

# BACTEREMIA AND ANTIMICROBIAL SUSCEPTIBILITIES IN HIV-INFECTED PATIENTS AT SIRIRAJ HOSPITAL

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**Abstract.** Bacterial infections in human immunodeficiency virus (HIV) infected patients may frequently develop into septicemia. Our study evaluated the bacterial pathogens isolated from hemocultures of HIV-infected patients at Siriraj Hospital and their antimicrobial susceptibility tests. The percentages of positive hemocultures were 24.64, 21.38, 23.88, and 28.46% in 1996, 1997, 1998, and 1999, respectively. *Salmonella* spp was the most pathogen isolated, followed by *Escherichia coli* (10.93%), *Staphylococcus aureus* (8.2%), coagulase-negative staphylococci (6.56%), nonfermentative gram-negative rods (6.01%), *Pseudomonas aeruginosa* (5.46%), *Klebsiella pneumoniae* (4.37%), and *Enterobacter* spp (4.37%). *Salmonella*, serogroup C was the most frequently isolated serogroup. It was sensitive to amoxicillin/clavulanate in 100%, ampicillin/sulbactam in 89%, cefazolin, cefuroxime, cefotaxime, ceftriaxone, ceftazidime, imipenem, gentamicin, amikacin, netilmycin, ofloxacin, and ciprofloxacin in 100%. The changing spectrum of bacteria and antimicrobial susceptibility patterns in HIV-1 infected patients may provide a guideline for the selection of appropriate drugs for treatment.

## INTRODUCTION

Bacterial infection occurs more frequently in HIV-infected patients than in HIV-negative patients, and is associated with higher rates of morbidity and mortality. Mortality rates in HIV patients compared to those without HIV differ between reports. It has been reported that bacterial infections are the leading cause of death in patients with the acquired immunodeficiency syndrome (AIDS); bacteremia was responsible for 8% of all AIDS deaths (Stein *et al*, 1992). A study in Florida, USA in 2001 stated that 88 patients (7%) had 89 episodes of bloodstream infection in 1,225 admissions. Of these 89 infections, 73 (82%) were community acquired and 16 (18%) were nosocomial infections (Afessa *et al*, 2001).

Several factors predispose patients with HIV infection to bacterial infections. These factors include abnormalities in humoral and cell-mediated immunity, phagocytic cell dysfunctions, skin

and mucous membrane defects, and depletion of CD4+ T-lymphocytes (Kovac *et al*, 1997). Consequently, the presence of bloodstream infections is associated with an increased mortality rate, length of hospital stay and intensive care unit admission rate. Recognition of the incidence and etiology of bloodstream infections in patients with HIV infection can lead to preventive and therapeutic measures that may reduce the associated increased mortality and morbidity. The purpose of this study was to evaluate the bacterial pathogens isolated from the hemocultures of HIV-infected patients at Siriraj Hospital and their antimicrobial susceptibilities, and to search for ways to improve the treatment of this infectious complication in HIV disease.

## MATERIALS AND METHODS

The study population was 730 adult HIV-positive patients treated and followed up at Siriraj Hospital during 1996-1999. All positive blood cultures from HIV-positive patients were included. The patient's blood was inoculated in conventional hemoculture broth using a ratio of 1:5 or inoculated into the automate Bactec system (Becton Dickinson), resin-containing media, to enhance isolation of pathogenic bacteria,

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particularly when patients were receiving antimicrobial agents. For conventional hemoculture, after 6 hours of incubation, most bacteria responsible for clinically significant infections were present in numbers large enough to recover by blind subculture. The latter was performed by aseptically removing a few drops of well-mixed media and spreading it onto blood agar. The plate was incubated in 5% CO<sub>2</sub> at 35°C for 2 days. Culture-negative bottles were reincubated until 7 days unless the patient's condition required special consideration. Each bottle was examined daily during incubation for evidence of growth, indicated by turbidity, hemolysis or the presence of small colonies. Bacterial pathogens were isolated and identified according to standard microbiological techniques (Murray *et al*, 1999).

#### Antimicrobial susceptibility testing

The Kirby-Bauer disk diffusion method was performed as recommended by the National Committee for Clinical Laboratory Standards (NCCLS, 2003). Muller-Hinton plates were incubated overnight at 35°C for 18-24 hours, after which the diameter of each inhibition zone was measured.

