

# Pneumococcal Infection and the Trend in Penicillin Resistance at Srinagarind Hospital 1995 to 1999

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## Abstract

Penicillin-resistant *Streptococcus pneumoniae* (PRSP) is a growing problem throughout the world including Thailand. We retrospectively reviewed antimicrobial susceptibility of *S. pneumoniae* to penicillin at Srinagarind Hospital from January 1995 to December 1999. The average annual incidence of invasive pneumococcal disease in our hospital was 0.6 per 1,000 hospital admissions per year. There were 107 clinical isolates of *S. pneumoniae* from 95 patients. The PRSP strains were screened by oxacillin-disk diffusion method. Bacteremia was the most common (68%) source, followed by cerebrospinal fluid (17%), pleural fluid (6.5%) and a variety of others (8.5%). The incidence of PRSP infection from 1995 to 1999 was 6.3, 5.3, 0, 30 and 14.3 percent, respectively. Accordingly, PRSP in pneumococcal-infected patients could be becoming a major therapeutic problem in our hospital in the near future and close monitoring is recommended. (*J Infect Dis Antimicrob Agents* 2000;17:97-100.)

## INTRODUCTION

Penicillin-resistant strains of *Streptococcus pneumoniae* (PRSP) have been reported worldwide and are becoming more prevalent. During the past decade, the emergence of pneumococcal resistance to many antimicrobial agents (drug-resistant strains of *S. pneumoniae*; DRSP) has also spread and complicated the treatment of invasive pneumococcal infections, especially meningitis.<sup>1-5</sup> A prevalence of resistance was reported in Europe, South Africa and the United States.<sup>1-7</sup> Recent data from a study by the Asian Network for Surveillance of Resistant Pathogens (ANSORP) revealed high rates of PRSP in many Asian countries, ranging from 21 to 80

percent.<sup>8</sup> In Thailand, between 1995 and 1999, the prevalence of PRSP ranged between 15 to 70 percent based on evidence from several university hospitals in Bangkok and a university hospital in Chiang Mai.<sup>9-10</sup>

High-dose penicillin or broad-spectrum cephalosporins have been used successfully to treat many types of invasive PRSP infections except for meningitis. Adding vancomycin to the broad-spectrum cephalosporins for empirical treatment of pneumococcal meningitis is recommended in areas where highly penicillin-resistant or intermediate-to highly-cephalosporin-resistant pneumococci become prevalent. Thus local prevalence of resistant pneumococci should be studied to determine the

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empirical regimen in treating meningitis.

## MATERIAL AND METHODS

We retrospectively reviewed invasive pneumococcal infections to find a trend in penicillin resistance from microbiological laboratory data in our hospital. Srinagarind Hospital is a tertiary care, 760-bed, university hospital located in Northeast Thailand. All pneumococcal isolates were collected from clinical specimens between January 1, 1995 and December 31, 1999. Only isolates obtained from normally sterile body sites were included in the analysis.

Pneumococci were screened for susceptibility to penicillin with a 1 µg oxacillin disk (BBL® Sensi-Disc® Antimicrobial Susceptibility Test Discs; Becton Dickinson, Cockeysville, USA) by the disk diffusion method. Isolates with an inhibition zone of <20 mm were considered resistant to penicillin. For these strains, the minimal inhibitory concentration (MIC) was determined by E-testing for penicillin (Etest®; AB Biodisk, Solna, Sweden). The MIC for cefotaxime is not a routine investigation in our microbiological labs so it was only done when required.

Clinical data (*i.e.*, age, sex, underlying diseases or predisposing factors, clinical presentation, treatment and clinical outcome) of patients with invasive PRSP diseases were obtained from the hospital records.

## RESULTS

During the 5-year study period, 107 clinical isolates of *S. pneumoniae* from sterile sites were collected from 95 patients at Srinagarind Hospital. Bacteremia was the most common source (73 isolates; 68%), followed by cerebrospinal fluid (18 isolates; 17%), pleural fluid (7 isolates; 6.5%) and the others (9 isolates; 8.5%), which included synovial fluid (2), sinus aspirates (1), vitreous fluid (2) and closed abscesses (4).

The average annual incidence of invasive pneumococcal disease (bacteremia, meningitis, empyema thoracis, endophthalmitis, septic arthritis and closed-space abscesses) in our hospital was 0.6 per 1,000 hospital admissions per year. Overall, the isolates from 85 cases (89.5%) were penicillin-susceptible and 10 (10.5%) were penicillin-resistant. The incidence of PRSP infection was 6.3, 5.3, 0, 30

and 14.3 percent for the years 1995 to 1999, respectively (Fig. 1). The clinical data of patients who had invasive PRSP diseases are shown in Table 1.

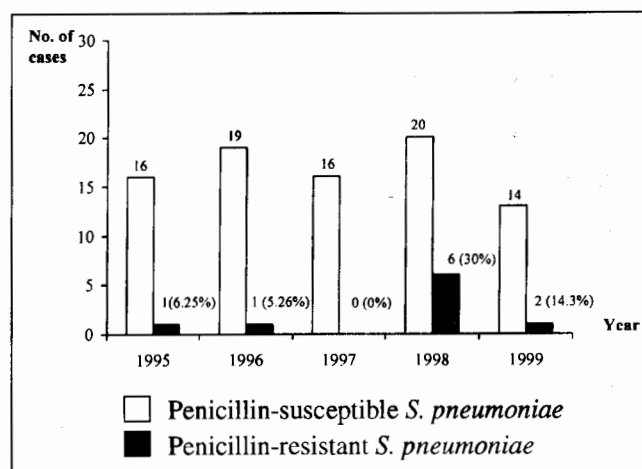


Fig. 1 Pneumococcal isolates by year, 1995-1999.

