RESPIRATORY TRACT INFECTION CAUSED BY BACTERIA (NON-*MYCOBACTERIUM*) AND THEIR ANTIBIOGRAM IN HIV- POSITIVE PATIENTS

Somporn Srifuengfung, Chanwit Tribuddharat, Thitiya Yungyuen and Thidarat Wensentia

Department of Microbiology, Faculty of Medicine at Siriraj Hospital, Mahidol University, Bangkok, Thailand

Abstract. This study was undertaken from 1995-2000 to investigate the cause of respiratory tract infection among 481 patients with human immunodeficiency virus (HIV) at Siriraj Hospital, Bangkok, Thailand. The positive rate of bacterial pathogens was 38.46%. *Pseudomonas aeruginosa* appeared to be the most common pathogen (32.97%), followed by *Staphylococcus aureus* (18.92%), *Klebsiella pneumoniae* (10.81%), *Haemophilus influenzae* (7.57%), and *Acinetobacter baumannii* (5.95%). *P. aeruginosa* was sensitive to netilmycin, amikacin, imipenem, meropenem, cefoperazone/sulbactam, piperacillin/tazobactam, and gentamicin (67-84%). *S. aureus* was sensitive to vancomycin and teicoplanin (100%).

INTRODUCTION

Bacterial pneumonia continues to be the primary cause of hospital admissions, and a major cause of morbidity and mortality, among HIV-infected patients. Nonetheless, risk factors for bacterial pneumonia remain under investigation. A lack of standardization of diagnostic criteria limits comparability of incidence rates between different risk groups. Data on the etiologic agents in bacterial pneumonia in the HIV/AIDS population have been chiefly derived from hospital studies, with isolation of the bacterial agents from sputum cultures (Caiaffa *et al*, 1993). New information leading to a broader understanding of the pulmonary diseases that are associated with HIV infection would be of major importance with relevance to both clinical and epidemiologic aspects of HIV disease. The data would be useful for long-term management of patients and assessing the magnitude and types of resources necessary in the future. The purpose of this study was to evaluate bacteria (non-*Mycobacterium*) which cause respiratory tract infections and their antibiogram in HIV- positive patients.

MATERIALS AND METHODS

HIV-infected patients with respiratory tract infection were enrolled in this study during the period January 1, 1995-December 31, 2000. Pathogens were isolated from sputa, bronchial washings, bronchoalveolar lavages, throat swabs and gastric washings.

Sputum samples were obtained when the patients were able to expectorate. Sputa were considered acceptable for culture if they contained >25 polymorphonuclear cells and <25 epithelial cells per low-power field. Clinical specimens were cultured on blood agar, MacConkey agar and chocolate agar. Plates were incubated in 5% CO_2 at 35ºC for 2 days. Bacterial pathogens were isolated and identified according to standard microbiological techniques (Murray *et al*, 1999).

Antimicrobial susceptibility testing

This was performed as recommended by the National Committee for Clinical Laboratory Standards (NCCLS, 2003). The Muller-Hinton plates were incubated overnight at 35ºC for 18-24 hours.

RESULTS

Over a 7-year period, 481 HIV-infected patients were enrolled in this study. Of these, 329 (64.8%) were male and 152 (31.6%) were female (Fig 1). The sources of specimens from which these isolates were grown are shown in Table 1. The most common specimens were sputa followed by bronchial washings, bronchoalveolar lavages, throat swabs and gastric washings, re-

Correspondence: Chanwit Tribuddharat, Department of Microbiology, Siriraj Hospital, 2 Prannok Rd, Bangkok 10700, Thailand.
Tel: 66 (0) 2419-7055; Fax: 66 (0) 2411-3106
E-mail: sissf@mahidol.ac.th

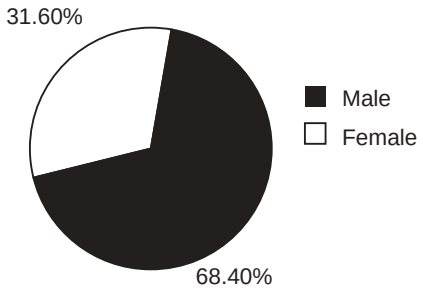

Fig 1–The percentage of patients by sex.

