

Bacteraemia in the Elderly

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Abstract

The aims of the study were to describe community-acquired and nosocomial bacteraemia in elderly patients and to determine the factors associated with increased mortality in these patients attending a tertiary hospital in Singapore. A consecutive series of 191 patients aged more than 60 years of age admitted in 1995 was studied-retrospectively. All of them had positive blood culture results obtained from the Department of Pathology and the case notes were reviewed and entered into a standard clinical protocol. They were analysed for age, sex, place of origin, race, sites of infection, clinical parameters and bacteriology. The mean age of the study population was 75 years ($SD = 8.9$ years). Bacteraemia was acquired from the community in 57.5% of patients, 33% was nosocomial in origin and 9.5% acquired it in chronic long term care facilities. The common organisms cultured in community-acquired infections were *Escherichia coli* (26.1%), *Klebsiella* species (25.4%), *Streptococcus* species (11.1%), methicillin sensitive *Staphylococcus aureus* (7.6%) and *Proteus mirabilis* (4.8%). The common organisms cultured in nosocomial infections were *Klebsiella* species (19.8%), *Enterobacter* species (14.6%), *E. coli* (11.8%), *Acinetobacter baumannii* (9.2%), methicillin sensitive *Staphylococcus aureus* (7.9%) and methicillin-resistant *Staphylococcus aureus* (7.9%). Whilst most cases of bacteraemia were single organism cultures, 13.5% were polymicrobial. The common sources of bacteraemia were chest (27.5%), urinary tract (24.5%), skin (12.5%), hepatic (8.8%), gut (4.3%), cardiovascular system (1%) and others (3.6%). In 12.5% of cases, the sources were multiple and in 5.3% of cases, the source could not be identified. Twenty-one per cent of patients with bacteraemia died. The following factors were associated with increased mortality rate: older age (median age of those that died was 78.5 years compared to survivors with a median age of 73 years, $P = 0.01$), patient's place of origin (patients in nursing home at higher risk of death, $P = 0.04$), patient's mobility status (immobile patients at higher risk, $P = 0.00297$), source of bacteraemia-respiratory infection at increased risk of death ($P = 0.00009$) but urinary tract infection had a better survival rate ($P = 0.03935$) and multiple sites of infection (patients with multiple sites of infection had higher risk, $P = 0.00897$). Methicillin-sensitive *Staphylococcus aureus* bacteraemia was associated with a mortality rate of 35.3%, followed by *Klebsiella* species 28.6%, *Pseudomonas aeruginosa* 28.6%, methicillin-resistant *Staphylococcus aureus* 25%, *Proteus mirabilis* 25% and *E. coli* 19.1%. Important clinical parameters which indicated a poor clinical outcome were: high pulse rate, hypotension, increased respiratory rate, low total white cell count, coagulopathy, hypoalbuminaemia and increased creatinine level.

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Introduction

The importance of infectious diseases in the elderly becomes more apparent as life expectancy improves and the proportion of elderly increases. The fact that infections are also more likely to occur over the age of 60 will make it a greater concern in terms of public health. The annual incidence of bacteraemia in some geriatric units is estimated to be about 14%.¹ Many studies have demonstrated that bacteraemia occurring in elderly patients is associated with a mortality rate ranging from 18.3% to 65%.²⁻⁵ The clinical predictors of bacteraemia noted in earlier studies were age, co-morbid diseases, diabetes

mellitus, presence of a rapidly or ultimately fatal disease, temperature of 38.3°C or higher, chills, acute abdomen, bladder catheter removal, rigors, shock, total band count equal or greater than 1500/mm³ and lymphocyte count equal or less than 1000/mm³.^{3,6,7} A retrospective study done to identify factors predictive of bacteraemia in elderly patients found that clinical indicators were unreliable predictors in the elderly.⁸ Another study which compared young and elderly patients with bacteraemia found that the elderly had fewer signs and symptoms.⁹

This report is a retrospective study of 191 consecutive patients aged 60 years and above with positive blood

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culture results seen in 1995 at Tan Tock Seng Hospital, a tertiary hospital in Singapore. The aims of the study were to describe the epidemiology of community-acquired and nosocomial bacteraemia in elderly patients, and to determine the factors associated with increased mortality in these patients.

Patients and Methods

The Diagnostic Bacteriology section of the Department of Pathology kept records of all positive blood cultures. From these records, we identified 212 consecutive patients aged more than 60 years with positive blood cultures results in the year 1995. Bloodstream infection was identified as present when there was consistent clinical setting and was considered significant by the primary treating physician. Cultures that grew *Corynebacterium* and *Bacillus* species were considered to be contaminants. Those that grew coagulase negative *Staphylococcus* species and *Staphylococcus epidermidis* were taken to be significant when there was more than one set of positive blood cultures. Out of 212 consecutive patients, 21 cultures were considered to be contaminated specimens.

