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Original Article

A Two-Year Analysis of Risk Factors and Outcome in Patients with Bloodstream Infection

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SUMMARY: A two-year analysis was performed at our hospital to evaluate the incidence and clinical impact of bloodstream infections (BSI) in medical, surgical, and intensive care unit patients. During 1999-2000 there were 521 cases of BSI with an incidence of 10.1/1,000 admissions. The most frequent predisposing factors for BSI were intravascular catheter (56.4%) and previous use of antibiotics (50.9%). Infections were considered as primary in 67.9% of cases. Urinary tract and intravascular catheter were the most frequent source of secondary bacteremia (43.1% and 35.9%, respectively). At the time of the first positive blood culture, 83.5% of patients were receiving empirical treatment, but it was adequate in only 53.9% of cases. After antimicrobial susceptibility testing, adequate antibiotic treatment was given in 67.9% of cases. Statistical analysis of independent risk factors showed that mortality was significantly related to age ($P < 0.048$), rapidly-fatal diseases ($P < 0.001$), septic shock ($P < 0.020$), multiorgan failure ($P < 0.001$), previous use of antibiotics ($P < 0.008$), *Enterobacteriaceae* producing extended-spectrum β-lactamases ($P < 0.036$), and inadequate empirical treatment ($P < 0.039$). Based on local epidemiology and susceptibility data, microbiology laboratories should periodically release recommendations on the optimal empirical treatment for different wards.

INTRODUCTION

Despite the introduction of new antimicrobial agents and progress in supportive therapy, bacteremias are related to up to 50% of a hospital's mortality rate and to excessive healthcare costs (1-3). Bloodstream infections (BSI) represent a leading cause of mortality in the United States (fourth to thirteen in rank) with 250,000 episodes of infections occurring annually and no less than 8,750 deaths per year due to these infections (4). Recent reports document an increase in age-adjusted death rates due to BSI, from 4.2 per 100,000 population in 1980 to 13.2 per 100,000 in 1992, related also to the increasing prevalence of opportunistic infections (5).

Underlying disease and risk factors such as immunosuppressive therapy and invasive or prosthetic devices may contribute to increase the number of hospital-acquired infections (6). Therefore, the identification of independent risk factors for the acquisition of BSI may be useful for the development of preventive measures (7,8). Furthermore, given that several types of infection may result in secondary BSI, early treatment of original infection is mandatory for preventing secondary BSI (9). Nosocomial bacteremias markedly influence the outcome of affected patients, especially in intensive care units (ICU), as a result of the severity of illness, multiple risk factors, and drug resistance. In particular, resistance to antibiotics is a major issue; multidrug-resistant bacteria are emerging worldwide, often as a result of selective pressure caused by broad-spectrum antimicrobial drugs (10).

The aim of this study was to investigate the BSI problem in an Italian teaching hospital by analyzing the risk factors, appropriateness of antimicrobial therapy, and mortality attributable to BSIs.

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MATERIALS AND METHODS

Blood collection and sample processing: Blood cultures were performed at the Microbiology Laboratory of the Ospedale di Circolo (Varese, Italy), an 800-bed university hospital that provides a full range of medical and surgical services, including heart surgery and neurosurgery, and is equipped with a kidney transplantation unit and a general ICU.

Standard criteria and methods for blood culturing have been in effect at our institution since 1997 (11). For example, blood should be obtained for culture prior to the administration of systemic antimicrobial therapy when there is fever ($\geq$38°C) or hypothermia ($\leq$36°C), leukocytosis (total peripheral leukocyte count of more than 10,000 leukocytes per liter), granulocytopenia (less than 1,000 polymorphonuclear leukocytes per liter), or a combination of any of the above. Blood should not be drawn through an indwelling intravenous or intraarterial catheter unless it cannot be obtained by venipuncture or if it is being drawn specifically to evaluate a potential catheter-related infection, in which case blood should be simultaneously drawn by venipuncture from another site. Blood should be drawn after cleansing the skin with 70% isopropyl alcohol for 30 s and applying 10% povidone iodine for 60 s. Eight to 10 ml of blood should be inoculated directly into couples of aerobic and anaerobic BACTEC Plus bottles (Becton Dickinson Diagnostic Systems, Sparks, Md., USA). Before inoculation, the rubber septum should be decontaminated with 70% isopropyl alcohol. We recommend a collection of three blood samples per set during the first 1 to 2 h of evaluation; if all these samples are negative 24 h later, we suggest that three more be obtained.

