



## **Bacteremia in a Multilevel Geriatric Hospital, Second Look 5 Years Later**

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### **Authors' contributions**

*This work was carried out in collaboration between all authors. Authors LE and LA designed the study, wrote the protocol, and wrote the first draft of the manuscript. Author KR made all records from charts of patients. Author DM, NRK and SR managed the analyses of the study and managed the literature searches. All authors read and approved the final manuscript.*

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### **ABSTRACT**

**Aims:** In a previous study (2004) we explored the clinical and microbiological aspects of bloodstream infections (BSI) in a multilevel geriatric hospital, and concluded that follow up and monitoring of these parameters is warranted.

The purpose of this new study is to evaluate the current BSI status and compare these data to those obtained previously.

**Study Design and Methodology:** We implemented the methodology developed for the initial study. Clinical features, microbiological characteristics and outcome of BSI over the year 2009 were investigated.

**Results:** The rate of positive blood cultures was similar (10% versus 12%). The rate of BSI was 1.35 per 1000 patients in 2004 and 1.7 per 1000 in 2009. The mortality rate at 2 weeks decreased significantly (from 42% to 22.5%,  $p=0.001$ ). The most common isolate was *Escherichia coli* in both studies, followed by *Proteus mirabilis*. Interestingly, antibiotic susceptibility of common pathogens between 2004 and 2009 remained unchanged in 40% while increasing in 32% of cases.

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**Conclusion:** This second look at BSI and revision of BSI parameters provides updated information that may be beneficial for further follow up and antibiotic stewardship program.

*Keywords: Bacteremia; multilevel geriatric hospital; long term care; blood stream infection.*

## 1. INTRODUCTION

The term bacteremia is defined as one or more positive blood-cultures (excluding contamination) in the presence of signs and symptoms of systemic infection [1].

Despite the availability of potent antimicrobial therapy and advances in supportive measures, BSI remains a major cause of morbidity and mortality. In the United States, septicemia was associated with the greatest increase in death rate throughout the years 1950-1997 compared with other causes and was among the 15 leading causes of death over that period [2].

Bacteremia is particularly devastating in the elderly population with hospitalization rates due to BSI in the US elderly population increasing more than 2-fold in 1986-1997 [3]. Contributing factors to the increased susceptibility of the elderly to infections include: senescence of both humoral and cell-mediated immune systems and an increased incidence of underlying illnesses [4]. All infections, bacteremia is the most threatening to the elderly patient and continues to carry a high rate of mortality [5].

The clinical presentation of bacteremia in the elderly patient may differ markedly from that in younger individuals. Localizing symptoms may be absent even when the etiologic cause of the bacteremia has been clearly established and the signs and symptoms are often atypical, blunted or non-specific. Signs and symptoms may consist solely of altered mental status, general deterioration, weakness and falls [6]. Accordingly, without sufficient vigilance and surveillance, BSIs may be overlooked or diagnosed too late. In addition to changes associated with aging, residents of long term care (LTC) facilities are at additional risk for the development of BSI [7]. Presence of indwelling catheters increase the risk of bacteremia 39-fold [8], a point of significance, given that urinary tract infections (UTIs) are the most frequent cause of septicemia in the geriatric population [9]. Complications such as pressure ulcers and colonization with gram-negative bacilli, combined with escalating antibiotic resistance, increase the probability of developing serious BSIs [10]. Bacteremia in the elderly remains a diagnostic and therapeutic challenge to the clinician.

Only a few studies on bacteremia in elderly have been published referring to general hospitals and long term care settings [11-13]. However, long term care is attributed to diverse types of facilities that care for elderly in various conditions: from nursing to skilled nursing and from acute to intermediate care. Many such facilities lack onsite resources for prompt diagnoses of infectious such as blood cultures [14]. Other than our previous study [13] we have found only two studies published in the last two years, referring to BSIs in multilevel geriatric hospitals, comprising acute, intermediate and LTC wards [15,16]. The need for more knowledge in this field and question of to screening for blood stream infections have been repeatedly debated [14,17,18]. In our previous study [13] we identified patients at risk for BSI based on accompanying signs (fever, dyspnea and clinical deterioration) and source of infection (UTIs, decubitus ulcers and respiratory tract infections)

and demonstrated that practitioners can use atypical signs or symptoms of sepsis, to consider obtaining blood cultures as part of the BSI workup in LTC patients.

