatic brain injury

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ABSTRACT

OBJECTIVE: This study aimed to determine the factors that increase nosocomial infections (NIs) in pediatric patients with traumatic brain injury (TBI) and the effects on both treatment cost and length of hospital stay.

METHODS: We performed a case-control study on patients admitted to the pediatric intensive care unit (PICU) with (n=66) or without (n=120) TBI between 2012 and 2014. The risk factors, length of stay, and costs of NIs were determined.

RESULTS: Data for 186 patients were analyzed. One hundred and twenty patients were controls (54 males vs. 66 females), while 66 were cases (27 males vs. 39 females). Seventeen out of the 186 PICU patients had NIs. About 7.6% of TBI patients had infections whereas 10% of control groups had NIs (p=0.58). The most isolated microbial agent was Acinetobacter baumannii (four cases). Thirteen (76.5%) out of the 17 infections were catheter-related bloodstream infections. The mean expenses per PICU patient were $762, with an additional cost of $2081 for patients with nosocomial contamination.

CONCLUSION: The use of catheters was the most critical risk factor for NIs in our study probably underestimated the cost for several reasons. Nevertheless, the findings supported our hypothesis about the additional burden of nosocomial spread on PICU patients. This study’s results should help provide evidence on cost-effectiveness or calculate the cost-benefit ratio of reducing NIs in children.

Keywords: Catheter-associated infections; cost; nosocomial infections; pediatric intensive care unit; traumatic brain injury.

Objectives
This study aimed to determine the factors that increase Nis in pediatric patients with TBI and the effects on treatment cost and hospitalization length.

MATERIALS AND METHODS

Study Design
We performed a case–control study. Our study was conducted in accordance with the Declaration of Helsinki. The Research Ethics Committee approved this study of Marmara University, Faculty of Medicine (Approval date: September 01, 2019; number: 09.2014.124).

Participants
This study was conducted in the PICU of Marmara University Hospital in Istanbul. The study period ran from 2012 to 2014. All patients aged 1 month to 17 years and hospitalized in the PICU for a minimum of 24 h were eligible for inclusion in the study. Patients admitted to the PICU with a TBI were classified as cases (n=66), while those hospitalized in the PICU for other reasons were taken as controls (n=120). Controls were selected randomly from the 1031 patients with diagnoses other than TBI, based on random numbers. All patient files (n=186) were searched for the development of NI from the day of PICU admission. Two patients in each group were excluded due to insufficient or incongruent data (Fig. 1).

Variables
The severity of the patients’ condition was estimated using the Pediatric Risk of Mortality III (PRISM) index. On the other hand, the Glasgow Coma Scale (GCS) was used to describe the level of consciousness in patients. Data on demographic features, injury, laboratory results, interventions, and treatments were extracted from the hospital’s electronic database system. The following variables were evaluated: Age, gender, length of stay (LOS) in hospital and PICU, mortality, the use of an invasive device, the presence of surgical operation, the type of ventilation (non-invasive or invasive mechanical ventilation), the type of invasive intervention (nasogastric and urinary catheters, central/venous/arterial catheters, hemodialysis, and peritoneal dialysis catheters, gastrostomy and tracheostomy, extra ventricular drainage, ventriculoperitoneal (v-p) shunt, chest tube, the use of total parenteral nutrition), the use of H2 blockers and steroids, the use of antiviral, antifungal and antibiotics, the presence of renal or hepatic dysfunction, the presence of NI, and the microbial agent.

The primary outcome variable of the study was the presence of nosocomial spread. Infections were identified from the trauma database and the hospital’s infection surveillance systems. All positive microbial cultures (cerebrospinal fluid, peripheral blood, urine, feces, and endotracheal tube samples) were identified during the PICU stay. The definition of NIs is defined 2 days after PICU admission and classified ventilator-associated pneumonia, central line-associated bloodstream infection, and catheter-associated urinary tract infection. There were no clusters or outbreaks of contamination or colonization during the study period.

The information in calculating the cost per patient was derived from the current price list of the Turkish Pharmaceuticals and Medical Devices Agency (https://www.titck.gov.tr/dinamikmodul/100) and the Social Security Department (https://tig.saglik.gov.tr). The total cost for each PICU patient was calculated in US Dollars.
Sample Size
The sample size calculation was based on the NI variable. To compare a 9% proportion of the expected event with an alternative hypothesis of 15% between two groups, giving an effect size of 0.2 (low) and an alpha error of 5%, a total of 179 patients are required to achieve a power of 80%.