Demographic data, source of infection, type of bacteria, clinical parameters, risk factors and underlying disease of these patients were entered into a standard protocol. Patients infected from their own homes and chronic long-term care facilities were considered together as infected from the community. Bacteraemia was classified as community-acquired if microorganisms were cultured from blood drawn within 48 hours of hospital admission.³ Nosocomial bacteraemia was defined as an infection acquired more than 48 hours after hospital admission for which the blood culture drawn grew microorganisms.³ When the blood culture drawn grew more than one type of organism, polymicrobial bacteraemia was considered to be present.³ The cause of death was recorded from the case records. The source of infection was recorded based on clinical evidence of infection and/or culture of same organism from the primary site and/or positive radiological evidence of infection. No attempt was made to differentiate between upper and lower urinary tract infection.

Statistical analysis was done using the Chi-square method to test for associations for categorical data and the Mann-Whitney U test for continuous data.

Results

Demographic

The median age of the patients was 75 years with a range of 60 to 97 years. There were 105 male (55%) and 86 female (45%) patients. The percentage of patients from surgical discipline was 35.6% and from medical discipline was 64.4%. Concurrent medical problems were common: 59 had diabetes mellitus, 38 had cardio-

vascular diseases, 36 had malignancy, 30 had strokes and 10 had dementia. The sources of admission were as follows: 87.4% were from their own homes in the community, 9.4% from chronic long term care facilities and 3.2% from other hospitals (Table I).

Bacteriology

Bacteraemia was acquired from the community in 57.5% of patients, 33% was nosocomial in origin and 9.5% acquired it in chronic long-term care facilities. A total of 221 isolates of bacteria were cultured from 191 patients. The common organisms cultured in community-acquired infections were *Escherichia coli* (26.1%), *Klebsiella* species (25.4%), *Streptococcus* species (11.1%), methicillin-sensitive *Staphylococcus aureus* (7.6%) and *Proteus mirabilis* (4.8%). The common organisms cultured in nosocomial infections were *Klebsiella* species (19.8%), *Enterobacter* species (14.6%), *E. coli* (11.8%), *Acinetobacter baumannii* (9.2%), methicillin-sensitive *Staphylococcus aureus* (7.9%) and methicillin-resistant *Staphylococcus aureus* (7.9%). Polymicrobial bacteraemia was noted in 13.5% of the cases and the rest was single organism culture (Table II). The three most frequent combination of organisms isolated were *Klebsiella* species and *E. coli* (6 patients), *Enterobacter* and *E. coli* (3 patients), and *Proteus mirabilis* and *E. coli* (2 patients).

Sources of Bacteraemia

The most common source of bacteraemia was the respiratory system (27.5%) followed by the urinary tract (24.5%), cutaneous system (12.5%), hepatobiliary tract (8.8%), gastrointestinal tract (4.3%), cardiovascular system (1%) and others (3.6%). In 12.5% of cases, the source was multiple and in 5.3% of cases, the source could not be identified. For those with more than one source of bacteraemia, the three commonest combinations were respiratory and urinary tract (7 patients), respiratory and cutaneous system (6 patients) and respiratory and hepatobiliary system (5 patients). In community-acquired bacteraemia arising from urinary tract infections, the common organisms were *E. coli* (40.5%), *Kleb-*

TABLE I: PATIENT'S CHARACTERISTICS

Age (years)	Males	Females
60 - 64	24 (80%)	6 (20%)
65 - 69	17 (54.2%)	14 (45.8%)
70 - 74	20 (60.6%)	13 (39.4%)
75 - 79	17 (50%)	17 (50%)
80 and above	27 (42.2%)	36 (57.8%)
Total	105	86
Sources of admission		
Community	87.4%	
Nursing home	9.4%	
Other hospital	3.2%	