The present study was carried out in 2009, 5 years after the previous one, to evaluate and compare the clinical data on bacteremia in our multilevel geriatric hospital. We focused on the rate of positive blood cultures, the mortality rate, the frequency of the most common isolated bacteria and their antibiotic susceptibility. The fact that this study was performed in the same hospital and with the same methodology as in the previous facilitates comparisons of these data and evaluation of emerging trends along these 5 years.

## 2. MATERIALS AND METHODS

**Setting:** The study was performed in a university affiliated 400-bed multilevel geriatric hospital with onsite full laboratory and radiographic imaging capabilities. Patients are admitted from the community, nursing-homes and general hospitals into acute, rehabilitation, intermediate or long-term care wards.

**Design and study population:** Data were collected retrospectively from bacteriology laboratory records from 2009. Charts of cases with positive blood cultures were identified and examined for demographic and clinical data. Patients were stratified by: age, source of infection, type of ward at which the patient was hospitalized when the infection occurred, underlying condition and appropriateness of empiric antibiotic therapy. The information retrieved from patients' files was recorded on data worksheets and then transferred to a database software program for statistical analysis. Comparisons with the data of our previous study [13] were performed. The study was approved by the local ethical committee.

**Blood cultures:** The hospital's standard practice is to draw aseptically from peripheral vein at least 20 ml of blood. Equal portions of the blood samples were inoculated into the sets of blood culture (aerobic and anaerobic). Bottles were incubated in the BacT/Alert system (bioMerieux, Inc, Durham, North Carolina) until flagged positive or for 7 days. A sample from a positive bottle was Gram stained and sub cultured. Isolates were identified using standard techniques. Susceptibility testing of isolates was performed by the Kirby-Bauer method according to guidelines established by the US National Committee on Clinical and Laboratory Standards.

**Definitions:** BSI was defined as at least one positive blood-culture from a patient. This applied to all pathogens except for common skin contaminants (such as coagulase-negative *Staphylococci*, *Bacillus spp.*, Diphtheroids, *Corynebacterium spp.*, *Propionibacterium spp.* In these instances, 2 or more positive blood-cultures drawn at different times and sites or alternatively, a single positive blood-culture accompanied by the isolation of the same organism from a normally sterile site were required for diagnosis of bacteremia. The outcome of the BSI episodes in terms of survival was defined as rapidly fatal (patients died within 3 days) or ultimately fatal (died within 2 weeks).

**Statistical analysis:** The clinical and laboratory data were coded and analyzed using SPSS software (SPSS 14.0, SPSS Inc, Chicago,IL). Univariate analysis, the chi-square with Yates correction as appropriate was used to determine significant associations. Fisher's exact test of probability for small number analysis was used when expected frequencies were fewer than 5 cases. The determination of significant differences between means was performed by way of Student's *t* test. A two tailed p-value less than .05 was considered significant.

### 3. RESULTS AND DISCUSSION

During the year of the study 2009, 1646 blood cultures were performed; 197 blood cultures (12%) were positive in 169 patients. Demographic and relevant clinical data of the patients are presented in Table 1. Seventy one patients (42%) had pressure wound grades greater than 3 and the rate of case fatality was 30%.

