



ORIGINAL ARTICLE

Updated antibiotic resistance and clinical spectrum of infections caused by *Streptococcus pneumoniae* in Taiwan: Emphasis on risk factors for penicillin nonsusceptibilities



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KEYWORDS

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Background/Purpose(s): *Streptococcus pneumoniae* is one of the leading pathogens causing community-acquired infection with high mortality rates in elderly patients. Emerging antibiotic resistance was found in past decades. Continuous surveillance to monitor changes in antibiotic resistance of *S. pneumoniae* and associated risk factors are important clinical issues.

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Streptococcus pneumoniae

Methods: Isolates of *S. pneumoniae* collected from six hospitals participating in the Taiwan Surveillance of Antimicrobial Resistance (TSAR) program III (2002) – VI (2008) were enrolled in this study. Bacterial susceptibilities were determined by minimum inhibitory concentration. The clinical data of source patients were collected retrospectively.

Results: A total of 330 nonduplicate *S. pneumoniae* isolates were enrolled in this study. Sputum was the most common specimen source, followed by pus. The mean age of the source patients was 38 years among these 330 patients, and 247 had various infections caused by *S. pneumoniae*. The overall in-hospital mortality rate was 6% and most (60%) of the mortality occurred in patients older than 65 years. The mortality rates among the patients age 65 years and older and those age 5 years and younger were 12.9% (9 of 70) and 2.4% (2 of 83), respectively. The rates of nonsusceptibility to penicillin by the meningitis criteria (PNSP-M) were 69.0% in 2002, 81.0% in 2004, 73.7% in 2006, and 74.5% in 2008. Resistance to erythromycin and trimethoprim/sulfamethoxazole remained high. Using multivariate analysis, patients with PNSP isolates were more likely to have a history of antibiotic exposure within the previous 15 days compared with patients with penicillin-susceptible (PSSP) isolates (nonmeningitis criteria: 29.70% vs. 18.34%, $p = 0.0288$; meningitis criteria: 25.30% vs. 9.88%, $p = 0.006$). Shock at presentation was the risk factor for in-hospital mortality.

Conclusion: Our study demonstrated that the rates of penicillin nonsusceptibility among *S. pneumoniae* remained high in Taiwan during the study period. Previous antibiotic exposure was the only risk factor for subsequent acquisition of penicillin-nonsusceptible *S. pneumoniae* compared with penicillin-susceptible *S. pneumoniae*. Judicious antibiotic use is important to control the spread of drug nonsusceptible *S. pneumoniae*.

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Introduction

Streptococcus pneumoniae is one of the most common pathogens causing community-acquired infections. The major invasive pneumococcal diseases include pneumonia, bacteremia, and meningitis and can result in high mortality despite antimicrobial therapy, ranging from 20% to 50%.^{1–4} Penicillin used to be the most important antibiotic against invasive pneumococcal diseases. However, resistance to penicillin has been noted since 1967.⁵ Prior to 2008, the penicillin susceptibility breakpoint for *S. pneumoniae* was 0.12 µg/mL.⁶ In 2008, Clinical and Laboratory Standards Institute (CLSI) provided two different criteria for penicillin susceptibility.⁷ For meningitis (M) isolates, *S. pneumoniae* with penicillin minimum inhibitory concentration (MIC) ≥ 0.12 µg/mL was classified as penicillin nonsusceptible *S. pneumoniae* meningitis (PNSP-M). For nonmeningitis (NM) isolates, *S. pneumoniae* with penicillin MIC ≥ 4 µg/mL was classified as penicillin nonsusceptible *S. pneumoniae* nonmeningitis (PNSP-NM). According to previous studies in other regions, the prevalence of penicillin nonsusceptibility among *S. pneumoniae* increased rapidly since the 1990s, regardless of using M or NM criteria.^{8,9}

High prevalence of PNSP-M (>60%) was reported by several studies conducted during the late 20th and early 21st centuries in Taiwan.^{3,10,11} However, two major public health events have occurred in Taiwan since those studies. First, prescription of antibiotics for patients with acute upper respiratory tract infection without clinical evidence of bacterial infection has been restricted since 2001.¹² Second, vaccination of seven-valent pneumococcal conjugated vaccine (PCV-7) for children with high risk for pneumococcal infection was implemented in October 2005. Introduction of PCV-7 might reduce the antibiotic resistance in pneumococci due to shifting of prevalent pneumococcal serotypes.⁹

Whether the penicillin susceptibility of pneumococci in Taiwan changed after these two major events remained unclear. The current study was conducted to investigate the secular trend of antibiotic susceptibility in *S. pneumoniae* and to identify factors association with acquisition of penicillin-nonsusceptible *S. pneumoniae* in Taiwan.