Blood cultures were incubated in the BACTEC 9240 instrument (Becton Dickinson) for 7 days at 35°C. Positive samples were Gram-stained and sub-cultured onto standard solid media. Isolates were routinely identified to the species level by the Sceptor System (Becton Dickinson) and/or the ATB System (bioMérieux sa, Marcy l'Étoile, France). Antimicrobial susceptibility testing was performed by microdilution Sceptor panels (Becton Dickinson). In particular cases (e.g., *Streptococcus pneumoniae*), antibiotic sensitivity was determined by disk diffusion and/or Etest (AB Biodisk, Solna, Sweden). According to the National Committee for Clinical Laboratory Standards (NCCLS) criteria for evaluating the production of extended-spectrum β-lactamases (ESBL), double-disk synergy test with clavulanate was routinely performed on members of the family *Enterobacteriaceae* that showed MICs for ceftazidime and/or aztreonam ≥ 2 μg/ml (12). Two Etest strips, one containing ceftazidime or cefotaxime alone, the other containing one of these plus clavulanate, were used as a confirmatory test. Results were interpreted according to the NCCLS guidelines (13,14).

Epidemiological and clinical data: The current study was a retrospective cohort study in which we examined the clinical records of all patients with BSI during 1999 and 2000. For each case of bacteremia or fungemia, the following information was recorded: age, sex, hospital admission and discharge dates, ward, underlying disease, primary source of infection leading to secondary BSI (when present and confirmed by culture), antimicrobial agents used before and after microbiological diagnosis, and cause of death. McCabe and Jackson groups were used to classify the severity of underlying disease (15).

Comorbidity scores were determined according to Charlson weighted index, whereas the severity of septicemia was classified according to the American College of Chest Physicians/Society criteria (16,17). The following predisposing conditions of infection (if present over 72 h before BSI onset) were studied: intubation; intravascular and bladder catheters; thoracic, abdominal, and other drainages; upper and lower endoscopy. In addition, previous use of antibiotics, previous surgical intervention, and immunosuppressive therapy were taken into account if present over two weeks before BSI. Patients were divided into three groups on the basis of admission to the ICU, medical, or surgical ward.

Finally, to better evaluate the BSI problem, we studied the admission data of all patients from whom blood culture had been aquired during hospitalization (including those with a negative result after 7-day incubation). The overall mean length of hospital stay (MLHS) and admission ward data were provided by the hospital administration.

Definitions: To evaluate both the epidemiology of BSI and the significance of the organism isolated in each septic episode, the Centers for Disease, Control and Prevention (CDC) definitions were adopted (18). Cultures taken from the same patient within 7 days were considered to be part of a single septic episode. Results were interpreted according to CDC guidelines, as follows: 1) significant bacteremia, in which either a known pathogen was isolated from one or more blood cultures, or a possible contaminant was recovered from at least two different blood cultures within the same set of samples; 2) pseudobacteremia, in which a possible contaminant (normal skin saprophyte) was isolated from only one out of two or more blood cultures within the same set of samples; and 3) polymicrobial bacteremia, in which two or more organisms were isolated from two or more cultures within the same set of samples (18). Hospital-acquired BSI was defined as bacteremia or fungemia occurring at least 72 h after admission. Primary BSI was related to bacteremia or fungemia for which there were no documented sources of infection, whereas secondary BSI showed laboratory evidence of infection at a distant site by the same organism. Antibiotic treatment was defined as empirical when administered before the results of cultures were available; it was considered adequate when the microorganism was subsequently found to be susceptible to the administered drug(s) (19). Antimicrobial treatment was defined as adequate when the patient received, for at least 7 days, one or more drugs active in vitro (19). Death was considered as attributable to BSI if it occurred during the acute phase of the infection or while the patient was still receiving antibiotic treatment.