**Table 1. Demographic and clinical data of hospitalized patients with positive blood cultures**

No. of patients	169
No. of positive blood cultures	197
Average age (years)	82.4±9.1
Male/female (numbers)	71/98
Medical Conditions	N (%)
Diabetes mellitus	110 (65.1)
Anemia	103 (60.9)
Hypoalbuminemia	102 (60.4)
Dementia	98 (58)
Sepsis per history	86 (50.9)
Hypertension	84(49.7)
Indwelling urinary catheter	75 (44.4)
Decubitus ulcer	71 (42)
Chronic renal failure	53 (31.4)
Cerebro-vascular accident	42 (24.9)
Feeding naso-gastric tube	35 (20.7)
Hypothyroidism	35 (20.7)
Ischemic heart disease	32(19)
Acute renal failure	31 (18.3)
Parkinson's disease	29 (17.2)
Congestive heart failure	26 (15.4)
Recurrent urinary tract infection	25 (14.8)
Laboratory data	mean±SD
Hemoglobin g/dl	10.8±1.9
White blood cells 10 <sup>3</sup> /mm <sup>3</sup>	11.3±1.97
Platelets 10 <sup>3</sup> /mm <sup>3</sup>	279±142
Urea mg/dl	72±54
Creatinine mg/dl	1.29±0.82
Albumin mg/dl	2.97±0.56

The isolated microorganisms and mortality rates are presented in Table 2. The case - fatality rate at two weeks was 22.5% with 16 (42%) of all deaths occurring in the first 3 days of the septic event (rapidly fatal period). *E. coli* detected in 32% of cases was the most common isolated pathogen, with a mortality rate of 9.5% amongst *E. coli* BSI cases, (13% of the overall mortality). Antibiotic susceptibility to *E. coli* was most prevalently observed for ertapenem (100%), amikacin (93%) and piperacillin-tazobactam (91%). The second most common isolate was *P. mirabilis* (17.8%) with mortality rate of 30% amongst *P. mirabilis* BSI cases (23.6% of all mortality). Highest susceptibility was observed to piperacillin-tazobactam (87%), amikacin (83%), ertapenem (73%). Bacteremia caused by *P. mirabilis* was significantly more prevalent in patients with pressure ulcers (29% versus 11% in those

without,  $P < 0.002$ ). The third microorganism was *Klebsiella pneumonia* (13%), with a mortality rate of 23%, which accounted for 13% overall mortality. *Proteus* was observed to be sensitive to amikacin (82%), piperacillin-tazobactam and ertapenem (68% each) and gentamicin (50%). Although less common, bacteremia caused by *Staphylococcus aureus* (10%) was associated with the highest death rate (35%), accounting for 15.7% of all mortality (Table 2). In each case of suspected septicemia a blood sample for culture was drawn and empirical antibiotic treatment was initiated immediately thereafter.

**Table 2. Bacteria isolated in BSI event (197isolates) and mortality (169 patients)**

Microorganism	N (%)	Fatal (1- 3 days) N (%) **	Fatal (4-14 days) N (%) **	Overall mortality N (%) ***
<i>Escherichia coli</i>	54 (32)	2 (4)	3 (5.5)	5 (13)
<i>Proteus mirabilis</i>	30(17.8)	4 (13)	5 (17)	9 (23.6)
<i>Klebsiella spp.</i>	22 (13)	2 (9)	3 (14)	5 (13)
<i>Enterococcus</i>	20 (11.8)	4 (20)	0	4 (10.5)
<i>Staphylococcus aureus</i>	17 (10.1)	0	6 (35)	6 (15.7)
MRSA*	10 (5.9)	1 (10)	0	1(2.6)
<i>Acinetobacter spp.</i>	9 (5.3)	1 (11)	1 (11)	2 (5.2)
<i>Streptococcus spp</i>	8 (4.7)	0	1 (12.5)	1 (2.6)
<i>Pseudomonas aeruginosa</i>	5 (3)	1 (20)	1 (20)	2 (5.2)
<i>Bacteroides</i>	4 (2.4)	1 (25)	1 (25)	
<i>Clostridium</i>	4 (2.4)	0	1 (25)	1 (2.6)

\*MRSA: methicillin resistant *Staphylococcus aureus*

\*\*percent calculated for each pathogen

\*\*\*percent from overall mortality (38 patients)

Particular interest was the appropriateness of the choice of drug for empiric antibiotic treatment and the death rate. In 71 (42%) of the 169 patients with positive blood culture empiric choice of treatment matched the antibiogram results, while in 98 (58%) cases did not. We calculated the death rate in the former group to be 15.3% as opposed to 32.4% in patients where choice of antibiotic was found to be inappropriate ( $p=0.009$ ).

