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# Polymicrobial bacteremia in critically ill patients

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**Abstract.** *Objective:* To characterize the epidemiology of polymicrobial bacteremia (PMB) among critically ill patients.
*Design:* Prospective clinical study.
*Setting:* University medical center.
*Patients:* All patients with positive blood cultures in a medical-surgical ICU.
*Measurements:* PMB represents 8.4% of all true bacteremia in our ICU. Most of these patients were postoperative but none had malignancies or significant immunodepression. Over three-quarters of the episodes were nosocomial. No significant differences in factors associated with PMB were found when they were compared with a cohort of 154 monomicrobial episodes. Enterobacteriaceae were the most common organisms. Intravascular devices (42.8%) were the most common source of PMB, followed by intra-abdominal origin (21.4%). The overall mortality was 7.1%, a lower rate than has previously been described.
*Conclusions:* We suggest catheter replacement in patients who develop PMB and improving techniques of catheter maintenance in order to reduce its incidence.

**Key words:** Polymicrobial bacteremia – Catheter-related bacteremia – Critically ill patients – Epidemiology

Polymicrobial bacteremia (PMB) is a major source of nosocomial infection, which has received considerable attention in previous studies [1, 2]. Prior investigations, however, have been limited to severe immunodepressed patients, such as those who suffered haematologic neoplasia, or unselected populations. Critically ill patients in intensive care units (ICUs) usually have their host defences altered by underlying diseases, are submitted to artificial and invasive procedures or immunosuppressive therapy. Although they are at high risk for the development of bacteremia [3], the study of PMB in this highly selected population has received scarce attention in the literature. In the present study, we sought to characterize this group in terms of sources, organisms and outcome, and compared these episodes to those with a single isolate.

## Patients and methods

### *Patients*

Our ICU is a 16-bed medical-surgical unit, in a 1000-bed teaching hospital that serves both as a referral center and a first line hospital. It is located in an urban area with a population of more than 3 million. Of the patients 63.2% underwent surgery and 10.9% were admitted by trauma. During the period of the study (January 1988–December 1990), all patients in our ICU with one or more positive blood cultures were initially eligible and prospectively evaluated by one of the investigators. Clinical, epidemiological, and laboratory data were prospectively recorded using a standardized worksheet and stored in a computer database.

Catheter insertions were performed by staff physicians using a strictly prescribed aseptic technique: the operator washed his hands and wore a mask, sterile gown, and gloves; the puncture site was prepared with povidone-iodine solution and surrounding areas were covered with sterile drapes. Once inserted, the catheter was secured with 1 or 2 silk sutures. Povidone-iodine ointment was applied to the insertion site, which was then covered with a sterile, transparent, occlusive dressing. The dressing was changed every 48 h.

### *Definitions*

We defined an episode of bacteremia as the first or any new positive blood culture obtained more than 2 days after the preceding positive blood culture. Positive cultures due to contamination were excluded from our study. The decision as to whether one or more positive blood cultures represented an episode of true bacteremia or contamination of the culture was reached by consensus between one of the authors (JR) and the physicians directly in charge of the patient. This decision was based on multiple factors, including the history of the patient, physical examination, body temperature, peripheral leukocyte count and differential, clinical course, results of cultures from other body sites, and percentage of blood cultures positive. According with Reuben et al. [1], PMB was defined as the isolation of two or more microorganisms from the blood on at least two ocasions within a 24 h period.

Any episode beginning 48 h after admission at the hospital was considered as nosocomial. Surgery was considered to be present if it took place within 2 weeks prior to the episode. Renal failure was defined as a serum creatinine level of more than 175 μmol/l. Cirrhosis was assumed if a positive liver biopsy was available or if the clinical presenta-

tion and follow-up were consistent with this diagnosis. A hematologic malignancy was considered to be present when the peripheral blood examination or the bone marrow or lymph node biopsy was consistent. Non hematologic malignancies were considered to be present only when the histologic diagnosis was available. We considered that leukopenia existed if the total leukocyte count was lower than $4\times10^9$/l. Shock was defined on the basis of a systolic blood pressure below than 90 mmHg, or a decrease greater than 30 mmHg in a hypertensive patient, associated with signs of systemic hypoperfusion over 4 h.

The source of infection was designated as one of the following – lower respiratory tract, intra-abdominal, urinary tract, wound infection, soft tissue, other or unknown- according to previously published criteria [3]; catheter-related bacteremia was diagnosed when the same strain was isolated in blood cultures and semiquantitative catheter tip cultures (15 or more colonies) [4] and if no primary site other than the intravascular catheter could be identified.