spectively. The rate of bacterial pathogens which could be isolated in this study was 38.46%, as shown in Table 2. Only 6.44% were yeast; 55% were normal flora. The reported incidences of bacterial pneumonia according to etiology varied widely. Our study showed that *Pseudomonas aeruginosa* was the most frequently isolated organism, followed by *Staphylococcus aureus*, *Klebsiella pneumoniae, Haemophilus influenzae* and *Acinetobacter baumannii*, respectively (Table 3). The percents of methicillin-sensitive and methicillin-resistant *S. aureus* were 52.75% and 47.25%, respectively.

Antimicrobial susceptibility testing

Both *P. aeruginosa* and *S. aureus* were tested for their antimicrobial susceptibilities. We found that *P. aeruginosa* was sensitive to netilmycin, amikacin, imipenem, meropenem, cefepime, cefoperazone/sulbactam, piperacillin/tazobactam and gentamicin, while *S. aureus* was sensitive to vancomycin and teicoplanin.

DISCUSSION

Bacterial pneumonia is a common complication of HIV infection, occurring at all stages of HIV disease, but more frequently as immune function declines. In this study, the most common bacterial pathogens isolated were *P. aeruginosa*, followed by *S. aureus, K. pneumoniae*, *H. influenzae* and *A. baumannii.* This is in contrast to that found in a previous study. For community-acquired pneumonia, the most important organisms identified were *S. pneumoniae* and *H. influenzae*, followed by *S. aureus, E. coli* and other gram-negative bacteria, including *Salmonella* species. Gram-negative bacteria were the leading cause of nosocomial pneumonia in HIV-seropositive patients including *K. pneumoniae, P. aeruginosa* and *E. aerogenes* (Witt *et al*, 1987; Cohn, 1991; Tudela *et al*, 1992). Similarly, a study in San Francisco County, California, reported that *S. pneumoniae* is the leading cause of community-acquired bacterial pneumonia in HIV-infected persons (Nuorti *et al*, 2000). Pneumococcal disease can occur early in the course of HIV infection, before the

Table 1
Sources of specimens.

Specimens	Number	%
Sputum	413	85.86
Bronchial washings	48	9.98
Bronchoalveolar lavages	7	1.46
Throat swabs	7	1.46
Gastric washings	6	1.24
Total	481	100

Table 2
Number of bacterial pathogens and yeast isolated.

Organisms isolated	Number	%
Bacterial pathogens	185	38.46
Yeasts	31	6.44
Normal flora	265	55.1
Total	481	100

Table 3
Bacterial pathogens isolated in decreasing order.

Bacterial pathogens	Number of strains	%
Pseudomonas aeruginosa	61	32.97
Staphylococcus aureus	35	18.92
Klebsiella pneumoniae	20	10.81
Haemophilus influenzae	14	7.57
Acinetobacter baumannii	11	5.95
Escherichia coli	10	5.41
Nonfermentative gram-negative rods	8	4.32
Enterobacter cloacae	6	3.24
Streptococcus pneumoniae	4	2.16
Proteus species	3	1.62
Nocardia species	2	1.08
Rhodococcus species	1	0.54
Moraxella catarrhalis	1	0.54
Salmonella serotype B	1	0.54
Others	8	4.33
Total	185	100

Table 4
Antimicrobial susceptibities of the 5 most common pathogens.