### RESULTS

One hundred eighty-three positive hemocultures from 730 HIV patients admitted to Siriraj Hospital during 1996-1999 were found. The percentages of positive hemocultures in 1996, 1997, 1998 and 1999 were 24.64, 21.38, 23.88, and 28.46%, respectively (Table 1). The average positive rate was 25.07%. Among the 7 most common pathogens (Table 2), *Salmonella* spp ranked first (44.81%), followed by *Escherichia coli* (10.93%), *Staphylococcus aureus* (8.2%), coagulase-negative staphylococci (6.56%), nonfermentative gram-negative rods (6.01%), *Pseudomonas aeruginosa* (5.46%), *Klebsiella pneumoniae* (4.37%), and *Enterobacter* spp (4.37%). For the *Salmonella* spp, the most common serogroup was C, followed by B, D, then E. Table 3 shows that the *Salmonella* group C was less-sensitive to ampicillin (26%), chloramphenicol (35%), and co-trimoxazole (48%), but highly-sensitive to amoxicillin/clavulanate (100%), ampicillin/sulbactam (89%), ceftazidime,

cefuroxime, cefotaxime, ceftriaxone, ceftazidime, imipenem, gentamicin, amikacin, netilmicin, ofloxacin, and ciprofloxacin (100%). The *E. coli* was less sensitive to ampicillin, amoxicillin/clavulanate, ampicillin/sulbactam, and cotrimoxazole (ranged 0-42%) but highly sensitive to cefuroxime, cefotaxime, ceftriaxone, ceftazidime, imipenem, gentamicin, amikacin, netilmicin, ofloxacin, and ciprofloxacin (ranged 78-100%). The *S. aureus* was highly sensitive to vancomycin, teicoplanin, netilmicin (100%), cotrimoxazole (88%), fosfomycin (83%), imipenem (88%), and ofloxacin (80%). Fifty percent were MSSA and 50% were MRSA. The results of antimicrobial susceptibilities for the other bacterial pathogens isolated in this study are shown in Table 3.

### DISCUSSION

In this study, the data of bacterial pathogens isolated from the hemocultures of HIV infected-patients at Siriraj Hospital and their antimicrobial susceptibilities during 1996-1999 were evaluated. In 6 prior studies, the incidence of bacteremia in hospitalized patients with HIV infection ranged from 5 to 28% (Northfelt and Polsky, 1991). Bacteremia occurred in 15% of patients with HIV infection admitted to Barnes Hospital, USA over a 2 year period (Fichtenbaum *et al*, 1995). A recent study in Brazil found that the mortality rate of patients was 39%, being 50% for patients with blood stream infections (Rosas *et al*, 2003). Another study showed that bacteremia occurred in 7% of adult patients with HIV infection who required hospital admission. Most blood stream infections in patients with HIV were community acquired (Afessa *et al*, 2001). The incidence of nosocomial infections has been 6-10.5% (Petrosillo *et al*, 2002).

As with studies elsewhere, we found HIV infection to be a significant risk factor for bacteremia. *Salmonella* was the most common pathogen associated with blood stream infections in our study. Some authors have stated that coagulase-negative staphylococci is the major cause of bacteremia in AIDS patients. Other investigators have found *S. aureus* to be the predominant agent of blood stream infection in gram-positive bacteremia (Banerjee *et al*, 1991).

Table 1  
The percentage of HIV-infected patients with a positive hemoculture.

Number of patients	1996	1997	1998	1999	Total
HIV-infected patients	138	145	201	246	730
HIV-infected patient with positive hemoculture	34	31	48	70	183
% positive	24.64	21.38	23.88	28.46	25.07

Table 2  
Bacterial pathogens isolated from the hemocultures of HIV-infected patients during 1996-1999.

