Invasive Pneumococcal Infection and Drug-Resistant *Streptococcus pneumoniae* in Thai Children†

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Abstract

Sixty-eight children with systemic *Streptococcus pneumoniae* infection were identified by hospital chart review between 1986-1997. The age distribution varied from 2 days to 15 years, with a mean age of 3.3 years. There were 35 boys and 33 girls. Four clinical entities included 30 cases of meningitis, 20 cases of pneumonia, 10 cases of peritonitis and 8 cases of septicemia/bacteremia. Forty patients (58.8%) had underlying diseases. Seventeen patients (25.0%) developed early complications and the mortality rate was 8.8 per cent. The percentage of susceptible isolates to penicillin, chloramphenicol, cefotaxime/ ceftriaxone, ciprofloxacin, imipenem and vancomycin were 69.6, 91.3, 100.0, 87.2, 100.0 and 97.1 per cent, respectively. There were six cases of drug-resistant *S. pneumoniae* (DRSP) infection; 3 cases of meningitis, one case of pneumonia, one case of infective endocarditis and one case of purpura fulminans. Our data indicate that *S. pneumoniae* infection is relatively serious and life-threatening. There is a trend of increasing prevalence of invasive pneumococcal and DRSP infections.

Key word : Pneumococcus, *S. pneumoniae*, DRSP, children

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Streptococcus pneumoniae (*S. pneumoniae*) is one of the leading bacterial pathogens causing illness and death among young children, the elderly, and immunocompromised patients[1]. The first isolate of drug-resistant *S. pneumoniae* (DRSP) was reported in 1967 and the prevalence of this organism is increasing alarmingly worldwide, including Southeast Asian countries and Thailand[2]. The authors

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conducted this study to elucidate the natural history of invasive pneumococcal disease and the prevalence of invasive DRSP infection in Thai pediatric patients.

MATERIAL AND METHOD

The authors reviewed the microbiology records of children aged between 0 and 15 years, who were admitted to King Chulalongkorn Memorial Hospital, from whom positive cultures for *S. pneumoniae* or positive antigen detection for pneumococcus were obtained from normally sterile clinical specimens including blood, cerebrospinal fluid (CSF), pleural fluid and ascitic fluid, from January 1986 to December 1997. The information obtained from the medical record of each patient included age, sex, month of admission, clinical presentation, underlying diseases, complete blood count, bacteriologic results, susceptibility test, minimum inhibitory concentration (MIC), early complications and mortality of the patients.

RESULTS

Of 82 cases from the microbiology records, 74 cases had positive culture for *S. pneumoniae* and 8 cases had positive countercurrent immunoelectrophoresis (CIE) for pneumococcal antigen only. Medical chart records of 68 patients (82.9%) were completely reviewed. Susceptibility tests were reviewed in 59 out of 74 isolates (79.7%). MIC was done in 8 out of 17 strains (47.1%) which were resistant to oxacillin disc.

Clinical Data

Ages of the 68 patients ranged from 2 days to 15 years, with a mean age of 3.3 years and a peak age of 0-2 and > 5 years. There were 35 males and 33 females with a male to female ratio of 1.1:1. The peak incidence was from December to February. Forty patients (58.8%) had underlying diseases. White blood cell (wbc) counts ranged from 2,900 to 52,600 cells/mm^3 and 74.2 per cent of patients had wbc count > 10,000 cells/mm^3. The percentage of neutrophils ranged from 10 to 95. Early complications developed in 17 patients (25.0%) and the overall mortality rate was 8.8 per cent.

Clinical presentations included meningitis (30), pneumonia (20), peritonitis (10) and septicemia/bacteremia (8) and microbiologic results are shown in Table 1.

Pneumococcal meningitis

Of 30 cases, there were 16 females and 14 males, with an age range between 2 days and 11 years and a mean age of 2.2 years. Thirteen patients had underlying diseases: thalassemia (3), meningocele (3), hydrocephalus (2), prematurity (2), malignancies (2) and malnutrition (1). Eleven patients developed early complications: subdural effusion (10), ventriculitis (2) and brain abscess (1). The mortality rate was 16.7 per cent.

Pneumococcal pneumonia

Of 20 cases, there were 11 females and 9 males, with an age range between 3 months and 15 years and a mean age of 4 years. Thirteen patients had underlying diseases: neurologic abnormalities (4), systemic lupus erythematosus (SLE) (3), human immunodeficiency virus (HIV) infection (2), malnutrition (2), biliary atresia (1) and postmeasles status (1). Six patients developed early complications: pleural effusion (3) and empyema (3). There was no mortality in this group.