TABLE II: MICROBIOLOGY OF BLOOD CULTURES

Organism	Community-acquired (%)	Nosocomial (%)
Gram-negative		
<i>Escherichia coli</i>	26.1	11.8
<i>Klebsiella</i> species	25.4	19.8
<i>Proteus mirabilis</i>	4.8	1.3
<i>Acinetobacter baumannii</i>	3.4	9.2
<i>Enterobacter</i> species	2.8	14.6
<i>Pseudomonas aeruginosa</i>	2.1	5.3
<i>Citrobacter</i> species	1.4	0
<i>Serratia</i> species	0.7	1.3
<i>Haemophilus influenza</i>	0.7	1.3
<i>Edwardsiella tarda</i>	0.7	0
<i>Pasteurella</i> species	0.7	0
<i>Providencia</i> species	0.7	0
<i>Salmonella</i> species	0.7	0
<i>N. meningitidis</i>	0	1.3
<i>Pseudomonas cepacia</i>	0	1.3
Gram-positive		
Methicillin-sensitive <i>S. aureus</i>	7.6	7.9
Beta-haemolytic <i>Streptococci</i>	5.2	1.3
Coagulase negative <i>Staphylococcus</i>	4.1	7.9
<i>Streptococcus pneumoniae</i>	3.7	0
Alpha-haemolytic <i>Streptococci</i>	2.2	0
<i>Enterococcus faecalis</i>	2.1	3.9
Methicillin-resistant <i>S. aureus</i>	1.4	7.9
<i>Enterococcus faecium</i>	0.7	3.9
<i>C. jeikeium</i>	0.7	0
<i>Gamella morbillorum</i>	0.7	0
Anaerobes		
<i>Bacteroides fragilis</i>	0.7	0
<i>Clostridium</i> (not <i>difficile</i>)	0.7	0

siella species (31%) and *Proteus mirabilis* (7.1%). In community-acquired bacteraemia arising from respiratory infections, the three common organisms were *Klebsiella* species (26.7%), *E. coli* (24.4%) and *Streptococcus* species (17.8%) which consisted of equal isolates of *Streptococcus pneumoniae* and Beta-haemolytic *Streptococci*. For hepatobiliary infections, the two common organisms were *E. coli* (52.4%) and *Klebsiella* species (28.6%). In nosocomial bacteraemia arising from urinary tract infections, the commonest organisms were *Klebsiella* species (35.3%), *E. coli* (11.8%), *Pseudomonas aeruginosa* (11.8%), *Acinetobacter* species (11.8%) and *Enterobacter* species (11.8%). In nosocomial bacteraemia arising from respiratory infections, *Klebsiella* species (25%) was the commonest microorganism cultured followed by methicillin-sensitive *Staphylococcus aureus* (10.7%), methicillin-resistant *Staphylococcus aureus* (7.1%) and *Acinetobacter* species (7.1%).

Mortality

The overall in-patient mortality rate of the patients was 21.2%. The mortality rate for patients from nursing homes was 38.9% and this was statistically significant

when compared to patients from their own homes 18.6% ($X^2 = 4.11$, $df = 1$, $P = 0.043$). Nosocomial bacteraemia had a mortality of 23.1% and this was not significant when compared to 20.3% seen in community-acquired bacteraemia. The presence of co-morbidity was not found to be associated with mortality in this study.

The factors that were associated with increased mortality were:

- 1) the age of the patients (the median age of those that died was 78.5 years compared to survivors with a median age of 73 years, Mann-Whitney $U = 2185.5$, $P = 0.0111$),
- 2) the mobility status of the patients (14.75% of mobile patients died compared to 33.3% of immobile patients, $X^2 = 8.83$, $P = 0.00297$),
- 3) multiple sites of infection (18.3% of patients with single sites of infection died compared with 41.7% of patients with multiple sites of infection, $X^2 = 6.829$, $P = 0.00897$),
- 4) the source of the bacteraemia:
 - (i) 36.1% with respiratory infections died compared with 12.1% with non-respiratory infections, ($X^2 = 15.33$, $P = 0.00009$).
 - (ii) 12.1% with urinary tract infections died compared with 25.4% with non-urinary tract infections, ($X^2 = 4.24$, $P = 0.03935$).

The clinical parameters associated with increased mortality were (Table III):

- 1) high pulse rate-greater than 100 beats/min,
- 2) hypotension-systolic blood pressure less than 100 mmHg,
- 3) high respiratory rate-respiratory rate of more than 15 breaths/min,
- 4) low total white cell count (less than $4000/\text{mm}^3$),
- 5) coagulopathy-partial thrombin time greater than 40 seconds,
- 6) hypoalbuminaemia-serum albumin level less than 35 g/l,
- 7) high creatinine level-creatinine level greater than 200 mmol/l.

Overall, taking into account all sources of infection, methicillin-sensitive *Staphylococcus aureus* bacteraemia had the highest mortality rate of 35.3%, followed by *Klebsiella* species 28.6%, *Pseudomonas aeruginosa* 28.6%, methicillin-resistant *Staphylococcus aureus* 25%, *E. coli* 19.1% and *Streptococcus* species 18.8% mortality rates. However, when only respiratory infections giving rise to bacteraemia were analysed, *Klebsiella* and *Streptococcal* bacteraemias were associated with 64.7% and 60% mortality rates, respectively.

