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Community- and healthcare-associated infections in critically ill patients: a multicenter cohort study

George Dabar [a,*], Carine Harmouche [a], Pascale Salameh [b], Bertrand L. Jaber [c], Ghassan Jamaleddine [d], Mirna Waked [e], Patricia Yazbeck [f]

[a] Hotel Dieu de France Hospital, Pulmonary and Critical Care Division, Saint Joseph University School of Medicine, PO Box 16-6830, Achrafieh Beirut, Lebanon
[b] Lebanese University, Faculties of Pharmacy and of Public Health II, Beirut, Lebanon
[c] Kidney and Dialysis Research Laboratory, Division of Nephrology, Department of Medicine, Saint Elizabeth's Medical Center, Boston, Massachusetts, USA
[d] Kings County Hospital Center, Pulmonary and Critical Care Department, Brooklyn, New York, USA
[e] Saint George Hospital, Pulmonary and Critical Care Department, Beirut, Lebanon
[f] Hotel Dieu de France Hospital, Anesthesia and Critical Care Division, Saint Joseph University School of Medicine, Beirut, Lebanon

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SUMMARY

Objective: To compare the spectrum of infection, comorbidities, outcomes, and mortality of patients admitted to the intensive care unit (ICU) due to community-acquired or healthcare-associated severe sepsis.

Methods: This prospective cohort study was conducted in three university medical centers in Lebanon from February 2005 to December 2006. Patients with severe sepsis were included and followed up until hospital discharge or death.

Results: One hundred and twenty patients were included of whom 60% had community-acquired infections (CAI) and 40% had healthcare-associated infections (HAI). The most common infection in both groups was pneumonia. Hematologic malignancies were the only comorbidity more prevalent in HAI than in CAI ($p = 0.047$). Fungal infections and extended-spectrum beta-lactamase (ESBL) organisms were more frequent in HAI than in CAI ($p = 0.04$ and 0.029, respectively). APACHE and SOFA scores were high and did not differ between the two groups, nor did the proportion of septic shock, while mortality was significantly higher in the HAI patients than in the CAI patients ($p = 0.004$). On multivariate analysis for mortality, independent risk factors were the source of infection acquisition ($p = 0.004$), APACHE II score ($p = 0.006$), multidrug-resistant Pseudomonas infections ($p = 0.043$), and fungal infections ($p = 0.006$).

Conclusions: Severe sepsis and septic shock had a high mortality rate, especially in the HAI group. Patients with risk factors for increased mortality should be monitored and aggressive treatment should be administered.

1. Introduction

Patients with severe sepsis admitted to the intensive care unit (ICU) require costly and time-consuming treatment, but have a high mortality rate, ranging from 30% to 50%.[1] Important contributors to this increased mortality risk include the underlying disease, comorbidities, type of infection, and microbiology. Previous studies addressing these infections in the ICU have focused on prevalence, the means to improve outcomes, and early goal-directed therapy.[2–5] Comparative data on the outcomes of patients with community-acquired infections (CAI) and healthcare-associated infections (HAI) requiring ICU care for severe sepsis are scarce.[6] It is unclear whether potential differences in outcomes between these two types of infection are due to differences in population characteristics (e.g., age, comorbidities) and/or to heterogeneity in disease traits (e.g., causative microorganisms, microbial resistance, and severity of the host inflammatory response). To help address this knowledge gap, a cohort study of patients with severe sepsis admitted to the ICU was performed, with a focus on comparing characteristics, disease severity, and outcomes of community- vs. healthcare-associated infections.

* Corresponding author. Tel.: +9611615300x9314; fax: +9611615295.
E-mail address: georges.dabar@usj.edu.lb (G. Dabar).

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2. Methods

2.1. Setting and patient selection

A prospective multicenter cohort study of critically ill patients admitted to the medical or surgical ICU at one of three tertiary teaching hospitals in Beirut, Lebanon was conducted (Saint Joseph University Faculty of Medicine, American University Hospital of Beirut, and Balamand University Faculty of Medicine and Medical Sciences). These were closed ICUs that were run by a team of critical care specialists assisted by physicians-in-training. Adults aged 18 years or older diagnosed with severe sepsis either at admission to the ICU or occurring during the ICU stay were included in the cohort, and followed until hospital discharge or death. The ethics committees at the three participating sites approved the study protocol and waived the need for patient informed consent due to the absence of interaction with patients.