The prevalence of positive blood cultures was similar in the acute geriatric (40%) and in the skilled nursing departments (53%) and only 7% in the rehabilitation ward. The clinical sign triggering for blood cultures were fever in 100% of patients. The presumed sources of bacteremia are shown in Table 3: urinary tract infection was the leading cause at 44%, followed by pressure ulcers (23%) and respiratory tract infections (18%).

**Table 3. Presumed source of infection in patients (N 169)**

Source of infection	N(%)
Urinary tract	74(43.8)
Decubitus ulcer	38 (22.4)
Respiratory tract	30(17.8)
Other	27(16)

The isolated microorganisms with their sensitivities to various antibiotic preparations in 2009 and 2004 are presented in Table 4. In 40% of cases there was no difference, in 32% cases susceptibility increased and in 28% it decreased.

**Table 4. Microorganisms' susceptibility to antibacterial drugs. Comparison of 2004 vs. 2009 (%)**

	<i>Escherichia coli</i>		<i>Proteus</i>		<i>Klebsiella</i>		<i>Enterococcus</i>		<i>Staphylococcus</i>		<i>MRSA</i>		<i>Acinetobacter</i>		<i>Streptococcus</i>		<i>Pseudomonas</i>		
	2004	2009	2004	2009	2004	2009	2004	2009	2004	2009	2004	2009	2004	2009	2004	2009	2004	2009	
Tetracycline	.																		12.5
Chloramphenicol	59	89	19	27	20	41					0.5				23				12.5
Amoxicillin	11	11		3				45			0.5				82				62.5
Amoxicillin/clavulanate	40	45	44	30	17	27		10	36	35	1				96				62.5
Cloxacillin sodium								75											
Vancomycin					8				82	100	95	90			91				
Rifampin	3								79	100	87	90							
Clindamycin									54	35	50	60							
Erythromycin										6									37.5
Trimethoprim sulfamethoxazole	42	37	19	17	43	36		20	29	88	53	100		11	46				50
Gentamycin	58	81	30	30	29	50		20						11	1				50
Tobramycin		4																	
Amikacin	83	93	95	83	80	82		10	18					22					80
Cefzolin	22	17	14	13	14	14			28	29					46				12.5
Cefuroxime	40	52	35	30	23	23									68				50
Ceftriaxone	56	52	46	37	34	27								11	59				75
Ceftazidime		2		10		5													
Fucidin										82		100							
Polymicin-B sulfate		2				18									78				80
Ciprofloxacin	40	44	25	27	25	23				12									12.5
Piperacillin-tazobactam	90	91	81	87	60	68		15						55.5	60				62.5
Ertapenem	95	100	77	73	65	68		10											80
Cefoxitin										29									
Oxacillin										12									

Twelve percent of the blood cultures performed during the year of the study grew bacteria representing a rate of 1.7 per 1000 patient days as opposed to 10%, 1.35 per 1000 patient days in our previous study five years ago [13]. A study from an Israeli LTC facility reported 15.8 % positive cultures and a rate of 0.46 isolations per 1000 patient's days over two years [16]. The study from a similar facility in France [15] reports on 224 blood cultures performed with 7% positive isolations, representing 66 episodes of bacteremia and a rate of 0.22 per 1000 patient days. This result is close to that of 0.3 per 1000 patient days reported by a previous study on nursing home patients [11,19]. Although similar analyses have been conducted in other LTC facilities, comparing these results is difficult because of the difference in the structure and the nature of the case mix of patients in each facility. As mentioned earlier the high prevalence of skilled nursing patients, with severe bed sores of grade 3 and over (42%) is characteristic of our hospital and is one plausible cause for the high rate of BSIs. Consequently, bed sores were the second most prevalent presumed portal of entry causing BSIs in our study whereas in several other studies the second most common source was the respiratory tract [19]. As reported in other studies the most prevalent presumed source of BSI in our patient population was the urinary tract.