Patients and methods

Bacterial isolates

S. pneumoniae isolates were collected as part of the Taiwan Surveillance of Antimicrobial Resistance (TSAR) program from medical centers and regional hospitals throughout Taiwan. The participating hospitals are located in the four geographic regions (northern, central, southern, and eastern) of Taiwan. TSAR has been conducted biennially since 1998 and data from TSAR I (1998) and II (2000) have been reported.^{13,14} TSAR III – VI (2002, 2004, 2006, 2008) isolates were collected between July and September from the same 26 hospitals, except for 2006 when isolates were from 25 hospitals. To obtain relevant clinical data, only the bacterial isolates and their source patients whose associated information could be obtained were enrolled in the current study. The associated demographic, clinical, and laboratory data of source patients from whom the bacteria were isolated were collected to investigate the risk factors for acquiring PNSP-M or PNSP-NM and mortality among patients with pneumococcal infections.

Antimicrobial susceptibility test

Antimicrobial susceptibilities to various antimicrobial agents, including penicillin, chloramphenicol, ceftriaxone,

erythromycin, trimethoprim/sulfamethoxazole, levofloxacin, and tetracycline were determined by MIC using the CLSI reference microbroth dilution method.¹⁵ For penicillin and ceftriaxone, NM and M criteria were used.⁷ PNSP-NM referred to isolates with penicillin MIC ≥ 4 $\mu\text{g}/\text{mL}$ whereas PSSP-NM (penicillin-susceptible *S. pneumoniae* nonmeningitis) referred to isolates with penicillin MIC ≤ 2 $\mu\text{g}/\text{mL}$ using the NM criteria. PNSP-M referred to isolates with penicillin MIC ≥ 0.12 $\mu\text{g}/\text{mL}$ whereas PSSP-M isolates had penicillin MIC ≤ 0.06 $\mu\text{g}/\text{mL}$ using the M criteria. Isolates with ceftriaxone MIC ≥ 2 $\mu\text{g}/\text{mL}$ and ≤ 1 $\mu\text{g}/\text{mL}$ were considered ceftriaxone nonsusceptible and susceptible, respectively, by the NM criteria. By the M criteria, ceftriaxone nonsusceptible and susceptible *S. pneumoniae* referred to those with ceftriaxone MIC ≥ 1 $\mu\text{g}/\text{mL}$ and ≤ 0.5 $\mu\text{g}/\text{mL}$, respectively.⁷

Statistical analysis

Continuous variables were described as mean \pm standard deviation (SD) and compared using the Student *t* test, or described as the median as well as range and compared with the Wilcoxon rank-sum test if their distributions were not normal. Categorical variables were compared with a chi-square test or Fisher exact test if the expected values were less than 10. Risk factors for penicillin nonsusceptibility and all-cause in-hospital mortality were identified using logistic regression models. Statistical analyses were performed using SAS 9.1.3 (SAS Institute, Cary, NC, USA). All tests were two-tailed and $p < 0.05$ was considered statistically significant.

Results

A total of 331 pneumococcal isolates collected between 2002 and 2008 (corresponding to TSAR III-VI) and their source patients from six hospitals, including three medical centers and three regional hospitals, were enrolled in the current study initially. One patient was excluded due to missing data. Information on patient demographics and clinical data is presented in Table 1. The mean age of the 330 patients from whom the isolates were obtained was 38 years. The male to female ratio was 217:96 (the sex of 17 patients was unknown). Sputum was the most common specimen source, followed by pus/wound. The most common underlying disease was cardiovascular disease. Based on clinical data, 247 of the 330 patients were determined to be infected and 70 were colonized (Table 1).

By NM criteria, the overall penicillin nonsusceptible rate among the 330 studied isolates was 30.4% (Table 2). During the study period, there was a transient decrease in PNSP-NM in TSAR V (2006) isolates compared with isolates of TSAR III, IV, and VI ($p = 0.031$) (Fig. 1). The overall nonsusceptibility to ceftriaxone was 19.4% by the NM criteria. Almost all (92%) of the study isolates were resistant to erythromycin and 70% were nonsusceptible to trimethoprim/sulfamethoxazole. Levofloxacin showed good activity (TSAR III: 100%; TSAR IV: 95.1%; TSAR V: 97.4; TSAR VI: 96.6%) against the tested isolates (Table 2).