Data analysis: Data from clinical records and results from blood cultures were analysed using a statistical PC software (Statistica; StatSoft, Tulsa, Okla., USA). Variance by logistic regression was calculated in order to compare patients who survived with those who died as a result of BSI. We used the Student's unpaired *t* test to compare continuous variables, the Mann-Whitney U-test to compare continuous variables not normally distributed, and Fisher's exact test to compare proportions. Differences were considered statistically significant when the *P* level was <0.050. Finally, the odds ratio (OR; 95% CI) for all significant risk factors was calculated.

RESULTS

During 1999-2000 there were 51,540 admissions with 2,338 suspected septic episodes and 521 (22.3%) BSI. The number of suspected septic episodes was 45.4/1,000 admissions; two or more blood cultures were performed in 66.2% of cases; the infections were hospital-acquired in 379/521 episodes (72.7%); and the incidence of BSI was 10.1/1,000 admissions. Table 1 shows the overall number of cases and their distribution in the ICU, medical, and surgical wards.

With regard to demographic and clinical data (Table 2), there were 196/521 female (37.6%) and 325/521 male (62.4%) patients, having an average age of 60.9 ± 17.2 years (range, 18-89). According to the McCabe and Jackson classification, 45.1% of patients had non-fatal diseases, 42.0% had ultimately-fatal diseases, and 12.9% had rapidly-fatal diseases. The mean Charlson weighted index was 3.0 ± 3.3 (range, 0-14). Sepsis was present in 80.4% of patients, 11.7% of whom had severe sepsis, 5.6% septic shock, and 2.1% multiorgan failure.

Table 3 summarizes the predisposing factors for BSI. Intravascular catheter, previous use of antibiotics, and bladder catheter were the most common predisposing factors. Most patients (423/521, 81.2%) had at least one predisposing factor, whereas 133/521 (25.5%) had two, and 288/521 (55.3%) had three or more. More specifically, three or more risk factors were present in all ICU patients, whereas in medical and surgical wards the numbers of such patients were 73/261 (28.0%) and 122/168 (72.6%), respectively.

Table 4 shows that BSI were considered primary in 354/521 (67.9%) cases, and secondary in the remaining 167 (32.1%). Overall, urinary tract and intravascular catheters were the most frequent source of secondary BSI (43.1% and 35.9%, respectively). In the ICU ward, in contrast the medical and surgical wards, the respiratory tract was the most frequent focus of infection (63.0%). Concerning the incidence

Table 1. Epidemiological data concerning blood cultures recovered from different wards during 1999-2000

	Medical	Surgical	ICU[1)]	Total
Admissions	16339	34131	1070	51540
Suspect septic episodes	1361	685	292	2338
Suspect septic episodes /1000 admissions	83.3	20.1	272.9	45.4
- Blood culture performed once[2)] (%)	431 (31.7)	277 (40.4)	83 (28.4)	791 (33.8)
Pseudobacteremias (%)	36 (8.4)	27 (9.7)	10 (12.0)	73 (9.2)
BSI[3)] (%)	72 (16.7)	52 (18.8)	10 (12.0)	134 (16.9)
- Blood culture performed twice[2)] (%)	474 (34.8)	237 (34.6)	70 (24.0)	781 (33.4)
Pseudobacteremias (%)	20 (4.2)	7 (3.0)	2 (2.9)	29 (3.7)
BSI (%)	100 (21.1)	59 (24.9)	33 (47.1)	192 (24.6)
- Blood culture performed ≥3[2)] (%)	456 (33.5)	171 (25.0)	139 (47.6)	766 (32.8)
Pseudobacteremias (%)	30 (6.6)	10 (5.8)	4 (2.9)	44 (5.7)
BSI (%)	89 (19.5)	57 (33.3)	49 (35.3)	195 (25.5)
Total Pseudobacteremias (%)	86 (6.3)	44 (6.4)	16 (5.5)	146 (6.2)
Total BSI (%)	261 (19.2)	168 (24.5)	92 (31.5)	521 (22.3)
Total Polymicrobial BSI (%)	10 (3.8)	8 (4.8)	3 (3.3)	21 (4.0)
BSI/1000 admissions	16.0	4.9	86.0	10.1
Hospital-acquired BSI (%)	150 (57.5)	142 (84.4)	87 (94.6)	379 (72.7)
Hospital-acquired BSI/1000 admissions	9.2	4.2	81.3	7.4