### *Cultures*

Blood samples were cultured aerobically by inoculating 5 ml in each of three culture bottles (TSB "liquoid"® (Roche), Hémoline® diphasique (BioMérieux) as aerobic media and Hémoline® anaerobic (BioMérieux) as anaerobic media). All specimens were incubated for 7 days at 35 °C and examined macroscopically once a day. Blind subcultures were made before descarding the negative bottles. A Gram stain and subcultures in adequate media were performed in all macroscopically positive bottles. Catheter tip cultures were performed according to the semiquantitative technique of Maki et al. [4]. Identification and sensitivity tests of isolated microorganisms were performed by methods previously described [5].

### *Statistical analysis*

Proportions were compared using the $\chi^2$-test with Yates correction or Fisher's exact test when necessary.

## Results

During the study period, 168 episodes of true bacteremia were detected in our ICU. Incidence and distribution by sources is shown in Table 1. These episodes formed a heterogeneous group and comparison of epidemiologic data between patients with mono- or polymicrobial bacteremia are shown in Table 2. A total of 14 episodes were PMB, and 11 of them were nosocomial; this represents 8.3% of all bacteremic episodes. Overall mortality was statistically greater ($p<0.05$) among patients with monomicrobial episodes (50 of 154, 32.4%) compared with patients with PMB (1 of 14, 7.2%). However, no significant differences were shown in mean age, sex or underlying conditions between both groups.

**Table 1.** Incidence and sources of 168 episodes of bacteremia

| Source | Total Incidence[a] | Polymicrobial[b] | Monomicrobial[b] |
|---|---|---|---|
| Catheter-related | 2.7 | 6 (42.8) | 39 (25.3) |
| Intra-abdominal | 0.9 | 3 (21.4) | 12 (7.7) |
| Lower respiratory tract | 1.2 | 1 (7.1) | 19 (12.3) |
| Urinary tract | 0.4 | 1 (7.1) | 7 (4.5) |
| Other | 2.4 | 2 (14.2) | 39 (25.3) |
| Unknown | 2.3 | 1 (7.1) | 38 (24.6) |
| Total | 10.1 | 14 (100) | 154 (100) |

[a] Episodes/100 discharges.
[b] Number of episodes. Percentages are shown between parentheses

**Table 2.** Clinical characteristics of 168 bacteremic episodes

| Characteristic | Polymicrobial[a] ($n=14$) | Monomicrobial[a] ($n=154$) | P value |
|---|---|---|---|
| Male gender | 8 (57.1) | 101 (65.5) | NS |
| Age in yr. | 46.0±9.6 | 62.1±10.1 | NS |
| Hospital acquisition | 11 (78.5) | 100 (64.9) | NS |
| *Underlying disorders* | | | |
| Prior surgery | 10 (71.4) | 95 (61.6) | NS |
| Mechanical ventilation[b] | 7 (50.0) | 92 (59.7) | NS |
| Coma | 5 (35.7) | 39 (25.3) | NS |
| Shock | 5 (35.7) | 31 (20.1) | NS |
| Hemodialysis | 2 (14.2) | 29 (18.8) | NS |
| Trauma | 4 (28.5) | 24 (15.8) | NS |
| Neoplasia | 0 (0) | 21 (13.6) | NS |
| Cytotoxic drug use | 0 (0) | 21 (13.6) | NS |
| Diabetes | 0 (0) | 13 (8.4) | NS |
| Leukopenia | 0 (0) | 11 (7.1) | NS |
| Mortality | 1 (7.2) | 50 (32.4) | <0.05 |

[a] Values shown Mean±SD or number of episodes. Percentages are shown between parentheses
[b] Longer than 48 h

Sources and pathogens isolated for the 14 episodes of PMB diagnosed in our study are listed in Table 3. A total of 30 organisms were cultured, with 12 cases having 2 isolates and two culturing three organisms. Aerobic Gram-negative bacilli represents 18 (60%) of isolates, with 11 patients growing at least one Gram-negative aerobe in blood culture. Gram-positive rods and anaerobic bacteria were isolated in 9 and 3 cases, respectively. Intravascular catheters were the most common identificable source, involved in six (42.8%) cases (Table 3), as determined by semiquantitative catheter tip cultures of 15 or more colonies. No episode was associated with peripheral catheters. The second most frequent source identified was intra-abdominal, responsible for 3 episodes (2 cholangitis and 1 abscess). Other identificable sources included urinary tract, sinusitis, pneumonia and wound infection (Table 3). In one case, despite work-up for a primary focus the source was undetermined.