*E. coli* was the most frequently isolated microorganism in both our studies followed by *P. mirabilis*. Blood stream infections due to *P. mirabilis* is significant with the increasing drug resistance, and its recognition is critical for the clinical management [16,20]. The overall mortality rate at two weeks in our study was 22.5%, significantly lower than the 42% reported in our previous study ( $p=0.001$ ). Despite its rare occurrence, bacteremia caused by *Staphylococcus aureus* was associated with the highest death rate (35%). Five years ago mortality rate was the highest attributed to *Acinetobacter* spp. (55%) and *Proteus mirabilis* (51%). The mortality rate associated with *E. coli* is the lowest in both our studies: in 2004 and 2009 (22% and 9.5% respectively).

The observed 22.5% mortality rate within 2 weeks is comparable with other studies that reported rates of 25% to 35% with mortality evaluated at different points in time from 1 to 4 weeks [15,16]. Worthy of mention is the impressive reduction in mortality rates between this present study and that of 2004. We attribute this finding to improved awareness of the risk of BSI amongst our staff physicians which has led to improved vigilance, prompt performance of blood culture and immediate initiation of empiric antibiotic treatment. These findings therefore demonstrate the importance of appropriate empirical antibiotic treatment as reflected by the difference in mortality: 15.3% vs. 32.4% ( $P=0.009$ ). Similarly, these findings show that precision in empiric antibiotic treatment can be enhanced by continuous monitoring of the local prevalence of pathogenic bacteria and their susceptibility patterns. In light of these findings the observed changes in antibiotic susceptibility along these five years (Table 4) is important. It was unchanged in 40% of cases and even increased in 32% - meaning that only in 28% it decreased. These numbers should also be evaluated in view of the 5 years difference between the two studies since in the last years multilevel geriatric facilities admit increasingly high numbers of complex patients in severe medical condition [21]. It is predicted that a substantial increase in the need for care LTC settings will be seen in the near future thereby amplifying the importance of infection control [17]. It is within this context that data captured from structured infection surveillance programs is essential for creating quality indicators for the management of medical conditions in nursing homes [22].

These considerations together with the concern that LTC facilities could evolve into reservoirs of resistant pathogenic microorganism, create the case for action for infection surveillance [23]. The issue of whether to perform blood cultures in LTC settings has also been questioned, and a consensus has not yet been reached [7,11,19]. With this respect it

should be mentioned that a recent guideline published by the Infectious Diseases Society of America stated that blood cultures may be appropriate for residents in whom bacteremia is highly suspected and who reside in facilities that have adequate diagnostic and therapeutic possibilities [24].

The issue of the appropriate trigger for performing blood cultures has been scarcely mentioned in most studies. The accepted practice in our facility is that blood cultures are performed upon presentation of fever > 38°C with or without chills. However, it is well known that bacteremia and sepsis are not necessarily accompanied by fever and chills. This is especially so in cases with a potential "portal of entry", such as pressure sores of high degree. The most frequent accompanying clinical sign in our study was clinical deterioration. As recently emphasized, conducting research on infections monitoring and reducing antibiotic resistance is essential for long-term care facilities [25].

#### **4. CONCLUSION**

We propose that routine clinical practice in such cases should be managed with high caution with blood cultures performed whenever bacteremia is suspected. We attribute the relatively high rate of BSIs in both our studies accompanied by a significant decrease in mortality, to the successful implementation of this policy. This study therefore complements the analysis performed in 2004 in that it provides evidence of the contribution of this policy for improving clinical care in multilevel geriatric hospitals.

#### **CONSENT**

Not applicable.

#### **ETHICAL APPROVAL**

All authors hereby declare that this study had been performed in accordance with the ethical standards of Declaration of Helsinki.

#### **COMPETING INTERESTS**

All authors have no any financial and personal relationships with other people or organizations that could inappropriately influence (bias) our work.

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