[1)] ICU, intensive care unit.
[2)] within the same set of samples.
[3)] BSI, bloodstream infections.

Table 2. Demographic and clinical data of patients with BSI

	Medical (*n*=261)	Surgical (*n*=168)	ICU (*n*= 92)	Total (*n*= 521)
Age (±SD)	65.0 (±17.0)	64.4 (±13.4)	53.6 (±17.3)	60.9 (±17.2)
Sex: (%):				
- Female	111 (42.5)	60 (35.7)	25 (27.2)	196 (37.6)
- Male	150 (57.5)	108 (64.3)	67 (72.8)	325 (62.4)
McCabe & Jackson groups (%):				
- Non-fatal	86 (33.0)	71 (42.3)	78 (84.8)	235 (45.1)
- Ultimately-fatal	121 (46.4)	84 (50.0)	14 (15.2)	219 (42.0)
- Rapidly-fatal	54 (20.7)	13 (7.7)	0 (0.0)	67 (12.9)
Charlson weighted index (±SD)	4.2 (±3.4)	3.5 (±3.5)	1.3 (±2.1)	3.0 (±3.3)
Severity of septicemia (%):				
- Sepsis	220 (84.3)	126 (75.0)	73 (79.3)	419 (80.4)
- Severe sepsis	25 (9.6)	29 (17.3)	7 (7.6)	61 (11.7)
- Septic shock	9 (3.4)	11 (6.5)	10 (10.9)	30 (5.6)
- Multiorgan failure	7 (2.7)	2 (1.2)	2 (2.2)	11 (2.1)

Table 3. Predisposing factors for BSI

	Medical (*n*=261)	Surgical (*n*=168)	ICU (*n*=92)	Total (*n*=521)
Intravascular catheter[1)]	92 (35.2)	115 (68.4)	87 (94.6)	294 (56.4)
Previous use of antibiotics[2)]	86 (33.0)	110 (65.5)	69 (75.0)	265 (50.9)
Bladder catheter[1)]	73 (28.0)	100 (59.5)	86 (93.5)	259 (49.7)
Previous surgery[2)]	35 (13.4)	116 (69.0)	60 (65.2)	211 (40.5)
Intubation[1)]	16 (6.1)	26 (15.5)	72 (78.3)	114 (21.9)
Drainages[1)]	45 (17.2)	32 (19.0)	27 (29.3)	104 (20.0)
Immunosuppressive therapy[2)]	45 (17.2)	29 (17.3)	22 (23.9)	96 (18.4)
Endoscopy[1)]	22 (8.4)	29 (17.3)	2 (2.2)	53 (10.2)

[1)] If present over 72 hours before BSI onset.
[2)] If present over 2 weeks before BSI onset.

Table 4. Primary BSI and sources of infection causing secondary BSI

	Medical (*n*=261)	Surgical (*n*=168)	ICU (*n*=92)	Total (*n*=521)
Primary BSI (%)	175 (67.0)	141 (83.9)	38 (41.3)	354 (67.9)
Secondary BSI (%):	86 (33.0)	27 (16.5)	54 (58.7)	167 (32.1)
- Urinary tract	38 (44.2)	23 (85.2)	11 (20.4)	72 (43.1)
- Intravascular catheter	25 (29.1)	18 (66.7)	17 (31.5)	60 (35.9)
- Lower respiratory tract	12 (14.0)	13 (48.1)	34 (63.0)	59 (35.3)
- Wounds	0 (0.0)	13 (48.1)	4 (7.4)	17 (10.2)
- Others[1)]	10 (10.5)	3 (11.1)	1 (1.9)	13 (7.8)

[1)] Others include upper respiratory tract (*n*=9), drainages (*n*=3), and pleural fluid (*n*=1).

