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Clinical Care of Hematological Patients in a Bone Marrow Transplant Unit: Do Human Resources Influence Infection Incidence?

To the Editor—Allogeneic stem cell transplantation (allo-SCT) is widely considered a curative option for many hematological malignancies. Bloodstream infections (BSIs) represent the most frequent infective event in allotransplanted patients, and their incidence may vary from 20% to 70%.[1–3] Prolonged neutropenia, gastrointestinal mucosal damage, and extensive use of central venous catheters (CVC) are the major risk factors for BSIs.[4,5] Usually, BSIs occur during the pre-engraftment phase, but they can occur in later phases, too.[4] Prophylactic antimicrobial therapy (namely with fluoroquinolones) is conventionally used during agranulocytosis, and empirical broad-spectrum antibiotics (namely third-generation cephalosporins, aminoglycosides, and glycopeptides) are promptly started in the event of fever or suspected infection while waiting for the results of microbiological cultures to initiate a target therapy.[6] Considering that only a minority of febrile episodes (30%–40%) in patients subjected to allo-SCT can be defined as BSIs, surveillance for infections in a bone marrow transplant unit is mandatory, to correctly drive the use of empirical therapy.

We recently published the data on the incidence and outcome of BSIs in a cohort of 162 patients who had allo-SCT, over a period of 6 years of transplant activity.[7] Briefly, 60% of the patients were transplanted for acute leukemias and 49% experienced a BSI, for a total of 119 isolates. The median time of blood culture positivity was 19 days from transplant (range day −4 to day +921). Half (n = 59) of the positive cultures were from peripheral blood samples and half (n = 60) were central-venous-catheter related, defined as a positive catheter blood culture that preceded a positive peripheral blood sample by 2 hours. In 77 of 119 cases (65%) and 42 of 119 cases (35%), a gram-positive or a gram-negative agent were isolated, respectively. *Staphylococcus epidermidis* and *Escherichia coli* were the most common isolates (35% and 57%, respectively). Concerning antimicrobial resistance, we observed fluoroquinolone resistance both among gram-positive (roughly 100%) and gram-negative bacteria (between 90% and 100%), together with methicillin resistance among gram-positive bacteria (100% of the *S. aureus*, *S. epidermidis,* and *S. haemolyticus,* and 75% of *S. hominis* isolates). Moreover, 67% of *E. coli* were extended-spectrum β-lactamase producers, and 40% of *Pseudomonas aeruginosa* were resistant to carbapenems. Interestingly, no carbapenemase-producing *Klebsiellae* were isolated. Overall, 15 of 162 allotransplanted patients (9%) died from BSIs. *Pseudomonas aeruginosa* is the most dangerous, with a 50% mortality rate. Enterococci, coagulase negative staphylococci, and *E. coli* showed mortality rates of 33%, 12%, and 4%, respectively.

The annual distribution of gram-positive and gram-negative bacteria and the gram-positive to gram-negative ratio are reported in Figure 1A and B. Within the 6-year observation period, we found a stable gram-positive to gram-negative ratio in all years except 2012 and 2013, when we observed a reduction in the number of positive blood cultures (11 in 2012 and 13 in 2013) and a reduction in the gram-positive to gram-negative ratio (1.2 in 2012 and 0.6 in 2013). Although these differences do not reach significance, they may be partially explained by different CVC management practices in 2012 and 2013, when we had a single dedicated nurse for CVC medications. Considering the high incidence of antibiotic resistance and the unavailability of prophylaxis other than fluoroquinolones, the adoption of clinical-care strategies, such as CVC medication given under optimal asepsis by dedicated nurses, may be the best way to prevent BSIs. This point is crucial, and we believe that the institution of a "CVC nursing team," trained to use the most stringent techniques for CVC management to limit the risk of CVC infection, may partially reduce the incidence of BSIs in allotransplanted patients. The problem, in daily clinical practice, is the lack of human resources to address this issue. Most Italian bone marrow transplant units suffer chronically from inadequate numbers of nurses to provide clinical care for patients. The clinical needs of allotransplanted patients during the first 40–60 days following transplant are very similar to those reserved for patients admitted to intensive care units. In theory, 1 nurse per 3 patients is the ideal ratio. In our unit, we now have 1 nurse for every 6 patients. Consequently, some simple activities, such as CVC medication management, may not be conducted with optimal attention to asepsis.

In conclusion, BSIs are a significant event in allotransplanted patients; they can significantly influence morbidity and mortality

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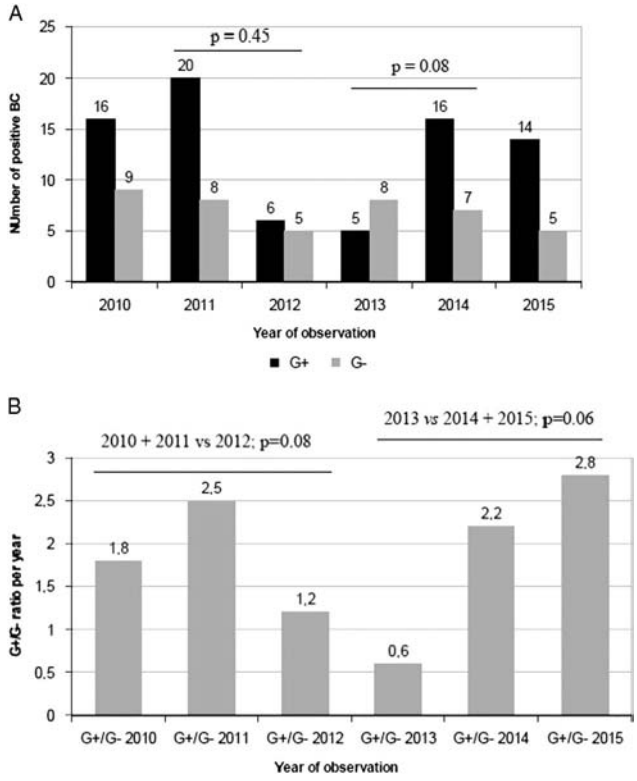

FIGURE 1. (A) Distribution of positive blood cultures over the study period (2010–2015). (B) Year distribution of gram-positive to gram-negative ratio.

of these patients. Moreover, BSIs may prolong the hospital admission of patients and significantly increase the costs of their clinical management. Thus, any strategy that may help reduce the incidence of infections in allotransplanted patients should be considered by hospital administrators. In our view, adequate nurse staffing levels to provide direct patient care should be considered as an important measure to reduce infection in allotransplanted patients.

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High Levels of Hand-Hygiene Compliance Are a Worthwhile Pursuit

To the Editor—We read with great interest the excellent review of evidence-based recommendations for the prevention of