Bacterial pathogens	1996	1997	1998	1999	Total	Percentage
<i>Escherichia coli</i>	2	4	6	8	20	10.93
<i>Klebsiella pneumoniae</i>	3	3	1	1	8	4.37
<i>Enterobacter</i> species	1	1	4	2	8	4.37
<i>Citrobacter diversus</i>	-	-	-	1	1	0.55
<i>Proteus</i> species	-	-	1	-	1	0.55
<i>Salmonella</i> :	16	11	17	38	82	44.81
group B	7	4	3	17	31	16.94
group C	6	3	8	16	33	18.03
group D	3	4	4	5	16	8.74
group E	-	-	2	-	2	1.09
<i>Aeromonas hydrophila</i>	-	-	1	1	2	1.09
<i>Pseudomonas aeruginosa</i>	1	1	4	4	10	5.46
<i>Acinetobacter anitratus</i>	-	-	3	-	3	1.64
Nonfermentative gram-negative rods	1	-	2	8	11	6.01
<i>Haemophilus influenzae</i>	-	1	-	1	2	1.09
<i>Staphylococcus aureus</i>	6	6	2	1	15	8.2
Coagulase-negative staphylococci	2	1	7	2	12	6.56
<i>Streptococcus pneumoniae</i>	1	2	-	1	4	2.19
Group A streptococci	-	1	-	-	1	0.55
Group D nonenterococci	-	-	-	1	1	0.55
<i>Enterococcus</i> species	-	-	-	1	1	0.55
$\beta$ -hemolytic streptococci not group A, B, D	1	-	-	-	1	0.55
Total	34	31	48	70	183	100

Long-term indwelling catheters were the most common predisposing factor. In addition, prior drug use was more frequently associated with *S. aureus* bacteremia in HIV-positive patients than in HIV-negative patients (Decker and Tazon, 1994). *Salmonella* infections in patients with AIDS have been reported to be an important cause of morbidity by several investigators. In San Francisco, *Salmonella* bacteremia was the most common pathogen, seen in 45% of patients with AIDS and 9% of patients without AIDS (Fernandez *et al*, 1996). Those results are similar to our findings. Infection with nontyphoid

strains of *Salmonella* were first described in patients with AIDS in 1983 (Pitchenik *et al*, 1983). A review of other studies in 1994 showed that HIV-infected patients have a 20 times higher risk than the general population of acquiring *Salmonella* infection, and blood stream invasion is 100 times more prevalent in HIV-infected patients than in immunocompetent ones (Gruenewald *et al*, 1994). Prior studies found that the number and proportion of *Salmonella* spp isolated from blood relative to those isolated from all body sites increased dramatically and progressively between 1983 and 1987 in the areas of the USA

Table 3  
Percentage of sensitivities test for bacterial pathogens isolated from the hemoculture of HIV-infected patients.

Antimicrobial agents	Sal. group B	Sal. group C	Sal. group D	E. coli	K. pneumo-niae	N.F.	P. aerugi-nosa	S. aureus	Coag. neg Staph	S. pneumo-niae
Penicillin	-	-	-	-	-	-	-	0 (8)	0 (5)	60 (5)
Ampicillin	19 (21)	26 (23)	76 (17)	15 (13)	0 (8)	0 (4)	-	0 (7)	0 (5)	80 (5)
Amoxicillin/clavulanate	90 (20)	100 (22)	100 (13)	42 (12)	75 (8)	67 (3)	-	71 (7)	100 (4)	100 (4)
Ampicillin/sulbactam	82 (17)	89 (18)	100 (15)	36 (11)	67 (6)	67 (3)	-	67 (6)	100 (5)	100 (4)
Oxacillin	-	-	-	-	-	-	-	50 (8)	80 (5)	60 (5)
Cefazolin	100 (21)	100 (15)	100 (10)	67 (12)	75 (8)	0 (3)	-	71 (7)	100 (4)	100 (5)
Cefuroxime	100 (10)	100 (8)	100 (9)	100 (5)	100 (1)	0 (1)	-	50 (2)	100 (3)	100 (2)
Cefotaxime	100 (19)	100 (21)	100 (17)	92 (12)	86 (7)	25 (4)	0 (10)	63 (8)	100 (4)	100 (3)
Ceftriaxone	100 (17)	100 (21)	100 (17)	100 (12)	100 (7)	25 (4)	40 (10)	57 (7)	100 (5)	100 (3)
Ceftazidime	100 (17)	100 (22)	100 (16)	92 (12)	83 (6)	50 (4)	60 (10)	63 (8)	100 (5)	100 (4)
Imipenem	100 (20)	100 (23)	100 (17)	100 (13)	100 (7)	75 (4)	90 (10)	88 (8)	100 (4)	100 (5)
Chloramphenicol	27 (22)	35 (23)	88 (16)	60 (10)	71 (7)	0 (2)	-	75 (8)	80 (5)	80 (5)
Erythromycin	-	-	-	-	-	-	-	50 (8)	60 (5)	60 (5)
Clarithromycin	-	-	-	-	-	-	-	50 (8)	50 (2)	100 (2)
Vancomycin	-	-	-	-	-	-	-	100 (8)	100 (4)	100 (4)
Teicoplanin	-	-	-	-	-	-	-	100 (7)	100 (5)	100 (4)
Fosfomycin	-	-	-	-	-	-	-	83 (6)	40 (5)	100 (4)
Co-trimoxazole	0 (22)	48 (23)	82 (17)	0 (13)	13 (8)	33 (3)	-	88 (8)	60 (5)	60 (5)
Gentamicin	41 (22)	100 (23)	87 (16)	100 (13)	100 (8)	50 (4)	60 (10)	50 (8)	80 (5)	0 (5)
Amikacin	100 (20)	100 (21)	100 (17)	100 (12)	100 (7)	50 (4)	56 (9)	67 (6)	100 (4)	0 (4)
Netilmicin	74 (19)	100 (22)	100 (15)	100 (12)	100 (7)	67 (3)	100 (7)	100 (7)	100 (5)	50 (4)
Ofloxacin	100 (15)	100 (16)	100 (9)	78 (9)	100 (6)	100 (3)	40 (5)	80 (5)	100 (3)	100 (3)
Ciprofloxacin	100 (16)	100 (16)	100 (16)	85 (13)	80 (5)	100 (4)	63 (8)	57 (7)	75 (4)	50 (4)

