

Community - Acquired Bacteremia in Srisaket Hospital a 1-Year Prospective Study

Nimit Lertpattanasuwan¹

Abstract

Over a one - year prospective study of community - acquired bacteremia in Srisaket Hospital revealed 261 patients with bacteremia. The overall incidence and mortality were 6.5/1000 admissions and 39.5 percent, respectively. 152 patients (64.7 percent) with bacteremia were community - acquired infection, of which 89 patients (58.6 percent) were males and 63 patients (44.4 percent) were females. The mean age was 51.9 years (range 15 - 90 years). The statistical difference of mortality in relation to sex or age was not significance. In 148 patients (98 percent) with community - acquired bacteremia a single organism was isolated, most commonly *Escherichia coli* (28.9 percent), *Staphylococcus aureus* (17.1 percent), *Burkholderia pseudomallei* (15.8 percent) and *Klebsiella* species (15.1 percent). Mortality rate directly related to bacteremia was highest in *Burkholderia pseudomallei* infection (4.2 percent) as compared to other organisms but there was no statistical significance. The most common source of infection was the respiratory system (22.4 percent), followed by the urinary system (13.2 percent) and hepatobiliary system (13.2 percent). In nearly 33 percent of cases, the primary site of infection was unknown. Mortality was significantly higher in patients with respiratory tract infection (69.7 percent ; $P < 0.001$). Three obvious clinical variables predicting the mortality included shock ($P < 0.00001$), Glasgow Coma Scale below 9 (15 in totals) ($P < 0.004$) and serum lactate level higher than 6.4 mEq / L ($p < 0.004$). Furthermore, the mortality was not related to the underlying disease or antibiotic treatment.

¹ Department of medicine, Srisaket Hospital, Srisaket, Thailand.

Introduction

Bacteremia remains a serious problem in infectious disease. The incidence and epidemiology of bacteremia have been widely reported in the United States and Europe⁽¹⁻¹⁴⁾ but few data are available from Africa and Asia, especially from Southeast Asia. The incidence and epidemiology of bacteremia from Southeast Asia may be different from those of the western countries. This prospective study was confined only to community-acquired bacteremia. The correlation between pathogenic organism, clinical aspects, laboratory tests and mortality was analyzed.

Materials and Methods

Setting

Sisaket Hospital in northeastern Thailand is a 500-bed general public hospital in a province with the population of 1,400,000. The service delivery are about 40,000 inpatients and 180,000 outpatients visits per year. The study of community-acquired bacteremia was conducted between 15th January 1997 to 28th February 1998. The history of illness, clinical data and laboratory tests of the

patients, age 12 and older, with community-acquired bacteremia were collected and analyzed.

Blood Culture Technique

Three blood cultures were taken in a patient with suspected bacteremia. A total 5 ml. of blood was injected through a clean rubber stopper into a sealed bottle prepared by the hospital laboratory department that contained 45 ml. of brain-heart infusion broth (Difco Laboratories, Detroit). The mixture was 24-hour aerobically incubated at 37 °c before it was smeared on a blood agar plate and the Mcconkey agar plate. (subculture) Then, both agar plates were incubated overnight at 37 °c before the organism was identified by biochemical test and gram stained technique. If there was not any colony growth on either agar plates within 24 hours, the cultured bottles were then reincubated and examined daily for 7 days before the subculture was repeated again. If the subculture again yielded no visible growth, then the cultured bottles were discarded. Additionally, the blood culture was continued for a 14-day period if the

clinical data was strongly suspicious of *Burkholderia pseudomallei* (*B.pseudomallei*) infection.

Definition

Community-Acquired Bacteremia

An episode of bacteremia was considered to be community acquired if the positive blood cultures were obtained within 48-hour of the patient's admission.^(4,9,15,16) If the blood cultures were taken more than 48 hours after hospital admission (i.e. probable hospital-acquired infection) or the organism isolated (usually *Acinetobacter* species or *Staphylococcus epidermidis*), and course suggested the cultured bacterium was a contaminant, then that will be excluded from the study.