Statistical Methods
Statistical analysis was performed with the Statistical Package for the Social Sciences version 21 (SPSS, IBM, Armonk, NY, USA). The “number (n), “percentage (%), “mean,” and “standard deviation (SD)” was used for the descriptive statistics of the continuous variables. The Student’s t-test or Mann–Whitney U-test compared two independent groups. The Pearson Chi-square or Fisher’s exact tests analyzed categorical data. Clinically, significant variables were used to create a logistic regression model to evaluate the factors associated with NI. Since the mean age and GCS differed significantly between the groups, comparisons were made after adjusting for these variables. The results were assessed with a confidence interval of 95%, and the level of significance, p, was set at 0.05.

RESULTS
Data for 186 patients were analyzed. One hundred and twenty patients were controls (54 males vs. 66 females), while 66 were cases (27 males vs. 39 females). There was no statistically significant difference between the patients and controls concerning sex. The mean age was 63.02±59.89 months, and the age range was 1–204 months. There was a statistically significant difference between control and case patients concerning age (Table 1).

Seventeen out of the 186 ICU patients had NIs. There was no difference in age and gender in the patient groups with and without infection. The overall mean GCS was 12.5±3.8. Patients with NIs had a higher mean GCS when compared with patients without NIs (14.4±1.9 vs. 12.3±3.9). On the other hand, all 17 patients with NIs had a lower mean PRISM score when compared with patients without NIs (3.4±14.0 vs. 8.9±18.2) (Table 2).

The microorganisms isolated in growth (between 80,000 and 100,000 CFU/mL) were Acinetobacter baumannii (four cases), Klebsiella pneumonia (three cases), Candida spp., Stenotrophomonas maltophilia (two cases), coagulase-negative Staphylococcus (two cases), Salmonella spp., Giardia intestinalis, Gram-negative bacilli, and Enterococcus faecalis. Antimicrobials (including penicillin, fourth-generation cephalosporins, aminoglycosides, macrolides, glycopeptides, carbapenems, polypeptides, tetracycline, rifampicin, and ciprofloxacin, as well as antifungal and antiviral agents) were administered to patients with NIs as monotherapy or combinations.

About 7.6% of TBI patients had infections whereas 10% of control groups had infections (p=0.58). One of the most probable risk factors was the use of catheters. Thirteen (76.5%) out of the 17 infections were catheter-related bloodstream infections (CRBSI), while the remaining 4 infections (23.5%) were detected in the cerebrospinal fluid, feces, urine, and tracheal aspirate. There was a statistically significant difference between the use of central/venous/arterial/urinary/nasogastric catheters concerning the groups (p<0.001). The mortality rate was 9.1% (n=11) among patients referred to the PICU with other reasons, and 18.1% (n=12) in patients referred with TBI.

The mean LOS in the hospital and PICU was 9.5 and 6.0 days, respectively. The LOS in hospital and PICU for patients with TBI was longer when compared with
the patients without TBI (11.9 days vs. 8.0 days and 7.7 days vs. 5.0 days, respectively); there were significant differences between the groups concerning the LOS in the hospital or PICU (Table 3). In addition, the LOS in the hospital and PICU for patients with NIs was longer as compared with the patients without NIs (26.3 days vs. 7.8 days and 20.0 days vs. 4.6 days) (p<0.001) (Table 2).

The mean total cost per control patient was $842, while $2509 for the patients with NIs. The only mean cost of having NIs (antibiotics, PICU costs) was $2081, while this was $330 for patients without NIs. As expected, the excess LOS increased the cost of patients with NIs due to antibiotic use and other PICU costs (Table 2).