**Table 3.** Sources and pathogens for 14 episodes of polymicrobial bacteremia in critically ill patients

| Case | Source | Microorganisms |
|---|---|---|
| 1 | Catheter | *E. aerogenes, E. cloacae* |
| 2 | Catheter | *E. aerogenes, P. aeruginosa* |
| 3 | Catheter | *K. pneumoniae, P. aeruginosa* |
| 4 | Catheter | *K. pneumoniae, E. coli* |
| 5 | Catheter | *E. coli, P. mirabilis* |
| 6 | Catheter | *P. aeruginosa*, Coagulase-negative *staphylococcus* |
| 7 | Cholangitis | *K. oxytoca, E. faecalis* |
| 8 | Cholangitis | *C. freundii, S. marcescens* |
| 9 | Intra-abdominal abscess | *C. freundii, Lactobacillus sp* |
| 10 | Wound infection | *S. aureus, C. perfringens, Streptococcus* viridans group |
| 11 | Urinary tract | *S. aureus, E. faecalis* |
| 12 | Sinusitis | *S. anginosus, B. intermedius, P. anaerobius* |
| 13 | Pneumonia | *P. aeruginosa, S. marcescens* |
| 14 | Unknown | *E. faecalis, P. maltophilia* |

## Discussion

Although PMB has been described in several previous series, there has been no recent study involving critically ill patients. The mean age of our population (46 years) was lower than the mean age reported in previous studies [6–9]. The majority of patients in our series were male, which reflects the demographics of our ICU, and they developed infection in the post-operative period; there is no evidence in the literature for a male or female predisposition to PMB.

Analysis of our patients corroborated what has been previously reported concerning nosocomial versus community-acquired infections [8–10]. Of the PMB bacteremias 78% were of nosocomial origin. In contrast to observations in previous series [1, 2, 6–14], none of our patients had malignancies or a well-recognized cause for major immunodepression. However, the majority of patients admitted to our ICU have intravascular catheters and underwent some invasive diagnostic and therapeutic procedures which predispose them to nosocomial infection.

Intra-abdominal, genito-urinary, and skin soft-tissue were the most common sources in the literature [1, 2, 8]. Strikingly, intravascular catheters were the most common source of infection in our series, representing 42.8% of episodes. Multiple organisms isolated from the blood were not unexpected, based on previous reports of catheter-related bacteremia [15–19]. Nevertheless, previous series that report sources of infection attributed this origin in only 5 to 10% of patients. Differences in study population, since central vein catheters are generally placed in more ill patients, could explain this observation in part. Furthermore, improving techniques for laboratory diagnosis of catheter-related bacteremia [19–22] in recent years and systematic withdrawal of catheters in febrile patients at our institution may be a complementary explanation. In fact, only 7.1% of our patients had no recognizable source of infection, a lower percentage than in previous series [1, 2, 8], and some authors recognize that central line infections probably represent a significant part of this group [1, 2]. Intra-abdominal infection caused PMB in 3 patients (two cholangitis and one intra-abdominal abscess) and was the second single source in the present series; the polymicrobial nature of biliary tract infections has been well documented, and up to 60% of bacteremia in these patients has been reported to be polymicrobial [23–25]. The remaining sources of PMB in our study have been previously reported [1, 2] and, although less usual, they should be considered as possible causes of infection.

Eleven patients had at least one facultative Gram-negative bacillus isolated from blood cultures and two Gram-negative bacilli was the most common combination. With the exception of a series by Kiani et al. [7] in which a high percentage of patients had burn infections, facultative Gram-negative are the predominant organisms. Our data agree with this observation.

Mortality has continued to remain high for PMB over the past [1, 6, 8]. Our experience has not supported this conclusion. With the exception of the series by Monif et al. [10], who do not report mortality in a review of 13 patients with PMB in an obstetric-gynecologic service, reports of general populations range from 21% to 54% [1, 7, 9, 13]. Ing et al. [6] studying 27 patients with PMB on a surgical ICU, between 1977 and 1978, reported a mortality rate of 48%. Predominance of sources associated with a lower risk of death, availability of newer antibiotics and development of techniques to provide better intensive care management may explain this improvement in prognosis.

When characteristics of PMB were compared with a cohort of 154 episodes of monomicrobial bacteremia, overall mortality was significantly lower for episodes of PMB; the high percentage of patients with catheter-related bacteremia in the group of PMB could explain in part this finding. However, no significant differences were shown in age, sex or underlying conditions, suggesting that factors associated with PMB in our ICU does not differ in respect to factors associated with monomicrobial episodes.

In summary, PMB remains an important entity in critically ill patients, but the epidemiological characteristics are different to other populations. Current mortality rate was lower than has previously been described and prognosis is not worse than for bacteremia due to a single organism. Since intravascular catheters were the most important source, it seems mandatory to remove these devices when a patient develops a PMB. Moreover, we suggest a strict policy of catheter placement and maintenance as a method to reduce its incidence.

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