Brief report

# Bloodstream infections and inpatient length of stay among pediatric cancer patients with febrile neutropenia in Mexico City

Martha Avilés-Robles MD [a], Rohit P. Ojha DrPH [b,*], Miriam González MD [c], Karla Ojeda-Diezbarroso MD [a], Elisa Dorantes-Acosta MD [d], Bradford E. Jackson PhD [e], Kyle M. Johnson PhD [f], Miguela A. Caniza MD [c,f]

[a] Department of Infectious Diseases, Hospital Infantil de México Federico Gómez, Mexico City, Mexico
[b] Department of Epidemiology and Cancer Control, St. Jude Children's Research Hospital, Memphis, TN
[c] International Outreach Program, St. Jude Children's Research Hospital, Memphis, TN
[d] Department of Oncology, Hospital Infantil de México Federico Gómez, Mexico City, Mexico
[e] Department of Preventive Medicine, University of Alabama at Birmingham, Birmingham, AL
[f] Department of Infectious Diseases, St. Jude Children's Research Hospital, Memphis, TN

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We assessed the association between bloodstream infections (BSIs) and inpatient length of stay among pediatric cancer patients with febrile neutropenia in Mexico City. The estimated length of stay for BSIs was 19 days, which corresponded with a 100% (95% confidence limits, 60%–160%) relative increase in the length of stay compared with patients for whom no pathogen was identified. Feasible options for reducing the length of stay should be considered to alleviate patient and resource burden.
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Infections are a major cause of morbidity and mortality for pediatric cancer patients.[1] Prior studies of pediatric cancer patients in high-income countries[2-5] suggest that bloodstream infections (BSIs) increase the inpatient length of stay, a marker of patient burden (eg, risk of nosocomial infection and antibiotic resistance)[6] and resource use. Nevertheless, the impact of BSIs on length of stay among pediatric cancer patients in low- and middle-income countries is unclear. Given the challenges of diagnosis and management in these areas because of limited resources,[6] BSIs may have a greater impact on length of stay than in high-income countries. Evidence of prolonged length of stay may warrant intervention to reduce patient and resource burden. Therefore, we aimed to assess the association between BSIs present at admission and inpatient length of stay among pediatric cancer patients with febrile neutropenia in Mexico City.

## METHODS

### Study population

Hospital Infantil de México Federico Gómez is a public multidisciplinary referral center in Mexico City for children aged <18 years. This 248-bed hospital includes a pediatric hematology and oncology unit with 32 beds. In 2013, the hematology and oncology unit documented 1,304 admissions attributable to 265 newly diagnosed pediatric cancer patients and 700 patients on active therapy. All episodes of febrile neutropenia (ie, temperature >38.3°C or 2 consecutive episodes of temperature >38.0°C, absolute neutrophil count <500 cells/mm$^3$)[1] among pediatric cancer patients admitted for inpatient care between November 2009 and September 2010 were eligible for our analysis. Consistent with institutional policy, only patients with leukemia received antimicrobial prophylaxis with trimethoprim/sulfamethoxazole and nystatin. Catheters are inserted on admission for patients with febrile neutropenia with hemodynamic instability, but they are removed at discharge. Implanted catheters are rarely used in our setting. This study was approved by the local institutional review board.

### Variables

We used a standardized data collection form to prospectively document age at admission, sex, cancer type, prophylaxis, and

**Table 1**
Characteristics of 142 pediatric cancer patients with febrile neutropenia who were admitted to Hospital Infantil de México Federico Gómez (Mexico City) between November 2009 and September 2010

| Characteristic | n (%) |
|---|---|
| Age | |
| <10 years | 103 (73) |
| ≥10 years | 39 (27) |
| Sex | |
| Girls | 72 (51) |
| Boys | 70 (49) |
| Cancer type | |
| Leukemia | 77 (54) |
| Lymphoma | 11 (7.8) |
| Solid tumor | 54 (38) |
| Relapse | |
| Yes | 25 (18) |
| No | 117 (82) |
| Prophylaxis | |
| Yes | 89 (37) |
| No | 53 (63) |
| Infection-related mortality* | |
| Deceased | 5 (3.5) |
| Alive | 137 (96) |

*Mortality during inpatient follow-up.