Pneumococcal peritonitis

Of 10 cases, there were 4 females and 6 males, with an age range between 7 months and 12 years and a mean age of 4.5 years. Nine patients

Table 1. Clinical presentations and microbiologic results in children with invasive pneumococcal infections.

Clinical presentation	Number of cases	Positive culture				CIE
		Blood	Pleural fluid	Ascitic fluid	CSF	
Meningitis	30	10	-	-	22	17
Pneumonia	20	18	2	-	-	2
Peritonitis	10	7	-	5	-	-
Septicemia/bacteremia	8	8	-	-	-	-

Note: CSF = cerebrospinal fluid, CIE = countercurrent immunoelectrophoresis

Table 2. Susceptibility of 59 strains of *S. pneumoniae* by disc diffusion method.

Antibiotics	Number of tests	% susceptibility
Amikacin	25	28.0
Pefloxacin	18	44.4
Penicillin	56	69.6
Clindamycin	40	77.5
Cotrimoxazole	28	85.7
Ciprofloxacin	39	87.2
Chloramphenicol	23	91.3
Amoxicillin/clavulanate	26	96.2
Vancomycin	35	97.1
Cefazolin	43	97.7
Cefotaxime/Ceftriaxone	8	100.0
Imipenem	13	100.0

had underlying diseases: cirrhosis (5) and nephrotic syndrome (NS) (4). One patient died.

Pneumococcal septicemia/bacteremia

Of 8 cases, there were 2 females and 6 males, with an age range between 5 months and 11 years and a mean age of 4.1 years. Five patients had underlying diseases: thalassemia (1), NS (1), cirrhosis (1), acute lymphoblastic leukemia (1) and congenital heart disease (1). There was no mortality in this group.

Microbiologic data

The susceptibility tests by disc diffusion method were performed on 59 strains of *S. pneumoniae* using 12 different antibiotics with results shown in Table 2.

MIC for penicillin and ceftriaxone using E-test were performed in eight strains resistant to oxacillin disc and revealed six cases of drug-resistant *S. pneumoniae* (DRSP) (MIC for penicillin $\geq$ 0.12 mcg/ml) with 4 cases of high level resistance (MIC for penicillin $\geq$ 2 mcg/ml) and 2 cases of low level resistance (MIC for penicillin = 0.12 -1.0 mcg/ml) (Table 3). All resistant strains were found between 1995-1997. There were nine more strains, eight of them were found between 1992-1997, which were resistant to oxacillin disc but MICs were not performed (Table 4). The prevalence of DRSP was approximately 10 per cent and 30 per cent of all invasive pneumococcal infections in children from 1986-1997 and 1995-1997 respectively.

Clinical and Microbiology data

Strain of *S. pneumoniae* categorized into penicillin-sensitive (PSSP), penicillin-resistant by oxacillin disc (MIC not performed) and DRSP in each clinical presentation is shown in Table 4.

Details of the patients with invasive DRSP infections are summarized in Table 5.

DISCUSSION

Our data show that systemic pneumococcal infection is a potentially serious illness in children, with significant complication and high mortality rate, especially in those with meningitis. These are not much different from previous reports on invasive

Table 3. MIC for penicillin and ceftriaxone in eight strains resistant to penicillin.

Oxacillin disc	MIC (mcg/ml)		Interpretation
	Penicillin	Ceftriaxone	
R	4	4	DRSP, high level
R	0.75	0.38	DRSP, low level
R	3	1.5	DRSP, high level
R	2	0.75	DRSP, high level
R	0.75	0.5	DRSP, low level
R	2	0.75	DRSP, high level
R	0.032	0.064	PSSP
R	0.023	ND	PSSP

Note: MIC = minimum inhibitory concentration,
mcg/ml = microgram per milliliter,
R = penicillin resistant by oxacillin disc, DRSP = drug-resistant *S. pneumoniae*, PSSP = penicillin-sensitive *S. pneumoniae*, ND = not done

Table 4. Types of *S. pneumoniae* and clinical presentation.

Clinical presentation	Number of cases	Types of *S. pneumoniae*		
		PSSP	Resist oxacillin	DRSP
Meningitis	24	18	3	3
Pneumonia	19	16	2	1
Peritonitis	10	9	1	-
Septicemia/bacteremia	8	3	3	2
Total	61	46	9	6

Note: PSSP = penicillin-sensitive *S. pneumoniae*,
Resist oxacillin = resistant to oxacillin disc (MIC not done),
DRSP = drug-resistant *S. pneumoniae*

Table 5. Details of children with DRSP infections.