Source of Infection

Clinically, the source of bacteremia was defined as known if there was an obvious source evidenced by clinical signs or the same organism was isolated from the blood and the local site of infection.⁽¹²⁾

Clinical Variables

The history of illness, clinical symptoms and signs of all the studied patients were recorded. The laboratory data such as complete blood count, hemoglobin typing (Hb typing), renal function tests, liver function tests, randomised blood sugar, glycosylated hemoglobin (HbA_{1C}), plasma cortisol level, plasma lactate level, plasma electrolytes (Na,K,Cl,HCO₃) and chest X-ray films were analyzed and recorded.

Shock

Shock was defined as a decrease in systolic blood pressure to 90 mmHg or less in a previously normotensive blood pressure.^(1,12,17)

Outcome

Survival was defined as the patient was discharged from hospital or transferred to be treated at the higher level hospital (regional hospital or University hospital). Death was defined when the patient died in the hospital or the patient or relatives denied treatment and the death was expected at home when his clinical prognosis was poor.

Statistical Analysis

All clinical and laboratory parameters were analyzed by the X^2 -test with Yates' correction, Fisher's exact test or Student's t-test.

Results

During the study, blood cultures were taken from 1,899 patients and a positive growth was obtained in 261 cases (13.8 percent). 83 cases (35.3 percent) of

these were considered to be hospital-acquired bacteremia. The remaining 152 patients (64.7 percent) were community-acquired bacteremia. Of these 89 were males (58.6 per cent) and 63 were females (44.4 per cent). Mean age was 51.9 years (range 15-90 years) and the overall mortality was 39.5 percent (60 patients). However, There was no statistical difference of mortality in relation to sex or age group ($p > 0.05$). (Fig. 1 and Fig. 2)

FIG.1 Mortality related to sex

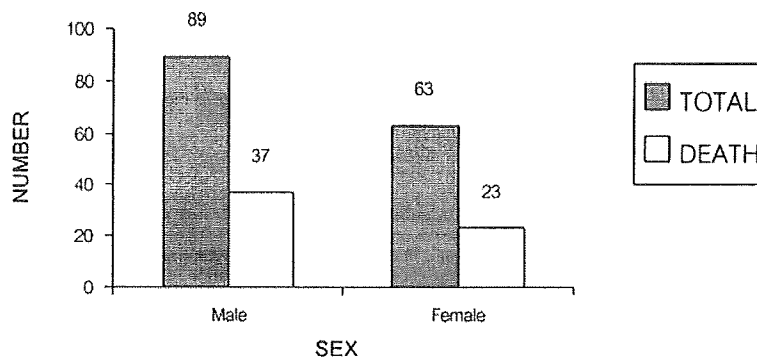
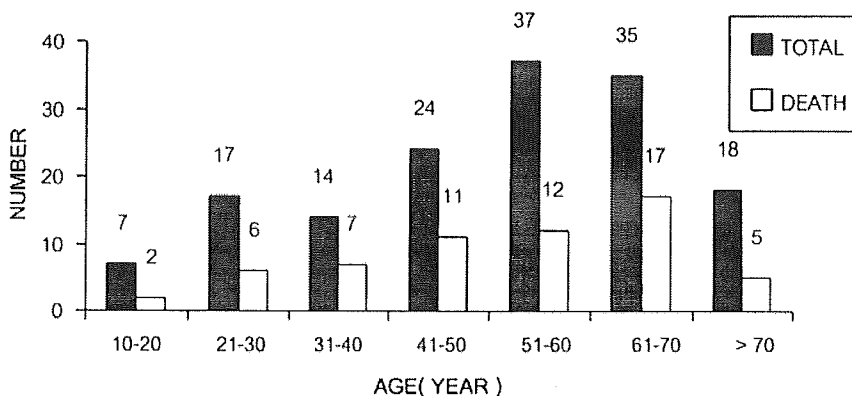


FIG.2 Mortality related to age



Incidence

In the same period, 40,368 patients were admitted into Sisaket Hospital. The overall incidence of bacteremia was 6.5/1000 admissions. The majority of patients were admitted in medical and surgical wards (151 of 152 patients, 99 percent). The remaining one patient was from gynecological ward.