By M criteria, the overall penicillin nonsusceptibility was 75.7%. The proportion of PNSP-M was also lower in isolates

of TSAR V compared with isolates of TSAR III, IV, and VI, but the difference was not statistically significant ($p = 0.549$). Sixty-three percent of the 330 pneumococci isolates were nonsusceptible to ceftriaxone by the M criteria (Table 2).

Patients with PNSP-NM or PNSP-M isolates were more likely to have a history of antibiotic exposure within the previous 15 days compared with patients with PSSP by either NM or M criteria (NM: 29.70% vs. 18.34%, $p = 0.0288$; M: 25.30% vs. 9.88%, $p = 0.006$). Using univariate and multivariate analysis by logistic regression models, previous antibiotic exposure was an independent risk factor for acquiring PNSP-NM or PNSP-M isolates (PNSP-NM, odds ratio [OR]: 2.848, 95% confidence interval [CI]: 1.374-5.901, $p = 0.0049$; PNSP-M, OR-3.730, 95% CI: 1.644-8.459, $p = 0.002$) (Table 3). No specific antibiotic used previously could be identified to be associated with acquiring PNSP.

Among the 247 pneumococci-infected patients, the mean age was 36 years and lower respiratory tract infection was the most common foci (144 of 247). PNSP-NM accounted for 32% (79 of 247) of all invasive pneumococcal infections and the overall in-hospital mortality was 6% (15 of 247). Sixty percent of the mortality cases (9 of 15) occurred in patients older than 65 years. The mortality rates among the patients older than 65 years and those younger than 5 years were 12.9% (9 of 70) and 2.4% (2 of 83), respectively. There was no difference in mortality between PSSP-NM and PNSP-NM infected patients or between PSSP-M and PNSP-M infected patients (PSSP-NM vs. PNSP-NM: 5.88% vs. 8.00%, $p = 0.5755$; PSSP-M vs. PNSP-M: 6.55% vs. 6.45%, $p = 1.000$). There was also no difference in mortality between patients with infection caused by ceftriaxone susceptible and nonsusceptible strains either by NM or M criteria (NM criteria: 5.91% vs. 9.09%, $p = 0.4960$; M criteria: 7.77% vs. 5.73%, $p = 0.5950$). Shock at presentation was the only risk factor for in-hospital mortality for patients with infection caused by *S. pneumoniae* either by univariate or multivariate analysis (OR: 40.1, 95% CI: 7.5 - 213.4, $p < 0.0001$).

Discussion

The emergence and rapid dissemination of antibiotic-resistant pneumococcal strains has been noted since the 1990s, and was found to be associated with previous antibiotic consumption.^{16,17} Our study of pneumococcal isolates from six hospitals showed that the rates of penicillin nonsusceptibility in *S. pneumoniae* in Taiwan, either by M or NM criteria, remained high in Taiwan. However, there was a transient decrease in penicillin nonsusceptibility in TSAR V (2006), especially by NM criteria ($p = 0.031$).

Transient decreased penicillin nonsusceptibility in pneumococci was also noted in the SENTRY Antimicrobial Surveillance Program,⁹ and in a surveillance system in Spain (Spanish Reference Laboratory for Pneumococci, SRLP).¹⁸ In the SENTRY program, it was found that the rates of β -lactam nonsusceptibility in pneumococci increased during 1998-2001 but later decreased during 2002-2003, and then increased again during 2004 and 2009. In that surveillance, penicillin and ceftriaxone nonsusceptibility of pneumococci (by NM criteria) in 2008 was

Table 1 Comparison of demographics and clinical characteristics of 330 patients with carriage or infection by *S. pneumoniae* stratified by penicillin susceptibility