Year	Age	Underlying	Presentation	MIC (mcg/ml)		Outcome
				Pen	Cro	
1995	3 years	Thalassemia	Meningitis	0.75	0.38	Survive
1996	1 $^{2}/_{12}$ years	HIV infection	Pneumonia	0.75	0.5	Survive
1996	10 months	No	Meningitis	4.0	4.0	Survive
1996	4 years	CHD	IE	3.0	1.5	Survive
1997	3 months	No	Meningitis	2.0	0.75	Survive
1997	3 years	No	Purpura fulminans	2.0	0.75	Survive

Note: MIC = minimum inhibitory concentration, Pen = penicillin, Cro = ceftriaxone,
mcg/ml= microgram per milliliter, CHD = congenital heart disease, IE = infective endocarditis

Haemophilus influenzae and meningococcal infections in Thai children and invasive pneumococcal infection in Thai adults[3-5]. Underlying diseases including immunosuppression in our subjects may be a major risk for pneumococcal infection.

There are increasing reports of Thai children with invasive DRSP infection[6,7]. Our data revealed that the prevalence of DRSP infection was approximately 30 per cent of invasive pneumococcal infections occurring in the past three years. The isolates were cultured from specimens obtained from normally sterile sites of hospitalized children. The prevalence in our study was less than that from other reports[8], probably due to the differences in specimens, year of study, age of patients and size of hospitals. Annual surveillance of this organism is essential.

Two-thirds of our patients occurred in the second half of the study period. The increasing trend may be due to the increasing risk of immunosuppression and the increasing trend of DRSP infection among Thai children which were found mostly in the second half of the study period.

In conclusion, *S. pneumoniae* infection is relatively serious and life-threatening. There is a trend of increasing prevalence of invasive pneumococcal and DRSP infections.

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การติดเชื้อ*นิวโมค็อคคัส*อย่างรุนแรงและการดื้อของเชื้อต่อยาต้านจุลชีพในเด็กไทย†

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การศึกษาผู้ป่วยเด็กที่ติดเชื้อ*นิวโมค็อคคัส*อย่างรุนแรงและได้รับการรักษาที่โรงพยาบาลจุฬาลงกรณ์ระหว่างปี พ.ศ. 2529-2540 จำนวน 88 คน พบว่าผู้ป่วยมีอายุระหว่าง 2 วันถึง 15 ปี (อายุเฉลี่ย 3.3 ปี) เป็นเพศชาย 35 คน เพศหญิง 33 คน อาการทางคลินิกจำแนกเป็นภาวะเยื่อหุ้มสมองอักเสบ 30 คน ภาวะปอดอักเสบ 20 คน ภาวะเยื่อบุช่องท้องอักเสบ 10 คน และภาวะติดเชื้อในกระแสโลหิต 8 คน ร้อยละ 58.8 ของผู้ป่วยมีภาวะนำเดิมมาก่อน ร้อยละ 25 เกิดภาวะแทรกซ้อน และร้อยละ 8.8 เสียชีวิต ความไวของเชื้อต่อยาต้านจุลชีพ penicillin, chloramphenicol, cefotaxime/ceftriaxone, ciprofloxacin, imipenem และ vancomycin คิดเป็นร้อยละ 69.6, 91.3, 100.0, 87.2, 100.0 และ 97.1 ตามลำดับ ผู้ป่วยจำนวน 6 คนติดเชื้อซึ่งดื้อต่อยาต้านจุลชีพ จำแนกเป็นผู้ป่วยที่มีภาวะเยื่อหุ้มสมองอักเสบ 3 คน ภาวะปอดอักเสบ ภาวะเยื่อบุลิ้นหัวใจอักเสบ และภาวะ purpura fulminans อย่างละ 1 คน ข้อมูลจากการศึกษาบ่งชี้ว่าการติดเชื้อ pneumococcus เป็นภาวะรุนแรงซึ่งอาจทำให้ผู้ป่วยเสียชีวิต มีแนวโน้มเพิ่มขึ้นของการติดเชื้อดังกล่าวรวมทั้งเชื้อซึ่งดื้อต่อยาต้านจุลชีพด้วย

คำสำคัญ : *นิวโมค็อคคัส*, ดื้อยา, เด็ก

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