Causative Organisms

The community-acquired bacteremia by type of organism and its relationship to mortality is shown in Table 1. There were 149 patients (98 percent) with bacteremia caused by monomicrobial

organism and 3 patients (2 percent) caused by polymicrobial organisms. Gram-negative bacilli were the most causative organisms (76.3 percent), the remaining 23.7 percent were caused by gram-positive cocci. *Escherichia coli* (*E.coli*) was by far the most common isolate (28.9 percent) followed by *Staphylococcus aureus* (*S.aureus*) 17.1 percent, *B. pseudomallei* 15.8 percent and *Klebsiella* species 15.1 percent. Mortality was observed highest in *B. pseudomallei* infection (54.2 percent) but there was no statistical difference of mortality between gram-negative and gram-positive organisms infection. (Table 1)

Table 1. Mortality related to pathogenic organisms.

	No.(%)	Death.(%)
Gram negative bacilli		
E.coli	44(28.9)	16(36.4)
B.pseudomallei	24(15.8)	13(54.2)
Klebsiella spp.	23(15.1)	11(47.8)
Pseudomonas spp.	13(8.6)	4(30.8)
Enterobacter spp.	6(3.9)	1(16.7)
Salmonella spp.	1(0.7)	0(0)
Other gram negative bacilli	2(1.3)	1(50)
Total	113(74.3)	46(40.7)
Gram positive cocci		
S.aureus	26(17.1)	10(38.5)
α -Streptococci	4(2.6)	2(50)
γ -Streptococci	3(2.0)	0(0)
Streptococcus pneumonia	2(1.3)	1(50)
β -Streptococci	1(0.7)	0(0)
Total	36(23.7)	13(36.1)
Polymicrobial organisms	3(2.0)	1(33.3)
Total	152(100)	60(39.5)

Source of Infection

The respiratory system was the most common source of bacteremia (21.7 percent), followed by the urinary system (13.2 percent) and the hepatobiliary system (13.2 percent).

In 33.2 percent of the bacteremic cases, the 1^o site of infection could not be identified with certainty (Table 2). Mortality was high when primary focus was within the respiratory system and the cases in which the source was unknown ($p < 0.001$ and $p < 0.01$, respectively).

Table 2. Mortality related to source of infection.

Source	No.(%)	Death.(%)	
Unknown	49(32.2)	27(55.1)	p<0.01
Respiratory system	33(21.7)	23(69.7)	p<0.001
Urinary system	20(13.2)	0(0)	
Hepatobiliary system	20(13.2)	4(20)	
Gastrointestinal system	10(6.6)	2(20)	
Skin and soft tissue	9(5.9)	4(44.4)	
Bone and joints	6(3.9)	0(0)	
Spleen	2(1.3)	0(0)	
Genital system	1(0.7)	0(0)	
Neurological system	1(0.7)	0(0)	
Other	1(0.7)	0(0)	
Total	152(100)	60(39.5)	

The common organisms identified in the unknown source of bacteremia were E.coli (30.6 percent), S. aureus (24.5 per cent), and Klebsiella species (16.3 percent), respectively. B. pseudomallei (30.3 percent), and Klebsiella species (24.2 percent) were the top - 2 common organisms of the respiratory system infection. In the urinary system and hepatobiliary system infection, E. coli was the most common organism, 61.9 percent and 20 percent, respectively (Table 3).

Table 3. Distribution of pathogenic organisms related to organic systems.

Organisms	Organic systems									
Gram-negative bacilli	RS	GUS	GIS	HBS	CNS	B&J	S&S	Sp	Lym	Unk
E.coli	4	13	4	7	-	1	-	-	-	15
B.pseudomallei	10	2	1	5	-	2	2	1	-	1
Klebsiella spp.	8	1	1	4	-	1	-	-	-	8
Pseudomonas spp.	1	1	3	-	-	-	1	1	-	6
Enterobacter spp.	-	1	-	2	-	-	-	-	-	3
Salmonella spp.	-	1	-	-	-	-	-	-	-	-
Other gram-negative	-	-	-	-	-	-	1	-	-	1
Gram-positive cocci										
S.aureus	4	2	-	2	-	1	5	-	1	11
α -Streptococci	3	-	-	-	1	-	-	-	-	-
γ -Streptococci	-	-	-	-	-	-	-	-	-	3
S.pneumonia	2	-	-	-	-	-	-	-	-	-
β -Streptococci	-	-	-	-	-	1	-	-	-	-
Polymicrobial organisms	1	1	-	-	-	-	-	-	-	1