Parameters	Nonmeningitis criteria			Meningitis criteria		
	PSSP-NM (N = 229)	PNSP-NM (N = 101)	<i>p</i>	PSSP-M (N = 81)	PNSP-M (N = 249)	<i>p</i>
TSAR (yr), <i>n</i> (%)						
III (2002)	41 (17.90)	18 (18.00)	0.0081	18 (22.20)	40 (16.06)	0.3620
IV (2004)	63 (27.51)	41 (41.00)		20 (24.69)	85 (34.13)	
V (2006)	64 (27.95)	12 (12.00)		20 (24.69)	56 (22.48)	
VI (2008)	61 (26.64)	29 (29.00)		23 (28.40)	67 (26.90)	
Age, mean ± SD (y)	38.27 ± 30.68	39.00 ± 32.59	0.2527	43.10 ± 29.46	36.98 ± 31.71	0.0760
Male to female	152/67	65/29	0.9630	48/29	168/67	0.1150
Isolated specimen site, <i>n</i> (%)						
Blood	16 (6.98)	14 (13.86)	0.2741	9 (11.11)	22 (8.84)	0.8770
Sputum	123 (53.71)	56 (55.45)		43 (53.09)	135 (54.21)	
Urine	1 (0.44)	0 (0.00)		0 (0.00)	1 (0.40)	
Pus/wound	47 (20.52)	20 (19.80)		15 (18.52)	52 (20.88)	
Others	24 (10.48)	9 (8.91)		9 (11.11)	24 (9.62)	
Throat swab	12 (5.24)	1 (0.99)		4 (4.93)	9 (3.61)	
Nasal swab	3 (1.31)	1 (0.99)		0 (0.00)	4 (1.61)	
Underlying condition, <i>n</i> (%)						
DM	30 (13.10)	14 (13.86)	0.7601	8 (9.88)	36 (14.46)	0.1950
Renal dx	7 (3.06)	2 (1.98)	0.7290	1 (1.23)	8 (3.21)	0.4520
CAD	45 (19.65)	23 (22.77)	0.4129	17 (20.99)	51 (20.48)	0.8740
GI dx	12 (5.24)	8 (7.92)	0.3047	3 (3.70)	17 (6.82)	0.2970
Cancer	15 (6.55)	8 (7.92)	0.5920	3 (3.70)	20 (8.03)	0.1450
Immunosuppression	5 (2.18)	6 (5.94)	0.0912	2 (2.47)	9 (3.61)	0.7330
Neutropenia	1 (0.43)	0 (0.00)	1.0000	0 (0.00)	1 (0.40)	1.0000
Other	39 (17.03)	13 (12.87)	0.3916	14 (17.28)	38 (15.26)	1.0000
Respiratory dx	30 (13.10)	20 (19.80)	0.0837	16 (19.75)	34 (13.65)	0.3720
Neurologic dx	23 (10.04)	16 (15.84)	0.1006	9 (11.11)	30 (12.05)	0.6970
Hepatic dx	13 (5.68)	8 (7.92)	0.3924	4 (4.94)	17 (6.83)	0.4590
Autoimmune dx	3 (1.31)	0 (0.00)	0.5567	1 (1.23)	2 (0.80)	1.0000
Living in LTCF or RCW within recent 1 y, <i>n</i> (%)	14 (6.11)	12 (11.88)	0.0778	6 (7.40)	20 (8.03)	1.0000
Hospitalization within recent 1 y, <i>n</i> (%)	90 (39.30)	50 (49.50)	0.0986	28 (34.57)	111 (44.57)	0.1220
Invasive therapy (H/D, C/T) within recent 1 y, <i>n</i> (%)	10 (4.37)	1 (1.00)	0.1829	0 (0.00)	11 (4.44)	0.0720
Antibiotic use within prior 15 days, <i>n</i> (%)	42 (18.34)	30 (29.70)	0.0288	8 (9.88)	63 (25.30)	0.0060
Infection or colonization, <i>n</i> (%)						
Colonization	51 (22.27)	19 (18.81)	0.4392	16 (19.75)	54 (21.69)	0.7570
Infection	168 (73.36)	79 (78.21)		61 (75.30)	186 (74.70)	
Mortality, <i>n</i> (%)	15 (6.98)	6 (5.94)	1.000	6 (7.41)	15 (6.02)	0.7930

CAD = coronary artery disease; C/T = chemotherapy; DM = diabetic mellitus; dx = disease; GI = gastrointestinal; H/D = hemodialysis; LTCF = long-term care facility; M = meningitis; NM = nonmeningitis; RCW = respiratory care ward; PNSP-M = penicillin-nonsusceptible *S. pneumoniae* meningitis; PNSP-NM = penicillin-nonsusceptible *S. pneumoniae* nonmeningitis; PSSP-M = penicillin-susceptible *S. pneumoniae* meningitis; PSSP-NM = penicillin-susceptible *S. pneumoniae* nonmeningitis; SD = standard deviation; TSAR = Taiwan Surveillance of Antimicrobial Resistance.