Table 5. Antimicrobial treatment of patients with BSI

	Medical (*n*=261)	Surgical (*n*=168)	ICU (*n*=92)	Total (*n*=521)
Empirical treatment given (%)	220 (84.3)	127 (75.6)	88 (95.7)	435 (83.5)
Empirical adequate treatment (%)	157 (60.1)	78 (46.4)	46 (50.0)	281 (53.9)
Overall adequate treatment[1)] (%)	182 (69.7)	110 (65.5)	62 (67.4)	354 (67.9)
Treatment adequate < 7 days[1)] (%)	23 (8.8)	13 (7.7)	6 (6.5)	42 (8.1)
Days of adequate treatment (±SD)	10.8 (±6.0)	9.1 (±3.4)	12.2 (±7.9)	10.1(±5.2)

[1)] After identification and antimicrobial susceptibility testing.

Table 6. Clinical data and outcome of patients with BSI

	Medical (*n*=261)	Surgical (*n*=168)	ICU (*n*=92)	Total (*n*=521)
Mean length of hospital stay[1)]	6.7	11.5	7.6	8.6
Length of stay in patients with BSI[1)] (±SD)	31.3 (±26.5)	54.6 (±45.5)	43.5 (±32.2)	43.1 (±37.7)
Time from admission to BSI[1)] (±SD)	11.8 (±15.8)	23.6 (±23.1)	14.9 (±10.1)	16.3 (±17.4)
Patient death (%)	48 (18.4)	24 (14.3)	17 (18.5)	89 (17.1)
Death attributable to BSI (%)	29 (11.1)	16 (9.5)	14 (15.2)	59 (11.3)

[1)] Results are expressed as days of hospital stay.

of microorganisms responsible for secondary infections, *Escherichia coli* was consistently associated with urinary tract infection (24/24), whereas *Staphylococcus aureus* was mostly related to intravascular catheter (26/35). Strains of *Enterobacteriaceae* other than *E. coli* were mainly recovered from respiratory (37/47) or urinary tract specimens (29/47), and sometimes from both (16/47).

As reported in Table 5, 83.5% of patients were receiving empirical treatment at the time of the first positive blood culture, but this treatment was adequate in only 53.9% of cases. After identification and antimicrobial susceptibility testing, adequate antibiotic treatment was given in 67.9% of cases, with an overall mean time of treatment of 10.1 ± 5.2 days (range, 3-40 days). No differences were found among ICU, medical, and surgical patients.

Table 6 shows that the overall MLHS was 8.6 days, whereas the MLHS of patients with BSI was 43.1 ± 37.7 days (range, 2-167 days). The MLHS from admission to BSI onset was 16.3 ± 17.4 days (range, 0-134 days). The mortality rate among patients with BSI was 17.1% (89/521), with death directly attributable to BSI in 59/521 cases (11.3%).

Table 7 reports the comparison between clinical data of BSI patients who survived and those who died. Statistical analysis of independent risk factors showed that mortality was significantly related to age (OR = 3.90; 3.39-29.6), rapidly-fatal diseases (OR = 12.32; 1.91-193.26), septic shock (OR = 5.39; 1.80-182.26), multiorgan failure (OR = 16.90; 11.36-1691.93), previous use of antibiotics (OR = 7.10; 1.23-123.44), infections caused by ESBL-positive enterobacteria (OR = 4.42; 1.58-157.56), and inadequate empirical treatment (OR = 4.28; 0.68-72.08). Among patients receiving inadequate empiric treatment (*n* = 240), 95 (39.6%) were infected by drug-resistant bacteria (methicillin-resistant *S. aureus* [MRSA], methicillin-resistant coagulase-negative staphylococci [MR-CNS], ESBL-positive enterobacteria). Drug resistance significantly affected patients' mortality due to BSI; the mortality rate was 23.2% (22/95) in the case of drug-resistant bacteria and 17.9% (26/145) in the case of other bacteria. It should be noted that among the factors not significantly related to mortality, ultimately-fatal diseases, drainages, and infections caused by MRSA had *P* levels very close to the significant value ($P < 0.071$, $P < 0.058$, and $P < 0.074$, respectively).