Drugs	% Sensitivity					
	P. aeruginosa	*S. aureus*		*K. pneumoniae*	*H. influenzae*	*A. baumannii*
		MSSA	MRSA			
Ampicillin	-	7	0	0	47	0
Amoxicillin/Clavulanate	-	100	3	74	97	2
Cefazolin	-	100	4	76	-	0
Cefotaxime	5	99	0	77	99	2
Ceftriaxone	-	98	0	76	-	2
Ceftazidime	65	95	0	78	100	31
Ceftibuten	-	100	0	87	-	8
Cefoperazone/sulbactam	69	100	4	98	-	91
Cefpirome	52	100	5	96	100	33
Cefepime	69	100	5	97	100	40
Imipenem	73	100	11	100	-	93
Meropenem	73	100	5	99	99	90
Erythromycin	-	91	0	-	15	-
Gentamicin (10 μg)	67	97	3	84	88	38
Amikacin	77	99	10	90	100	38
Netilmicin	84	100	58	86	-	47
Ofloxacin	62	98	4	90	98	35
Ciprofloxacin	68	-	-	-	-	-
Levofloxacin	64	100	8	89	100	44
Co-trimoxazole	-	96	49	65	44	29
Piperacillin/tazobactam	68	99	7	97	-	41
Oxacillin	-	100	0	-	-	-
Vancomycin	-	100	100	-	-	-
Teicoplanin	-	100	100	-	-	-
Fosfomycin	-	100	49	-	-	-

onset of other opportunistic infections specifically associated with AIDS (Redd *et al*, 1990). Isolates from patients with lower respiratory tract infection who requires hospitalization or intensive care have included both gram-positive and gram-negative species (Marrie *et al*, 1989; Fang *et al*, 1990). A previous study indicated that most frequently isolated pathogens includes *S. pneumoniae, S. aureus, H. influenzae* and other gram-negative rods, including *P. aeruginosa* (Fang *et al*, 1990). Since the beginning of the AIDS epidemic, bacterial pneumonia in HIV-infected individuals has been suggested as a sentinel to declining immune function and the onset of other opportunistic illnesses. The incidence of pneumonia increases as the immune status declines. HIV-infected individuals with CD4 cell counts of less than 200 cells/ml are four times more likely to have one episode of bacterial pneumonia in one year than those with higher CD4 cell counts. For multiple episodes, the risk increases to about 20 times in the same immunosuppressed group. Whether bacterial pneumonia is a marker of immune deficiency or acts as an immune system activator, contributing causally to HIV disease progression is unclear. Bacterial pneumonia is a predictor of progression to AIDS and a source of HIV-related morbidity and mortality before AIDS (Selwyn *et al*, 1992). Antimicrobial therapy of bacterial pneumonia must be prompt and adequate, but in HIV-infected patients there are no guidelines for the empirical treatment of bacterial pneumonia (Burack *et al*, 1994; Huang and Stansell, 1996). On the basis of retrospective studies, the use of second or third-generation cephalosporins or co-trimoxazole has been necessary. Our study demonstrates that *P. aeruginosa* was highly sensi-

tive to amikacin, netilmicin, ciprofloxacin, imipenem, and meropenem, whereas *S. aureus* was highly sensitive to vancomycin and teicoplanin, but less sensitive to fosfomycin and co-trimoxazole.

Prior studies have demonstrated that cefepime, a broad-spectrum cephalosporin, has actively against both gram-positive and gram-negative bacteria (Barckow and Schwigon, 1993). Compared with ceftazidime, cefepime is more active in various experimental models against *S. pneumoniae* and *S. aureus* respiratory infection, while its efficacy against *K. pneumoniae* and *P. aeruginosa* is comparable to that of ceftazidime (Leophonte *et al*, 1993). I*n vitro* studies performed in Spain have documented that cefepime's activity against *S. pneumoniae* is better than ceftazidime's, and similar to that of cefotaxime. It also has good activity against methicillin-sensitive *S. aureus*, Enterobactericeae, *H. influenzae* and *P. aeruginosa* (Kessler *et al*, 1985; Doern and Vautour, 1992; Watanabe *et al*, 1992). Data from our study may be useful clinically, considering the high prevalence of some respiratory bacterial pathogens and their antimicrobial susceptibilities in HIV infection. The antimicrobial pattern may provide guidelines for physicians in treatment, while waiting for antimicrobial susceptibility results from the microbiological laboratory.

