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Microbiologic characteristics and predictors of mortality in bloodstream infections in intensive care unit patients: A 1-year, large, prospective surveillance study in 5 Italian hospitals



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Background: Bloodstream infections (BSIs) from multidrug-resistant (MDR) bacteria cause morbidity and mortality in intensive care unit (ICU) patients worldwide. This study investigated the incidence of BSIs in 5 adult general ICUs in Rome, Italy, and evaluated the mortality rate and risk factors associated with these infections. **Methods:** Over a 12-month period, 1,318 patients were enrolled. Demographic characteristics, Simplified Acute Physiology Score II (SAPS II), comorbidities, and BSI isolate data were collected. After stratification for the outcome, statistical analysis was performed to assess the impact of patient risk factors on in-hospital mortality. **Results:** There were 324 BSIs in 175 patients recorded, with an in-hospital mortality rate of 46%. Univariate analysis revealed that SAPS II, cardiac comorbidity, and *Klebsiella pneumoniae* BSI were significantly associated with a higher risk of death. Having a *K pneumoniae* BSI and cardiac illness at admission were both confirmed to be associated with death by multivariate analysis ($P = .0162$ and $P = .0158$, respectively). Most of the *K pneumoniae* isolates showed high resistance rates to carbapenems. **Conclusion:** BSIs caused by *K pneumoniae* and cardiovascular comorbidity in ICU patients are associated with a higher risk of death. Thorough surveillance for MDR pathogens and stratification of the patients' risk on admission into the ICU are key to improving the outcomes of these infections.

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Author contributions: D.D.R. contributed to the design of the study and wrote the manuscript. G.P.T., M.A., L.S., and P.S. designed the study and coordinated the field sampling. L.S. and M.A. reviewed the manuscript. S.G., G.R., M.M., M.T.G., G.P., R.C., M.D., G.C., M.R., F.L., S.N., C.F., M.F., M.G.C., and T.F. performed the data collection at the hospitals involved and performed the microbiologic analysis. C.C. contributed to the final manuscript. S.B. helped with the statistical analysis.

Conflicts of interest: None to report.

¹ Deceased.

Bloodstream infections (BSIs) and septicemia resulting from infections with antibiotic-resistant gram-negative and gram-positive bacteria are recognized as one of the most significant causes of morbidity and mortality in intensive care unit (ICU) patients worldwide. These conditions have been estimated to complicate between 1.2% and 6.7% of all ICU admissions, with a high case mortality rate of >40% in different studies.^{1,2} Globally, nearly 70% of the BSIs in ICUs are secondary to another primary infection (eg, central line, urinary or respiratory tract infections), whereas the remaining BSIs are of unknown origin.^{3,4} A recent Italian study conducted in 125 ICUs reported that BSIs, particularly catheter related-BSIs, are the second most frequent ICU-acquired infection, with an incidence of 1.9 cases per 1,000 central venous catheter days.⁵ At the time of admission into the ICU, a higher Acute Physiology and Chronic Health Evaluation II or Sequential Organ Failure Assessment score, clinical presentation with septic shock or severe sepsis, multiple comorbidities (>2), and receiving inadequate antimicrobial therapy in the first 48 hours are all generally considered to be the predictors of mortality after BSI that occur in medical or ICU wards.^{6–9}

Bacterial resistance to many antimicrobial classes, which is often encountered in the ICU environment, is nowadays a major concern for the clinician because it might be associated with increased length of hospital stay, worse outcomes, and difficulty of treatment.^{10,11} In particular, according to a recent consensus statement issued by an international panel of experts, a multidrug-resistant (MDR) pattern can be defined as nonsusceptibility to at least 1 agent in ≥ 3 antimicrobial categories, whereas an extremely drug-resistant pattern is defined as nonsusceptibility to at least 1 agent in all but ≤ 2 antimicrobial categories.¹²

In the EUROBACT cohort study, which included 1,156 patients from 162 ICUs in Europe, 88% of the subjects developed at least 1 episode of bacteremia, with an overall mortality rate of 35.7%, and the presence of an MDR or an extensively drug-resistant pattern in the microbiologic isolate was generally associated with a worse outcome and a higher risk of death.¹³