where the incidence of AIDS is high (Levine, 1991). This increase is mostly due to an increase in the number of individuals with septicemia caused by *S. typhimurium* (Levine, 1991). A full explanation of the salmonellosis problem in AIDS patients must account for the increased incidence of this agent, the high frequency of bacteremia and the high relapse rate. Defective cell mediated immunity (CMI) was noted early in the study of AIDS, and is believed to be the basis for the majority of the infectious consequences of this disease. In addition, impaired B cell function is also recognized. Another factor that may play a role in potentiating *Salmonella* infections in patients with AIDS is prior drug use. The latter changes the normal intestinal flora, a known defense against *Salmonella*, thus increasing the likelihood of clinically apparent disease caused by a smaller inoculum of organisms. Thus antimicrobial agents in combination with impaired

CMI may lead to a higher frequency of bacteremia and a relapse in patients with AIDS (Steven and Charles, 1987). We found *Salmonella* to be the most common gram-negative organism, unlike the findings of some previous studies. Some have found *E. coli* to be the most common etiologic agent of infection in HIV-infected patients (Afessa *et al*, 2001). In the same study, a significant percent of patients with blood stream infection were women, who are at higher risk for genitourinary infection. The relative number of infected woman may explain the high rates of *E. coli* blood stream infection in their study (Afessa *et al*, 2001).

Recognition of risk factors for HIV infection is important. If the risk of HIV infection is present, the physician should be aware of the high incidence of recurrent bacteremia among HIV-infected patients. For this reason, an adequate course of antimicrobial agents should be admin-

istered. Regarding antimicrobial susceptibility tests, prior studies had reported that more than 20% of *S. typhimurium* strains were resistant to ampicillin. Furthermore, chloramphenicol may not be bactericidal to *Salmonella*. This may be associated with a higher relapse rate than ampicillin and does not affect the gastrointestinal carrier state. In salmonellae resistant to ampicillin and chloramphenicol, co-trimoxazole and zidovudine have been used successfully; however, these may be poorly tolerated by patients with HIV infection (Sperber and Schlepner, 1987). Similarly, a recent report showed that the emergence of resistance to ampicillin and other compounds in strains of non-typhoid *Salmonella* complicated the choices for therapy. In some geographic areas 30%-45% of isolates were resistant to ampicillin, and although rare, resistance to third-generation cephalosporins and fluoroquinolones has also been reported (Morosini *et al*, 1995). Initial therapy should include intravenous administration of a third-generation cephalosporin until susceptibility tests have been determined, then a switch to ampicillin can be made, if indicated (Guerrero *et al*, 1996). Consequently, recognition of pathogens and early administration of appropriate antimicrobial agents is important in reducing the morbidity and mortality associated with bacteremia in HIV-infected patients.

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