RS = Respiratory system GUS= Genitourinary system GIS= Gastrointestinal system

HBS = Hepatobiliary system CNS= Central nervous system B&J= Bone&joints

S&S = Skin&soft tissue Sp= Spleen Lym= Lymphoma Unk= Unknown

Underlying Disease

In this study, the group of underlying disease was not categorized by severity such as the rapidly fatal (e.g. adult with acute leukemia, or blastic relapse of chronic leukemia) ; the ultimately fatal (disease likely to be fatal within 5 years) ; the non fatal (disease unlikely to be fatal within 5 years) ; and none

(previously healthy) according to McCabe and Jackson's categories.⁽²¹⁾ The underlying disease was just classified by the real underlying disease or condition rather than by category. Mortality related to underlying disease was significantly lower in patients with malignancy ($p<0.02$), but there was no statistical difference in the other groups (Table 4).

Table 4. Mortality related to real underlying disease or condition.

Underlying disease	No.(%)	Death.(%)	
Malignancy*	10(6.6)	0(0)	P<0.02
Diabetes mellitus	35(23.0)	14(40.0)	
Renal diseases**	8(5.3)	1(12.5)	
Pulmonary tuberculosis	7(4.6)	2(28.6)	
Heart diseases***	6(3.9)	2(33.3)	
AIDS	5(3.3)	3(60.0)	
Steroid drugs abuse	12(7.9)	4(33.3)	
No underlying condition	69(45.4)	34(49.3)	
Total	152(100)	60(39.5)	

*7 patients with cholangiocarcinoma, 1 patient with colon cancer,
1 patient with pancreatic cancer, 1 patient with Hodgkin lymphoma

** Chronic renal failure, renal stones.

*** Valvular heart disease, coronary heart disease.

Clinical Variables

Variables on history of illness, clinical signs and symptoms were all shown in Table 5, 6 and 7. The patients who had the Glasgow coma scale lower than 9 out of 15, or shock on admission,

were correlated with higher mortality ($p < 0.004$ vs $p < 0.0001$) (Table 8 and 10). However, the other clinical variables were not significantly correlated with mortality.

Table 5. Symptoms of bacteremia

Symptoms	No.(%)
Fever	49(96.7)
Cough	15(23.4)
Dyspnea	32(62.7)
Confusion	17(33.3)
GI symptoms?	28(54.9)
GU symptoms??	9(17.6)

*nausea, vomiting, diarrhea,

**nocturia>2 times, dysurea, pass stones

Table 6. Signs of bacteremia

Signs	No.(%)
Low systolic BP.?	25(49.0)
Anemia	19(37.3)
Jaundice	19(37.3)
Legs edema	3(5.9)
Hepatosplenomegaly	14(27.5)
Abscess	11(21.6)
Respiratory signs	21(41.3)
Urinary signs	17(33.3)
Neurological signs	10(19.6)

*systolic BP < 90 mmHg

Table 7. Clinical signs of bacteremia

Signs	Mean	Range
Temperature (C°)	38.5	36.0-41.0
pulse (per min)	106.7	62.0-166.0
Systolic BP (mmHg)	97.8	50.0-150.0
Diastolic BP(mmHg)	63.2	30.0-90.0
Respiratory rate (per min)	28.7	20.0-62.0
Glasgow coma scale	13.3	3.0-15.0

Table 8. Glasgow coma scale related to mortality

GCS#	No.(%)	Death.(%)
≤ 9	7(13.7)	6(85.7)
> 9	44(86.3)	13(29.5)
Total	51(100)	19(37.3)

GCS = Glasgow coma scale

p<0.004

Liver Function Tests

The study revealed no statistical difference in the liver function tests between the two groups of patients

(p > 0.05). One group who had underlying hepatobiliary disease and another one who had no previous hepatobiliary disease. (Table 9)

Table 9. Liver function tests of two groups of patients with or without hepatobiliary disease