Furthermore, over the last decade, there has been a dramatic increase in nosocomial MDR bacterial strains in the United States and Europe, particularly among isolates recovered from ICU patients.^{14–17} In particular, carbapenem resistance was reported in nearly 70% of *Acinetobacter* spp and 40% of *Klebsiella* spp, and an extended spectrum beta lactamases pattern was expressed in up to 30% of *Enterobacteriaceae* isolates globally.^{18–20}

The present study investigated the annual incidence of BSI in adult ICUs of 5 hospitals (3 teaching hospitals and 2 nonteaching hospitals) in Rome, Italy, in an attempt to quantify the rate of bacteremia per year, the microbiologic epidemiology and diffusion of antibiotic-resistant pathogens, and the risk factors associated with in-hospital mortality after a BSI episode.

METHODS

This was a prospective study conducted over a period of 12 months (September 2010–September 2011). Three of the hospitals involved in the study were teaching hospitals (University of Tor Vergata, University of La Sapienza, and S. Andrea Hospital), whereas 2 were nonteaching hospitals (S. Giovanni Hospital and S. Gallicano Hospital).

All patients who were admitted into the ICUs of the 5 participating hospitals, from baseline to 12 months thereafter, were enrolled in the study. Patients were enrolled regardless of the demographic characteristics and underlying clinical conditions. No exclusion criteria was provided, and no admitted patient was excluded. To collect all of the data of the enrolled patients, a database was created ad hoc. Preliminary meetings, involving the

5 participating centers, have enabled the sharing of databases for the collection of data, and the training of personnel of each center was made before enrolling patients. The preliminary meetings involved clinicians and microbiologists. On that occasion, diagnostic protocols for sample collection and laboratory microbiologic methods were shared by the participating centers. All other issues relating to data collection and statistical analysis, which emerged during the study period, were reported to the National Institute of Health, which developed the database and collaborated on the study.

All of the patients enrolled in the study were monitored daily by attending physicians for the subsequent development of BSI. According to the Centers for Disease Control and Prevention definitions for nosocomial infections, a primary BSI was considered to be the occurrence of any bacteremia not known on admission and acquired in the ICU and was defined by the isolation of ≥ 1 organism from the same patient on ≥ 1 occasion when the clinical evidence suggested signs or symptoms of sepsis.²¹ An episode was considered to be a new episode when a new positive blood culture result was obtained >48 hours after a preceding positive blood culture result. Furthermore, a BSI was defined as the identification of a high-grade pathogen (eg, *Pseudomonas aeruginosa*, *Staphylococcus aureus*) in a blood culture specimen or the identification of a common contaminant or skin flora (eg, coagulase-negative staphylococci [CoNS]) in at least 2 separate blood culture specimens from the same patient. Polymicrobial bacteremia was defined as the isolation of >1 microorganism during a single bacteremic episode.

The demographic characteristics, Simplified Acute Physiology Score II (SAPS II), causes of admission, comorbidities, and BSI isolate data were collected in the database. After antimicrobial susceptibility testing, the most common patterns of drug resistance for gram-positive and gram-negative isolates were identified. Blood cultures were collected at the discretion of the attending physicians in the presence of clinical signs or symptoms of sepsis according to the surviving sepsis campaign guidelines,²² to which all the hospitals were compliant. The cultures were processed using standard microbiologic methods. The blood cultures were performed using an automated BacT/ALERT system (bioMérieux, Durham, NC). The identification of the isolates was performed using the VITEK (bioMérieux, Durham, NC) and API automated systems (bioMérieux, Marcy l'Etoile, France). Organism identification and susceptibility classification were completed with the Vitek 2 system (bioMérieux, La-Balmes-les-Grottes, France) and by manual biochemical identification when necessary. Antimicrobial susceptibility testing was performed on all of the isolates with the Vitek 2 system, as approved by the United States Food and Drug Administration, to determine the minimal inhibitory concentrations. Organism susceptibility was interpreted according to the Clinical and Laboratory Standards Institute guidelines.²³ For the purposes of the statistical evaluation, in the cases where bacteremia was caused by >1 gram-negative isolate at the same time, the most resistant specimen was used for antimicrobial susceptibility. In all of the participating centers, an infectious diseases specialist consultation was available to manage the antimicrobial therapy of the BSI episodes along with the ICU physicians.

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