Other clinical parameters such as high temperature, hyponatremia and thrombocytopenia were not associated with increased mortality but subthermic, hyponatremic and thrombocytopenic patients have 50%,

TABLE III: CLINICAL PARAMETERS

Pulse rate (beats/min)	Percentage Mortality (%)
100 or less	17.5
More than 100	31
$(X^2 = 4.3, df = 1, P = 0.038)$	
Systolic blood pressure	Percentage Mortality (%)
70 to 99 mmHg	56
100 to 119 mmHg	20.5
120 to 139 mmHg	21.3
140 mmHg and higher	17.1
$(X^2 = 11.71, df = 3, P = 0.0084)$	
Respiratory rate (breaths/min)	Percentage Mortality (%)
15 and less	6.3
16 to 25	22.6
26 and more	37.5
$(X^2 = 6.37, df = 2, P = 0.041)$	
Total white cell count	Percentage Mortality (%)
Less than 4000	66.7
4000 to 11 000	22.2
Greater than 11 000	16.4
$(X^2 = 16.18, df = 2, P = 0.003)$	
Partial thrombin time (seconds)	Percentage Mortality (%)
More than 40	60
Less than 40	17.5
$(X^2 = 12.43, df = 1, P = 0.0004)$	
Serum albumin (g/l)	Percentage Mortality (%)
Less than 35	29.4
Greater than 35	12.2
$(X^2 = 4.86, df = 1, P = 0.028)$	
Serum creatinine level (mmol/l)	Percentage Mortality (%)
Less than 200	40.7
Greater than 200	18.9
$(X^2 = 6.25, df = 1, P = 0.0124)$	
Temperature (°C)	Percentage Mortality (%)
Less than 37	50
37 to 38	25
38 to 39	19.2
Greater than 39	20.3
$(X^2 = 2.44, df = 3, P = 0.486)$	
Serum sodium level (mmol/l)	Percentage Mortality (%)
125 and below	40
126 to 134	21.9
135 and above	16.7
$(X^2 = 3.11, df = 2, P = 0.211)$	
Platelet count (per ml)	Percentage Mortality (%)
Less than 150000	28.6
Greater than 150000	18.7
$(X^2 = 2.23, df = 1, P = 0.135)$	

40% and 28.6% mortality rates, respectively (Table III). However, this was not statistically significant.

Discussion

Our study revealed that the overall mortality of bacteraemia in elderly patients from a tertiary hospital in Singapore was 21.2% which is comparable to the mortal-

ity rates reported in previous studies.³⁻⁶ We found that older patients, those from nursing homes, with poor mobility status, with multiple sites of infection and a respiratory source of bacteraemia were associated with increased mortality rates. Important clinical parameters which indicated a poor clinical outcome were: high pulse rate, hypotension, increased respiratory rate, low total white cell count, coagulopathy, hypoalbuminaemia and increased creatinine level.

Comparative studies between the young and the elderly have shown that bacteraemic episodes increased sharply with increasing age. It had been suggested that age might be an independent risk factor for acquiring bacteraemia.¹⁰ In our series, 50% of the patients with bacteraemia were 75 years and older, and 34% were greater than 80 years of age. We found that mortality from bacteraemia was strongly associated with increased age. This was similar to previous reports linking advanced age with increased mortality.^{11,12} However, a study found that to be true only in a certain subgroup of patients such as those with ultimately fatal/non fatal illness.¹⁰

The mortality rate of patients with bacteraemia originating from nursing homes was twice that from their own homes (38.9% compared with 18.6%). The functional status was an important confounding factor because the nursing home patients had a higher proportion with immobility, that is, 83% compared to 28% of patients with immobility coming from their own homes. Nursing home patients had been showed in earlier work to be associated with increased mortality from bacteraemia^{13,14} and those with higher dependence in activities of daily living have a greater risk of dying from respiratory infection.¹⁵

Most of our patients had community-acquired infections. The chest was the commonest source of infection followed by the urinary tract. The majority of nosocomial infections were from the surgical disciplines (56%). The incidence of nosocomial bacteraemia in this study was about 33% reflecting the level of care provided by the hospital. The incidences of nosocomial infection in the elderly varied from 16% in a chronic long-term hospital, 18.5% in an acute assessment and rehabilitation unit, and 53% in an acute hospital.^{11,16,17} The elderly has been shown to have a 2- to 5-fold increased risk of acquiring nosocomial infections.¹⁸ Some of the risk factors associated with acquiring nosocomial infections were poor performance status and duration of hospital stay.^{17,19}

