Clinical outcome, healthcare cost and length of hospital stay among patients with bloodstream infections and acute leukemia in a cancer center in Eastern India

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To the Editor—Acute leukemia is one of the most common forms of malignancy reported globally. Patients with acute leukemia acquire infections for many reasons related to disease, chemotherapy, immunosuppression, the use of vascular access devices, and mucosal barrier injury. Bloodstream infections (BSIs) are potentially the most serious infections in leukemic patients; they often lead to morbidity, hospitalization, and sometimes death. In a previous study, we reported the impact of BSI as a predictor of length of hospital stay (LOS) and cost of care in patients with cancer.[1] In this study, conducted from April 2015 to March 2016, we investigated the effect of BSI on LOS, mortality rates, and healthcare cost among patients with acute leukemia. In total, 350 patients were analyzed during the study period: 234 acute lymphoblastic leukemia (ALL) patients (median age, 8 years; range, 1.5–68.6 years; male:female ratio, 1.8:1) and 116 acute myeloblastic leukemia (AML) patients (median age: 32 years; range, 2.8–71.1 years; male:female ratio, 1:1).

Among patients with gram-positive bacterial BSIs only 1 methicillin-resistant *Staphylococcus aureus* (MRSA) BSI was detected, and 5 methicillin-sensitive *S. aureus* BSIs were detected. Among gram-negative bacillary BSIs, carbapenem resistance varied from 22% to 81%. This resistance was greatest among *Klebsiella* spp., but it was also observed in *Escherichia coli, Pseudomonas aeruginosa,* and *Acinetobacter* spp. We detected 2 cases of colistin-resistant *Klebsiella.* Surveillance cultures from stool samples showed carbapenem resistance in gram-negative bacilli in 59% of patients, and surveillance cultures from throat swabs showed carbapenem resistance in gram negative bacilli in 18% of patients.

Gram-negative bacterial BSIs were the most common, followed by BSIs due to gram-positive cocci and *Candida parapsilosis* (Table 1). The median duration of hospital stay for patients with a BSI was highest for those with *Candida* BSIs (32 days) followed by those with gram-positive bacterial BSIs (25 days) and those with gram-negative bacterial BSIs (22 days). The intensive care unit (ICU) admission rate was highest for patients with gram-negative bacterial BSIs (23 of 69, 33.3%) followed by those with gram-positive bacterial BSIs (8 of 43, 18.6%). The ICU admission rate was least for *Candida* cases in this study (0 or 2, 0%). The 30-day all-cause mortality and BSI-related attributable mortality rate was highest for gram-negative bacterial BSI patients (20.3%).

The clinical outcome data of the present study assume significance in view of the high prevalence of multidrug-resistant (MDR) gram-negative bacterial infections in this setting.[2,3] We have previously reported cases from our center of colistin-resistant *Klebsiella* among both pediatric and adult patients.[4,5] In the period between 2014 and 2015, we reported 30-day all-cause mortality among patients with carbapenem-resistant *E. coli* (0%), *Klebsiella pneumoniae* (40%), *P. aeruginosa* (50%), and *Acinetobacter baumannii* (60%).[6]

In the current study, the average cost for hospital stay was highest for patients with *Candida* BSIs (US$12,232 [Rs. 795,134]), followed by those with gram-negative bacterial BSIs (US $4,945 [Rs. 321,433]). The average cost for hospital stay was lowest for those with gram-positive bacterial BSIs (US$4,163 [Rs. 270,607]). In our previous study, among all cancer patients (and not restricted to those with BSIs), we found that the overall mean LOS was 5.9 days, the average cost of care per admission was US $1,413 (Rs. 95,208), and the all-cause mortality rate was 5.7%.[1]

The comparison of healthcare outcome measures helps us to understand the efficacy of various clinical interventions, such as chemotherapy regimens and infection prevention and control measures, as well as the effect of infrastructure development or resource allocation. Data on these measures are far less commonly available from low- or middle-income countries than from developed economies, but they are important globally because of the migration of people for work, exigencies or medical tourism. A study from the United States showed that for patients with neutropenia plus infection, the mean hospitalization costs were $27,587, the LOS was 12.6 days, and the mortality rate was 19.4%.[7] In a study from Mexico, the mean cost per hospital stay was US$2,246 among patients with ALL.[8] An Indian study on patients undergoing cardiothoracic surgery, patients with hospital-acquired bacteremia experienced a significantly longer total hospital stay (mean, 22.9 days), longer ICU stay (mean, 11.3 days), a higher mortality rate (mean, 54%), and higher cost (mean, US$14,818) than similar patients without bacteremia.[9]

Healthcare service providers must take appropriate measures to mitigate the negative effect of infections on clinical and health economic outcome measures. One of the key interventions to achieve a positive change is an awareness, education, and training program for care providers regarding matters related to infection epidemiology, diagnosis, and appropriate management. An Indian study from a tertiary-care teaching hospital reported that for every dollar spent on training, the return of investment was $236 in avoidance of healthcare-associated infections (HAIs).[10]

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Table 1. Patient Profiles: Bloodstream Infections, Length of Hospital Stay, and Hospital Cost from April 2015 to March 2016

Cause of BSI	No. of BSIs	No. of Patients	Neutrophil Count During BSI, median cells/μL (range)	LOS, median d (range)	ICU Admission, no./total (%)	All-Cause (Crude) Mortality at Day 30 from BSI, no./total (%)	Attributable Mortality at Day 30 from BSI, no./total (%)	Total Hospital Bill During the Admission Episode, median cost (range)
Gram-negative bacilli	113	69	33 (0–50,730)	22 (3–55)	23/69 (33.3)	14/69 (20.3)	11/69 (15.9)	US$4,945 (267–62,910) Rs. 321,433 (17,358–408,918)
Gram-positive cocci	53	43	136 (4–23,700)	23 (5–47)	8/43 (18.6)	7/43 (16.3)	1/43 (2.3)	US$4,163 (367–42,317) Rs. 270,607 (23,870–2,750,653)
Candida spp	2	2	220 (30–410)	32 (12–51)	0/2 (0)	0 (0)	0/2 (0)	US$12,232 (4,116–20,349) Rs. 795,134 (267,560–1,322,708)

NOTE. BSI, bloodstream infection; LOS, length of hospital stay; ICU, intensive care unit; Rs, rupees.

The infection prevention and control measures introduced in our hospital to mitigate the problem of infection in patients with acute leukemia have included numerous interventions: (1) surveillance culture for detection of MDR bacteria in stool samples and throat swabs, (2) use of direct susceptibility tests on positive blood cultures for early detection of resistant organisms, (3) use of polymerase chain reaction–based rapid detection of carbapenem-resistant genes, (4) early empirical therapy with polymyxin based treatment regimens in those previously infected or colonized with carbapenem-resistant multidrug-resistant gram-negative bacteria (MDR-GNB), and (5) accreditation of our infection control systems (NABH Safe I: National Accreditation Board for Hospitals and Healthcare providers). Cost of health care, length of hospital stay, and deaths from infections are affected by many factors, such as human resources, technology, clinical care strategies, which we wish to explore in future controlled studies.

Potential conflicts of interest. All authors report no conflicts of interest relevant to this article.

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