**Table 2**
Pathogens associated with 24 episodes of bloodstream infections among pediatric cancer patients with febrile neutropenia in Mexico City

| Pathogen | n (%) |
|---|---|
| *Escherichia coli* | 7 (29) |
| *Pseudomonas aeruginosa* | 5 (21) |
| Coagulase-negative *Staphyloccoccus* | 5 (21) |
| *Klebsiella pneumoniae* | 3 (13) |
| *Staphylococcus aureus* | 2 (8.3) |
| *Enterococcus* sp | 1 (4.2) |
| *Streptococcus viridans* | 1 (4.2) |

**Table 3**
Overall and subgroup-specific time ratios and corresponding 95% confidence limits comparing length of stay between febrile neutropenic pediatric cancer patients with bloodstream infections and patients for whom no pathogen was identified

| | Median length of stay (days)* | | | |
|---|---|---|---|---|
| Group | Bloodstream infection | No pathogen identified | Time ratio[†] | 95% confidence limit |
| Overall | 19 | 10 | 2.0 | 1.6-2.6 |
| Age | | | | |
| ≥10 years | 17 | 10 | 1.8 | 1.4-2.5 |
| <10 years | 20 | 8.0 | 3.1 | 1.7-5.7 |
| Sex | | | | |
| Girls | 19 | 10 | 2.2 | 1.6-3.2 |
| Boys | 18 | 10 | 1.8 | 1.2-2.8 |
| Cancer type[‡] | | | | |
| Leukemia | 20 | 10 | 2.4 | 1.7-3.2 |
| Solid tumor | 17 | 10 | 1.9 | 1.2-3.0 |
| Prophylaxis | | | | |
| Yes | 18 | 10 | 2.0 | 1.5-2.6 |
| No | 20 | 10 | 2.7 | 1.4-5.0 |

*Estimated using Kaplan-Meier method.
[†]Adjusted for age at admission, sex, cancer type, and antimicrobial prophylaxis.
[‡]Insufficient sample size for subgroup analysis of other cancer types (lymphoma: n = 14).

treatment phase, diagnosed infections, and length of stay for each episode of febrile neutropenia. Inpatient length of stay, our outcome of interest, was defined as the duration of hospitalization (ie, admission to discharge or death). Laboratory-confirmed BSIs, our exposure of interest, were defined according to the United States Centers for Disease Control and Prevention's National Health Surveillance Network criteria.[7] Blood culture samples for aerobic and anaerobic cultures were drawn 15-30 minutes apart at admission and cultured in BacT/ALERT PF (bioMerieux Inc, Durham, NC) bottles according to the manufacturer's guidelines. Among the 3 patients with implanted catheters (none of whom had incident BSI), blood samples were obtained through the port and a peripheral vein, whereas blood samples were obtained from peripheral veins or from a central vein during placement of a central venous catheter for all other patients.

*Data analysis*

We used Kaplan-Meier methods to estimate the overall and subgroup-specific median inpatient length of stay. In addition, we specified accelerated failure time shared frailty models[8] with log-logistic distributions to compare length of stay between febrile neutropenic pediatric cancer patients diagnosed with BSIs at admission and patients for whom no pathogen was identified (ie, fever of unknown origin). Log-logistic distributions were selected based on empirical evidence that the discharge rate rapidly increases within the first week then decreases over time. The shared frailty component (random effect) of the model addresses within-person dependence for individuals with multiple episodes of febrile neutropenia during the study period.[8] Our models were also adjusted for age, sex, cancer type (leukemia, lymphomas, solid tumors), and prophylaxis (yes or no) to reduce confounding bias. Persistent fever, an intermediate on the causal pathway, was not adjusted in the model to avoid potential overadjustment bias.[9] The time ratios (TRs) and corresponding 95% confidence limits (CLs) estimated from our models reflect the length of stay (eg, TR = 1.2 indicates a 20% longer length of stay for patients with BSIs compared with patients for whom no pathogen was identified).

**RESULTS**

Our study population was composed of 142 pediatric cancer patients admitted with 217 episodes of febrile neutropenia between November 2009 and September 2010. Table 1 summarizes the characteristics of the study population. Briefly, most patients were aged <10 years (70%), and the sex distribution of patients was similar (girls = 51%, boys = 49%). Patients with leukemia comprised most (54%) of the study population. Antimicrobial prophylaxis was administered to 63% of patients. BSIs were diagnosed in 11% of febrile neutropenia episodes, of which 54% (13/24) were gram-negative organisms. Table 2 summarizes the specific pathogens associated with BSIs. The most commonly isolated pathogen was *Escherichia coli* (29%). The total inpatient length of stay from all episodes of febrile neutropenia during our study period was 3,058 days (median = 11 days, interquartile range = 7-17).

Table 3 summarizes the overall and subgroup-specific associations between BSIs and length of stay. Overall, patients with BSIs had a 100% longer relative length of stay compared with patients for whom no pathogen was identified (TR = 2.0; 95% CL, 1.6-2.6). BSIs consistently increased the relative length of stay within subgroups of patients, ranging from an 80% (TR = 1.8; 95% CL, 1.4-2.5) increase among boys to a 210% increase among patients aged <10 years (TR = 3.1; 95% CL, 1.7-5.7).

**DISCUSSION**

Our analysis suggests that the median inpatient length of stay of patients diagnosed with a BSI at admission is 19 days, whereas the median inpatient length of stay for patients for whom no pathogen was identified is 10 days. After adjustment for covariates to reduce confounding bias, our results suggest

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