Abnormal mental state and low activity of daily living scores have been shown to be independent predictors of death in patients admitted to hospital.²⁰ Our study also indicated that immobility was strongly associated with increased risk of mortality from bacteraemia. However, we were unable to demonstrate the increased mortality

in those patients with other co-morbid illnesses. This could be the result of the retrospective nature of the study and that the severity of concurrent diseases could not be ascertained accurately from the case records. Likewise, Whitelaw et al,²¹ using McCabe and Jackson's classification of underlying disease into non-fatal, ultimately fatal and rapidly fatal disease were unable to demonstrate the association between underlying diseases and mortality.

Patients with respiratory source for bacteraemia had very poor survival rate and this high mortality rate had also been demonstrated in other studies.¹¹ The common organisms cultured in community-acquired bacteraemia from the chest were *Klebsiella* species and *E. coli*. *E. coli* pneumonia had a higher incidence in the elderly especially those with chronic debilitation where the organism could be isolated from the oropharynx in 50% of the patients.²² Although this is commonly a nosocomial infection, it has also been described in community-acquired infections.²³

Urinary tract infections had the lowest mortality compared to bacteraemia from other sources, a finding similar to that reported by Meyers and Whitelaw.^{11,21} Ackerman and Monroe¹³ showed that 80% of bacteraemic urinary tract infection were caused by gram-negative organism principally *E. coli*. In our study, *E. coli* was the cause in 40.5% of the cases of community-acquired urinary tract infections followed by *Klebsiella* species. Other investigators had reported a higher mortality associated with bacteraemic urinary tract infection in men and those with chronic indwelling catheter.^{13,21}

We found a high mortality rate of 35.3% associated, with *S. aureus* bacteraemia in the elderly. This was also seen in other studies with reported rates between 54% to 67%.^{6,11,21} This high mortality rate underscores the importance of appropriate antimicrobial coverage for this organism and other gram-negative bacilli when treating elderly patients with bacteraemia especially those with multiple medical problems from chronic long-term care facility.

In our series the rate of polymicrobial infection was 13.5%, the common sources of infection were the chest and urinary tract and 64% were nosocomial infection. Cooper et al²⁴ reported the rates of polymicrobial bacteraemia to be between 6% and 13% with an associated mortality of 21% to 54%. They found it to be associated with the elderly, malignancy, neurological disorder, diabetes, peripheral vascular disease, nosocomial infection and the common source of infection was the gastrointestinal tract, urinary tract and skin.

Fever, raised erythrocyte sedimentation rate and clinical indication of source of infection were found to be more common in the bacteraemic elderly than those without bacteraemia, hypothermia and leukopenia, and

altered mental state had a specificity rate of about 80% in diagnosing bacteraemia.' We found that patients with ill general condition, hypothermia and hypotension had a very high mortality rate. These clinical signs reflect the presence of septic shock, a condition associated with high mortality in the elderly."

Significantly lower survival was shown to be associated with a total white count of less than 4 000/mm³, similar to the findings described by other investigators,^{12,21} but whether this reflects overwhelming sepsis or an immunocompromised state needs further investigation.

A low albumin concentration was often noted in non-survivors and this might be an indicator of chronic ill health or an acute phase response to the infection. Liebovici et al¹² found serum albumin to be a strong predictor of early and late mortality from bacteraemia. In a comparative study of nursing home's pneumonia and community-acquired pneumonia, Marrie et al¹⁴ found a significantly lower levels of serum albumin in patients with nursing home acquired pneumonia compared to patients without pneumonia and those with community-acquired pneumonia.

In our study, we found that a high creatinine level and coagulopathy were associated with increased mortality but not with thrombocytopenia and hyponatremia. The latter two parameters had been shown by Sonnenblick et al³ to be significant factors associated with high mortality using univariate analysis. We did not consider the appropriateness of antibiotic treatment in this study but several studies have demonstrated that inappropriate empirical antibiotics in the elderly leads to higher mortality in the short term as well as affecting long term survival.^{11,12}

In conclusion, bacteraemia in the elderly from a tertiary hospital in Singapore is associated with a mortality rate of 21.2%. Patients with advanced age and poor functional status have a grim outcome. Those with chest infection have a poor prognosis. Although, gram-negative organisms accounted for the majority of the bacteraemia, one must always consider the possibility of *S. aureus* infection because it carries a high mortality in the elderly. Thus, timely and appropriate broad-spectrum antibiotics in clinically septic elderly patients would improve survival.

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