REFERENCES

Barckow D, Schwigon CD. Cefepime versus cefotaxime in the treatment of lower respiratory tract infections. *J Antimicrob Chemother* 1993; 32: 183-7.

Burack JH, Hahn JA, Saint-Maurice D, Jacobson MA. Microbiology of community-acquired bacterial pneumonia in persons with and risk for human immunodeficiency virus type 1 infection. *Arch Intern Med* 1994; 154: 2589-96.

Caiaffa WT, Graham NMH, Vlahov D. Bacterial pneumonia in adult population with human immunodeficiency virus (HIV) infection. *Am J Epidemiol* 1993; 138: 909-21.

Cohn DL. Bacterial pneumonia in the HIV-infected patient. *Infect Dis Clin N Am* 1991; 5: 485-507.

Doern GV, Vautour R. *In vitro* activity of cefprozil (BMY28100) and cefepime against *Streptococcus pneumoniae*, *Branhamella catarrhalis* and *Haemophilus influenzae* and provisional interpretative criteria for disc diffusion and dilution susceptibility test with *Haemophilus influenzae*. *Diag Microb Infect Dis* 1992; 15: 633-40.

Fang GD, Fine M, Orloff J, *et al*. New and emerging etiologies for community-acquired pneumonia with implications for therapy. A prospective multicenter study of 359 cases. *Medicine* 1990; 69: 307-16.

Huang L, Stansell JD. AIDS and the lung. *Med Clin North Am* 1996; 80: 775-801.

Kessler RE, Bies M, Buck RE, *et al*. Comparison of a new cephalosporin, BMY-28142 with other broad-spectrum β-lactam antibiotics. *Antimicrob Agents Chemother* 1985; 27: 207-16.

Leophonte P, Bertrand A, Nouvet G, Muir JF, Lucht F, Delaval P. A comparative study of cefepime and ceftazidime in the treatment of community-acquired lower respiratory tract infection. *J Antimicrob Chemother* 1993; 31: 165-73.

Marrie TJ, Durant H, Yates L. Community-acquired pneumonia requiring hospitalization: 5-year prospective study. *Rev Infect Dis* 1989; 11: 586-99.

Murray PR, Baron EJ, Pfaller MA, Tenover FC, Yolken RH, eds. Manual of clinical microbiology. 7thed Washington, DC: American Society for Microbiology, 1999: 283-96.

National Committee for Clinical Laboratory Standards. Performance standard for antimicrobial susceptibility testing, twelfth informational supplement. Approved Standard NCCLS document M100-S13, 2003.

Nuorti JP, Butler JC, Gelling L, Kool JL, Reingold AL, Vugia DJ. Epidemiologic relation between HIV and invasive pneumococcl disease in San Francisco county, California. *Ann Intern Med* 2000; 132: 182-90.

Redd SC, Rutherford GW, Sande MA, Lifson AR, Hadley WK, Facklam RR. The role of human immunodeficiency virus infection in pneumococcal bacteremia in San Francisco residents. *J Infect Dis* 1990; 162: 1012-7.

Selwyn PA, Alcabes P, Hartel D, *et al*. Clinical manifestations and predictors of disease progression in drug users with human immunodeficiency virus infection. *N Engl J Med* 1992; 327:1697-703.

Tudela P, Tor J, Llibre JM, *et al*. *Haemophilus influenzae* pulmonary infection in patients with the human immunodeficiency virus. *Med Clin* (Barc) 1992; 99: 324-6.

Watanabe NA, Hiruma R, Katsu K. Comparative *in vitro* activities of newer cephalosporins cefcidin, cefepime and cefpirome against ceftazidime- or imipenem-resistant *Pseudomonas aeruginosa*. *J Antimicrob Chemother* 1992; 30: 633-41.

Witt DJ, Craven DE, McCabe WR. Bacteremia infections in adult patients with the acquired immune deficiency syndrome (AIDS) and AIDS-related complex. *Am J Med* 1987; 82: 900-6.