2.2. Definitions

Sepsis was defined as a suspected or confirmed infection and the presence of at least two systemic inflammatory response syndrome criteria: fever or hypothermia, tachycardia, tachypnea, and altered leukocyte count.[7] Severe sepsis was defined as sepsis and the presence of at least one sepsis severity criterion (i.e., evidence of organ dysfunction such as hypotension or hypoperfusion).[4] Septic shock, a subset of severe sepsis, was defined as sepsis-induced hypotension (systolic blood pressure $\leq$90 mmHg or a reduction of $\geq$40 mmHg from baseline) despite adequate fluid resuscitation and the presence of perfusion abnormalities such as lactic acidosis, oliguria, and altered mental status.[8,9]

Critically ill patients were considered 'medical' if admitted to the ICU for a medical problem, and 'surgical' if admitted following scheduled or unscheduled surgery. ICU criteria for admission were according to each unit's specific protocol.

Infection was identified based on clinical history, physical examination, laboratory and microbiological data, and the administration of antibiotics (excluding antimicrobial prophylaxis) according to the International Sepsis Forum Consensus Conference.[6] Categorization of infection as clinically documented was assessed on a daily basis by the treating physician along with a consultant infectious disease specialist; a diagnosis of microbiologically documented infection was based on the same clinical information complemented by microbiology data such as cultures of blood or body fluid from a suspected site of infection.[6] Any organism found in clinical cultures can cause infection or colonization; the latter is defined by positive cultures without signs and symptoms related to an infectious syndrome. This situation can be transient where some microbes are finally eradicated by the host immune response, while others can later promote symptomatic infections when they gain access to usually sterile body sites, e.g., the bloodstream. Investigating clinical circumstances surrounding positive cultures helped in the differentiation between infection and colonization.[10]

In accordance with the criteria of the Centers for Disease Control and Prevention,[11] an infection developing >48 h after hospital admission or within 30 days after hospital discharge was defined as healthcare-associated. An infection present on admission to the hospital or developing within 48 h or less from the time of admission was defined as community-acquired.

Gram-negative bacteria were considered to be extended-spectrum beta-lactamase (ESBL)-producing pathogens if they belonged to the *Enterobacteriaceae* family and were resistant to more than one third-generation cephalosporin or aztreonam. Multidrug-resistant *Pseudomonas* species were defined based on resistance to at least three of the following antibiotics: Pseudomonas acting beta-lactams, carbapenems, aminoglycosides, and quinolones.[12] The consideration of fungal infection was challenging. Isolation in cultures or identification techniques is not a surrogate for infection and the clinical status of the patient often prevented biopsy sampling. Consequently, the diagnosis of fungal infection required early recognition of clinical and radiological signs and interpretation of microbiological results in context.[13]

2.3. Data collection

At the time of admission to the ICU, data collection included demographic characteristics (age, sex), the presence of comorbid conditions (liver cirrhosis, cancer (metastatic and non-metastatic), severe chronic obstructive pulmonary disease, bone marrow transplantation, hematological malignancy, diabetes mellitus, heart failure, and chronic renal failure requiring renal replacement therapy), and the presence and site of infection (if known). In addition, the severity of the acute illness and organ dysfunction at the time of ICU admission was assessed using the Acute Physiology and Chronic Health Evaluation (APACHE) II score and the Sequential Organ Failure Assessment (SOFA) score. ICU and hospital length of stay and ICU and hospital all-cause mortality were also recorded.

2.4. Statistical analyses

Continuous variables are reported as the mean with standard deviation. Categorical variables are reported as the count with percentage. Comparisons between groups were made with the Kruskall–Wallis test and the Student *t*-test or Wilcoxon test for continuous variables, and with the Chi-square test or Fisher's exact test for categorical variables.

Stepwise backward multivariable logistic regression analyses were performed to examine whether the location of infection acquisition (HAI vs. CAI), as the main variable of interest, was associated with in-hospital mortality. Due to the small sample size, a parsimonious regression model was used, which included for covariates, sex, APACHE II score (which encompasses age and comorbid conditions), septic shock, multidrug-resistant Pseudomonas infection, and fungal infection. The Hosmer–Lemeshow test was used to assess goodness-of-fit for the logistic regression models.

All statistical analyses were performed using SPSS software version 13 (SPSS Inc., Chicago, IL, USA). Differences were considered statistically significant at a *p*-value of less than 0.05.

3. Results

3.1. Characteristics of the cohort

Between February 2005 and December 2006, a total of 1464 critically ill patients were admitted to the ICU, of whom 120 with severe sepsis fulfilled the eligibility criteria. The characteristics of the cohort are summarized in Table 1, stratified according to whether the infection was community- or hospital-acquired. Fifty-four percent were men, mean age was 65 years, and at the time of ICU admission, the mean APACHE II score was 21 and SOFA score 8. Seventy-eight percent of patients suffered from septic shock. Patient characteristics did not differ significantly between the two groups with the exception of a higher prevalence of hematologic malignancies among patients with HAI compared to CAI (22.9% vs. 9.7%; $p = 0.047$).

Infectious characteristics of the cohort are displayed in Table 2. Sixty percent of patients had microbiologically documented infections, which was almost the same in the two groups.