	No.	Mean	with HBD***		without HBD	
			No.	Mean	No.	Mean
Albumin (gm/dl)	39	2.8 (1.5-4.0)	11	2.8 (1.6-4.0)	28	2.8 (1.5-3.9)
Globulin (gm/dl)	39	3.8 (2.4-6.9)	11	4.2 (3.3-6.9)	28	3.6 (2.4-6.0)
SGOT (U/L)	40	189.5 (4.0-3310.0)	11	116.9 (4.0-326.0)	29	217.1 (13.0-3310.0)
SGPT (U/L)	38	79.0 (3.0-1046.0)	10	54.5 (5.0-107.0)	28	87.6 (3.0-1046.0)
TB* (mg/dl)	39	5.5 (0.2-24.1)	11	8.8 (0.2-24.9)	28	4.2 (0.3-17.1)
ALP** (U/L)	37	533.4 (65.3-1867.0)	9	841.6 (373.0-1867.0)	28	434.4 (65.3-1625.0)

*TB = Total bilirubin **ALP = Alkaline phosphatase ***HBD = Hepatobiliary disease

Shock

Of the 51 patients whose complete data was recorded, 25 patients (49 percent) were in shock upon admission and 24 patients were treated with inotropic drugs. The mortality rate of patients admitted with shock was statistically the same for those treated with inotropic drugs as those who were not treated with the drugs ($p < 0.00001$). (Table 10)

Table 10. Mortality related to shock on admission

Shock	No.(%)	Death.(%)	
Present	25(49)	17(68.0)	$p < 0.00001$
Absent	26(51)	2(7.7)	
Total	51(100)	19(37.3)	

Serum Lactate

Randomized serum lactate was studied in 51 patients. The study showed that whose serum lactate level more than 6.4 mEq/L (range 0-19.8 mEq/L) were correlated with high mortality ($p < 0.004$) (Table 11).

Table 11. Correlation between mortality and serum lactate level

Lactate level (mEq/L)	No.(%)	Death.(%)	
≤ 6.4	34(66.7)	8(23.5)	$P < 0.004$
> 6.4	17(33.3)	11(64.7)	
Total	51(100)	19(37.3)	

Antibiotic Treatment

Of the 51 patients, there were 23 cases (45 per cent) who were treated with appropriate antibiotic within 24 hours after admission (prompt and appropriate antibiotic treatment).⁽¹⁷⁾ The remaining 28 cases (55 per cent) were at first treated with inappropriate choice of antibiotic,

or the appropriate antibiotic was introduced when the pattern of antibiotic susceptibility test was known more than 24 hours after admission (delay and inappropriate antibiotic treatment).⁽¹⁷⁾ There were no statistical difference in mortality between the two groups of patient ($p > 0.05$) (Table 12).

Table 12. Correlation between mortality and antibiotic treatment

Treatment	No.(%)	Death.(%)	
Prompt and appropriate	23(45)	8(34.8)	$p > 0.05$
Delay and inappropriate	28(55)	11(39.3)	
Total	51(100)	19(37.3)	

Discussion

There have been many reports about bacteremia studied in the United States and Europe.^(1-14,16,18,19) Experience of bacteremia varies widely depending on the level of hospital and its facility. Most studies of bacteremia have concentrated on the overall incidence (hospital-acquired and community-acquired) in many diverse hospital departments and settings. The overall incidence was about 3-12/1000 admissions.^(1-4,13,17,19) The incidence of bacteremia was reported to be more than

7/1000 admissions from those studied at a University hospital or referral center,^(1,4,13) but lower at the community hospitals.^(2,3,17,19) In our study, the overall incidence of bacteremia was 6.5/1000 admissions, which is similar to that report from the community hospitals.^(2,3,17,19) Approximately two-thirds (64.7 percent) of the patients with bacteremia were considered to be community-acquired cases. The remaining one-third were hospital-acquired patients. The proportion of bacteremic incidence is similar to other

previous studies reported by Ispahani P. and colleague, Scheckler WE. or French GL. and colleague.^(1-2,20) From the total of 152 patients with community - acquired bacteremia (64.7 percent), 89 (58.6 percent) were males and 63 (44.4 percent) were females. The distribution by sex was similar to various reports.^(1,4,9,12,17,20) The incidence of bacteremia trends to be higher in the patients who are more than 50 years of age (the mean age was 51.9 years). This result was quite similar to other studies.^(1,4,9) In our study, the overall mortality rate was 39.5 per cent, which is not different from those reported by Weinstein MP. and colleague (42 per cent)⁽¹²⁾ or in the study of Usha Setia (35 per cent).⁽³⁾ However, mortality related to bacteremia did not show a steady increase with age in this study which was difference from other authors who reported that mortality increases with age.^(9,12,17)