DISCUSSION

Our study was performed to evaluate the incidence and clinical impact of BSI in different hospital wards. More specifically, we examined risk factors, treatment, and outcome in medical, surgical, and ICU patients.

The overall incidence rate of BSI at our institution was comparable to the rates reported in other European studies

Table 7. Comparison between patients who survived BSI and those who died as a result of BSI[1)]

	Survived (*n*=432)	Dead (*n*=59)	*P* level
Age (±SD)	59.3 (±17.7)	67.9 (±10.2)	<0.048
Sex (%):			
- Female	162 (37.5)	16 (27.1)	NS
- Male	270 (62.5)	43 (72.9)	NS
McCabe & Jackson groups (%):			
- Non-fatal	241 (55.8)	25 (42.4)	RC[2)]
- Ultimately-fatal	162 (37.5)	23 (39.0)	NS
- Rapidly-fatal	29 (6.7)	11 (18.6)	<0.001
Severity of septicemia (%):			
- Sepsis	374 (86.6)	19 (32.2)	RC[2)]
- Severe sepsis	45 (10.4)	11 (18.6)	NS
- Septic shock	13 (3.0)	20 (33.9)	<0.020
- Multiorgan failure	0 (0.0)	9 (15.3)	<0.001
Charlson weighted index (±SD)	2.8 (±3.2)	3.6 (±3.1)	NS
Hospital-acquired BSI (%)	332 (76.9)	52 (88.1)	NS
Predisposing factors (%):			
- Intravascular catheter	273 (63.2)	45 (76.3)	NS
- Previous use of antibiotics	239 (55.3)	44 (74.6)	<0.008
- Bladder catheter	246 (56.9)	36 (61.0)	NS
- Previous surgery	191 (44.2)	39 (66.1)	NS
- Drainages	81 (18.8)	25 (42.4)	NS
- Intubation	126 (29.2)	30 (50.8)	NS
- Immunosuppressive therapy	91 (21.1)	11 (18.6)	NS
- Endoscopy	41 (9.5)	5 (8.5)	NS
Secondary BSI (%):			
- Urinary tract	60 (13.9)	7 (11.9)	NS
- Intravascular catheter	53 (12.3)	7 (11.9)	NS
- Lower respiratory tract	67 (15.5)	11 (18.6)	NS
- Wounds	12 (2.8)	5 (8.5)	NS
Microorganisms (%):			
- *Staphylococcus aureus*	100 (23.1)	25 (42.4)	NS
- methicillin-resistant *S. aureus*	69 (15.9)	16 (27.1)	NS
- Coagulase-negative staphylococci (CNS)	76 (17.6)	9 (15.3)	NS
- methicillin-resistant CNS	50 (11.6)	6 (10.2)	NS
- *Enterobacteriaceae*	160 (37.0)	14 (23.7)	NS
- ESBL[3)]-producing *Enterobacteriaceae*	18 (4.2)	6 (10.2)	<0.036
- Nonfermenting gram-negative bacteria	24 (5.6)	7 (11.9)	NS
- *Candida* spp.	48 (11.1)	4 (6.8)	NS
Empirical treatment inadequate (%)	159 (36.8)	48 (81.4)	<0.039

[1)] Thirty patients who did not die because of BSI have been excluded.
[2)] RC, reference category.
[3)] ESBL, extended-spectrum β-lactamases.