Logistic regression analysis was used to identify independent risk factors for NIs (Table 4). Patients who had multiple central venous or arterial catheters (p=0.005, 95% CI: 0.000–0.162) and hemodialysis catheters (p=0.009, 95% CI: 0.000–0.207) were more likely to develop bloodstream infections than patients who were not exposed to these factors. The mean scores of LOS in hospital/PICU, GCS, and PRISM points were not associated with the risk factors in our study. This model had a sensitivity of 98.2% and a specificity of 64.7% in predicting NIs.
DISCUSSION

NIs are common complications of more extended hospitalizations that result in severe mortality, morbidity, and excessive cost [15]. Bloodstream infections caused by catheters or related invasive interventions are common sources of NIs in patients admitted to PICUs [16]. In this study, there was no significant association between TBI and NIs in PICU patients. According to the multiple regression analysis, the presence of catheters (central/venous/arterial) increased the risk of CRBSI in both the cases and the control patients.

One study detected a similar result about the independent risk factors of NIs and reported that the use of multiple central venous and arterial catheters increased the risk of catheter-borne bloodstream infections 6-fold. Another related study also reported that numerous central catheters increased the risk of CRBSI almost 10 fold [17]. The same study also stated that the use of TPN was another risk factor for CRBSI. However, TPN was not a risk factor in our research. On the other hand, most related studies declared that NIs were associated with a statistically significant increased mortality rate [18, 19]. Although there was no apparent influence of NIs on mortality in our study, they were associated with a longer LOS in the hospital and PICU.

In the present study surprisingly, the logistic regression model revealed a significantly lower incidence of
NIs in patients with hepatic dysfunction (OR 3.9). We attribute this finding to the special attention given to these patients concerning their care. These patients received medications, including antibiotics, in especially adjusted doses, and medications metabolized by the liver were avoided. Furthermore, in our study, only one patient with NI had hepatic dysfunction. Thus, this interpretation requires caution from the sample size perspective. This apparent discrepancy needs to be studied in future investigations.

The mean duration of stay in the hospital and PICU for the cases in our study was 3.9 and 2.0 days longer than that of the controls (8.0 and 5.0 days, respectively). These data confirmed the excess LOS in hospitals and ICUs, ranging from 3.1 to 23 days [20–22]. There were statistically significant differences between both case/control groups and patients with/without NIs regarding LOS in hospital and PICU in our study. The literature shows that if a patient has a NI in the ICU, the length of hospitalization will be longer [23]. Besides, an increased mortality rate (up to 35%) was detected depending on the excessive LOS in hospitals and ICUs [24, 25]. As expected, the excess LOS by NIs leads to an increase in hospital costs and frequency of antibiotic use. In developing countries, the expenditure on antibiotics constitutes a large part of the cost [26]. We detected that only antimicrobial use and related expenses were $474 (mean per patient) for traumatic PICU patients without NIs, while this amount was $3030 (mean per patient) for traumatic PICU patients with NIs. On the other hand, the mean total cost per control patient was $842, while it was $2509 for the patients with NIs. Some similar national studies support our findings. The additional cost for ICU patients was reported as ranging between $1500 and $5800 [27–30]. However, this range expands considerably ($2500–40000) in international studies, leading to a 2–47% of additional cost in ICUs per patient [31–33].

**Limitations**

Our work has some limitations. First, it is conducted retrospectively in a single center. A larger data set may allow more accurate sampling and detailed results. Second, we calculated costs using the price chart issued by the Turkish Ministry of Health, which uses a diagnosis-related grouping. Hence, some expense items such as anesthesia fees during surgery,
hospital/PICU standard expenses, and workforce expenses were not calculated. At that point, an itemized price list, including all interventions, could be obtained from the Hospital Billing Unit to get more accurate cost data.

**Conclusion**

In light of the findings, parallel with the current literature, we detected that NIs had an essential effect on the LOS in hospitals and PICU, as well as on additional and total costs of both controls and cases. In our study, it can be concluded that hospital infections are less common in patients followed up with TBI compared to the control group, due to the need for a shorter duration of invasive ventilation, TPN, and interventions such as invasive catheterizations. However, TBI did not have any significant extra effect on the presence of NIs. On the other hand, the NIs caused a substantial burden to both PICU patients and the health-care system regarding the treatment and hospitalization costs. In our study, the cost was probably underestimated for several reasons. Nevertheless, the findings supported our hypothesis about the additional burden of NIs on PICU patients. The results of this study should help provide evidence on cost-effectiveness or calculate the cost-benefit ratio of reducing nosocomial bloodstream infections in children.

**Ethics Committee Approval:** The Marmara University Clinical Research Ethics Committee granted approval for this study (date: 01.09.2019, number: 09.2014.124).

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**REFERENCES**