In this study, as mentioned in other literatures,^(1-4,13,17,18,20) *E.coli* was the most common pathogen among all positive blood cultures (28.9 per cent), followed by *S.aureus* (17.1 percent), *B.pseudomallei* (15.8 per cent), then *Klebsiella* species

(15.1 percent). *B.pseudomallei* was still the major pathogenic organism of community-acquired bacteremia in northeastern Thailand, particularly in diabetic patient and patients with renal stone or in chronic renal failure states.⁽²¹⁾ The highest mortality rate (54.2 percent) was found with *B.pseudomallei* septicemia, but the statistics was not significantly different from other causative organisms.

Respiratory system was the most common source of bacteremia (21.7 percent), followed equally by urinary system and hepatobiliary system (13.2 per cen), but nearly 33 per cent of the cases, source of bacteremia was unknown, the same figure was reported in 1983 by Weinstein MP. and colleague.⁽¹²⁾ Nevertheless, many studies have reported that urinary tract infection was the principal source of bacteremia.^(1-3,18,20) *B. pseudomallei* bacteremia, the most common organism of respiratory tract infection (30.3 percent) in this study (Table 3), brought about 90 percent (9 out of 10) in mortality. The majority of urinary tract and hepatobiliary tract infection were due to *E.coli* and this may account for the lower mortality. Mortality

rate was significant higher in respiratory tract infection ($p < 0.001$) and case with unknown source of bacteremia ($p < 0.01$) than other sources (Table 2). This difference is probably account by the extreme virulence of *B.pseudomallei* in respiratory tract infection.

Analysis of mortality related to clinical variables revealed that it was higher in patient with Glasgow coma scale under 9/15 or who was presently shock (systolic blood pressure < 90 mmHg) on admission ($p < 0.05$). Other clinical variables such as body temperature, total peripheral leukocyte count, renal function or liver function tested values had no correlation with the mortality. This result was difference from other reports in which mortality and those clinical variables were highly statistical significant related.^(1,13,17)

Overproduction of lactate is due to anaerobic pathway metabolism. Serum lactate level is about 0.5-1.5 mEq/L for normal daily metabolism, but it will be as high as 4.5 mEq/L⁽²²⁾ whenever shock or hypoxemia appear. In our study, serum lactate level was concerned and found that the patient whose serum lactate level

more than 6.4 mEq/L was prognosed with high mortality ($p < 0.004$) (Table 11). This preliminary observation may merely reflect the severity of shock associated with high mortality which was discussed above.

According to our knowledge, the mortality will be higher in the patient with rapidly fatal or ultimately fatal underlying disease than who were previously healthy.^(1-3,17,19) The surprising result in this study was that the patients with underlying malignancy had significantly lower mortality ($p < 0.02$) than whoever with diabetes mellitus, heart disease, AIDS, steroid drug abuse or previously healthy. If we looked through all 10 patients with malignancy there were 7 patients with cholangiocarcinoma, the remaining patients were colon cancer, pancreatic cancer and Hodgkin lymphoma, respectively. None of them had ever been chemotherapeutic treated, thus their immunoprotective mechanism might not difference from the patient without underlying disease. As well as the source of bacteremia and type of pathogenic organisms in these cases still being the confound factors to be analyzed.

For the aspect of antibiotic treatment, mortality will be significantly decreased in patients treated with prompt and appropriate antimicrobial agent^(1,3,13,17) but there was not such statistical difference between a group received prompt and appropriate antibiotic treatment comparing with another one received delayed and inappropriate antibiotic treatment in this study. This may reflect the assumption that the resistant pattern of antibiotics from susceptibility test in vitro may, in fact, had some degree of bacteriostatic or bactericidal activities in vivo condition. Thus, the patient who was treated with insensitive tested antibiotic could have some clinical improvement before the appropriate one was given. But in the delayed treatment of bacteremia many uncertainties have to be explored.

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