There were ten cases of PRSP infection; six were children below 15 years of age. Most of them had underlying illnesses such as: human immunodeficiency virus infection (2 cases), steroid use (3 cases), alcohol-induced liver cirrhosis (1 case), acute leukemia (1 case) or systemic lupus erythematosus (1 case). Six cases presented with pneumonia, three had bacteremia and another three developed complicated empyema thoracis. Two cases presented with primary pneumococcal septicemia and another two presented with meningitis. One had severely complicated meningitis with cerebritis and subdural empyema at admission.

Different antimicrobial agents were given to these ten patients: high-dose penicillin G sodium (2), ceftriaxone (2), cefotaxime (2), ampicillin (1), cefotaxime and vancomycin (1), amoxicillin/clavulanate (1), cotrimoxazole (1). All the patients responded well to the treatment given. However, two cases died due to hospital-acquired sepsis.

The MIC to penicillin was performed in five cases and ranged from 0.064 to 0.5 µg/mL. The MIC to cefotaxime was performed for only the case complicated with meningitis, and was 0.06 µg/mL.

## DISCUSSION

The increasing numbers of drug-resistant *S. pneumoniae* in various parts of the world during the past decade have raised the concern that we shall soon not have adequate, effective antibiotics to

**Table 1. Clinical features of patients infected with penicillin-resistant *S. pneumoniae*.**

No.	Age (yr.)	Sex	Risk factors/ Underlying Disease	Diagnosis	Antibiotic treatment	Outcome	MIC (mg/L)
1.	3/12	M	Biliary atresia	Meningitis Septicemia	Ampicillin	Recovered	ND
2.	5/12	M	No	Meningitis Cerebritis Subdural Empyema	Cefotaxime Vancomycin	Death	0.125
3.	41	M	Cirrhosis	Pneumonia Empyema	Coamoxiclav	Recovered	ND
4.	3	M	AIDS Tuberculous lymphadenitis	Pneumonia Septicemia	Cotrimoxazole	Recovered	ND
5.	4	F	Nephrotic syndrome Steroid user Hb E disease	Septicemia	Ampicillin	Death	ND
6.	9	M	Nephrotic syndrome Steroid user	Pneumonia Septicemia	PGS	Recovered	ND
7.	73	M	Old CVA	Pneumonia Septicemia	PGS	Recovered	0.25
8.	18	F	SLE Steroid user	Pneumonia Empyema	Ceftriaxone	Recovered	0.5
9.	9	M	AMMoL Neutropenia AIDS	Septicemia	Cefotaxime	Recovered	0.064
10.	31	M		Pneumonia Empyema	Ceftriaxone	Recovered	0.125

Note: ND: not done, CVA: cerebrovascular accident, SLE: systemic lupus erythematosus, AMMoL: acute myelomonoblastic leukemia.

AIDS: acquired immunodeficiency syndrome, Hb: hemoglobin, MIC: minimal inhibitory concentration to penicillin, PGS: penicillin G sodium

fight life-threatening bacterial infections. Recent data from the ANSORP study showed an alarming prevalence of penicillin resistance in Thailand (57%). However, data collection was limited to two university hospitals in Bangkok and might not represent the overall prevalence of PRSP in the country.<sup>8</sup>

The emergence of pneumococcal resistance and documented microbiological failure of the treatment regimen for pneumococcal meningitis with broad-spectrum cephalosporins led to the accepted empirical therapy of ceftriaxone or cefotaxime plus vancomycin for cases of suspected pneumococcal meningitis.<sup>11-14</sup> This combination therapy is expensive and not cost-effective in areas where resistant pneumococci is uncommon. Moreover, this treatment may put antibiotic pressure on this organism to develop resistance. As a consequence, establishing the local prevalence of resistant pneumococci is crucial, and should rather guide initial antibiotic

therapy in the invasive pneumococcal infection cases. In areas where high resistance to penicillin and intermediate- to high-resistance to ceftriaxone and cefotaxime (MIC  $\geq 1.0$   $\mu\text{g/mL}$ ) are significant (>5%), the addition of vancomycin to ceftriaxone or cefotaxime is necessary in pneumococcal meningitis cases until antibiotic susceptibility testing has been completed.<sup>9</sup>

According to our data, in our hospital, the average annual incidence of invasive pneumococcal disease is low. The incidence of invasive PRSP diseases has tended to rise over the 5-year study period, even without including all cases of pneumonia. This is because we included only pneumococcal pneumonia cases, who had positive blood culture or who were complicated with empyema thoracis and had culture-proven of *S. pneumoniae*. Moreover, in our retrospective of microbiological laboratory data, we could not differentiate between true pathogens or

colonized isolates in the sputum.

In our study, only 4 isolates were tested for penicillin MIC by E-test, and they showed an intermediate-resistance to penicillin (0.064-0.5 µg/mL). The only isolate tested for third-generation-cephalosporin MIC showed susceptible to cefotaxime (0.06 µg/mL). Combining these MIC results and the clinical response to high-dose penicillin and third-generation-cephalosporins, suggested that the prevalence of high penicillin resistance or intermediate and high cephalosporin resistance in our hospital is low.

In conclusion, however, the upward trend of drug-resistant pneumococcal infection in our hospital is a warning that we may also have an emerging problem, therefore, close monitoring is essential.

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