(20-23). It should be noted, however, that a relatively high rate of BSI (27.2 per 1,000 admissions) was found in a large one-day multicenter study by the European Study Group on Nosocomial Infections (19). In our survey, the majority of BSI were hospital-acquired, confirming the data in the above mentioned European study and differing from previously reported data that showed a virtually equal number of hospital- and community-acquired BSIs (9,19). This discrepancy may be due to the different study periods (1992 versus 1999-2000), given that the number of risk factors and complexity of treatment have been on the increase. As expected on the basis of multiple risk factors, the incidence of BSI was higher in the ICU than in the medical or surgical ward (5 and 17 times higher, respectively) (8). Notably, the most frequent predisposing factors observed herein implied the rupture of natural barriers (e.g., intravascular and bladder catheters) and/or altered mechanisms of defense (e.g., the use of antibiotics and immunosuppressive agents).

With regard to the number of blood cultures performed within the same set of samples during septic episodes (i.e., the number of bottles obtained from each patient), two or more samples were obtained as recommended (11, 18) in only 66.2% of cases.

The inability to determine the focus of BSI remains an important problem. In our study, the source of BSIs was often unknown (67.9%). Considering that we included only sources confirmed by cultures, this figure is comparable to that reported by Weinstein et al. (9). Overall, the sources and the focuses of infection most frequently causing secondary BSI were urinary tract and intravascular catheters, and the

lower respiratory tract infection. Urinary tract infections were comparatively more frequent in medical wards, whereas episodes associated with intravascular catheter occurred with comparable frequency in all three wards. Astoundingly, the most frequent focus of infection in ICU was the respiratory tract (63.0%), probably due to the high frequency of intubation and use of mechanical ventilation.

With regard to the outcome of patients with BSI, our data indicated that 83.5% of patients received empirical treatment, and that it was adequate in only 53.9% of cases. More specifically, 81.4% of the deceased and 36.8% of the surviving patients received inadequate empirical treatment ($P < 0.039$). It should be noted that only 50.0% of ICU patients received adequate empirical treatment, mainly due to infection with multidrug-resistant strains (10). During 1999-2000, in fact, a large number of MRSA (80.0%), MR-CNS (96.3%), and ESBL-producing *Enterobacteriaceae* (54.3%) were detected in the blood cultures of ICU patients. The high percentage of ESBL-producing enterobacteria was reflective of an outbreak (August 1999 to July 2001) of TEM-52-producing *Klebsiella pneumoniae*. In fact, among 35 cases of BSI caused by enterobacteria, 16 (45.7%) were cases of ESBL-positive *K. pneumoniae* and 3 (8.6%) were cases of ESBL-positive *Enterobacter cloacae*.

Our findings demonstrates that despite the availability of susceptibility results, only 354/521 (67.9%) of patients received adequate treatment. Further analysis of clinical records showed that this situation was related to different factors: 1) 58/521 (11.1%) patients died as a result of BSI in less than 7 days from diagnosis; 2) 22/521 (4.2%) patients did not receive any treatment; 3) 45/521 (8.6%) received inadequate treatment because the drug(s) administered were ineffective in vitro; 4) 42/521 (8.1%) were given adequate drugs for less than 7 days.

The MLHS in infected patients was significantly longer than that in uninfected patients (43.1 versus 8.6 days), confirming the impact of costs associated with BSI on public health (2,3). Overall, the mortality and death rates attributable to BSI (17.1 and 11.3%, respectively) were similar to results reported by Bouza et al. (19), though other previous studies have reported higher rates (21-23). However, it must be considered that the latter studies focused on hospital-acquired BSI.

Statistical analysis demonstrates that a high rate of death attributable to BSI is certainly associated with age, underlying disease, severity of septicemia, previous use of antibiotics, infections caused by ESBL-positive enterobacteria, and inadequate empirical treatment.

Our data emphasize the importance of the collaboration between the microbiologist and the infectious disease physician in providing the patient with an appropriate therapy. Finally, based on local epidemiology susceptibility data, internal recommendations for empirical treatment of suspected BSI should be elaborated on and periodically revised.

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