13.5% and 8.7%,⁹ values that were lower than our study of 30.4% and 19.4%, respectively. In SRLP, the prevalence of PNSP-M decreased in the past decade, especially during 2005–2008.¹⁸ The decrease of penicillin nonsusceptibility rate in both programs was proposed to be associated with

the introduction of pneumococcal vaccine, which resulted in clonal shifts from multidrug-resistant (MDR) clones to non-MDR clones not covered by the vaccine.¹⁹ Studies on resistance in different serotypes in Taiwan have also shown that serotypes in PCV-7 vaccine have higher rates of

Table 2 Antibiotic susceptibilities of *S. pneumoniae* in different years

TSAR (y)	% of isolates susceptible								
	PEN-NM	PEN-M	CRO-NM	CRO-M	ERY	TMP/SMX	LVX	CHL	TCY
TSAR-III (2002)	69.5	31.0	78.1	44.1	10.2	37.2	100	49.2	3.3
TSAR-IV (2004)	60.5	19.0	85.6	32.7	9.4	23	95.1	55.1	6.7
TSAR-V (2006)	84.2	26.3	90.7	43.4	10.5	26.3	97.4	60.6	5.3
TSAR-VI (2008)	67.7	25.5	78.9	32.2	5.6	33.3	96.6	41.7	4.4
Overall	69.6	24.3	80.6	37.1	7.9	29.2	97	55.7	5.2

CHL = chloramphenicol; CRO-M = ceftriaxone by meningitis criteria (susceptible, minimum inhibitory concentration [MIC] \leq 0.5 μ g/mL; nonsusceptible, MIC \geq 1 μ g/mL); CRO-NM = ceftriaxone by nonmeningitis criteria (susceptible, MIC \leq 1 μ g/mL; nonsusceptible, MIC \geq 2 μ g/mL); ERY = erythromycin; LVX = levofloxacin; PEN-M = penicillin by meningitis criteria (susceptible, MIC \leq 0.06 μ g/mL; nonsusceptible, MIC \geq 0.12 μ g/mL); PEN-NM = penicillin by nonmeningitis criteria (susceptible, MIC \leq 2 μ g/mL; nonsusceptible, MIC \geq 4 μ g/mL); TCY = tetracycline; TMP/SMX = trimethoprim/sulfamethoxazole; TSAR = Taiwan Surveillance of Antimicrobial Resistance.

penicillin nonsusceptibility.^{20,21} Therefore, the transient decrease of penicillin nonsusceptibility in *S. pneumoniae* isolates collected in TSAR V (2006) might be related to the introduction of PCV-7 in Taiwan in 2005.

Our study also found that the proportion of PNSP-M was also lower in isolates of TSAR V compared with those of TSAR III, IV, and VI, but the difference was not statistically significant ($p = 0.549$). Fig. 2 demonstrates the cumulative distribution of MICs to penicillin of tested isolates. For the proportion of isolates with penicillin MIC \leq 1 μ g/mL, that of isolates from TSAR V was only slightly higher than those from TSAR III, IV, and VI. However, for the proportion of isolates with a penicillin MIC of 2 μ g/mL, that of isolates from TSAR V was much higher than those from TSAR III, IV, and VI. This is why there was a statistically significant decrease in PNSP-NM in TSAR V, but only a slight decrease (without statistical significance) in PNSP-M.

Decreased antibiotic usage resulting from restriction of antibiotics among patients in Taiwan with acute upper respiratory tract infection without clinical evidence of bacterial infection since 2001 has been reported.²² However, we did not find any decrease in rates of nonsusceptibility to erythromycin, tetracycline, and trimethoprim/sulfamethoxazole, three of the commonly used first-line antibiotics in Taiwan outpatients, in pneumococci in Taiwan. One reason for this is that pneumococci in Taiwan are mostly MDR.^{10,11,14} Thus, the use of one of the

antimicrobial agents would select for the MDR strains. The rates of erythromycin (92%) and trimethoprim/sulfamethoxazole (70%) nonsusceptibility in pneumococci in Taiwan remained much higher than isolates from the United States where nonsusceptibility to these two agents was 37% and 33%, respectively.⁹ Therefore, treatment choices are more limited for pneumococcal infections in Taiwan. Although resistance of pneumococci to levofloxacin did not increase significantly and remained at less than 5% overall during the study period, a finding similar to those from other countries,^{9,18,23} judicious use of this class of antibiotics is warranted.

Our study found that previous antibiotic exposure within 15 days before isolation of pneumococci was the only independent factor associated with penicillin nonsusceptibility using either N or NM criteria. Previous antibiotics exposure would facilitate the subsequent acquisition of drug-resistant bacteria due to selection pressure.^{24,25} It was therefore reasonable that we found previous antibiotic use to be associated with PNSP-M or PNSP-NM carriage/infection in the current study. Although previous studies from other countries have reported similar findings,^{24,26–28} this is the first report demonstrating the association of antibiotic use and penicillin-nonsusceptible pneumococci in Taiwan.

Compared with PSSP-M, infection caused by PNSP-M has been associated with higher mortality in some studies,^{1,29} but some studies found no association between penicillin-nonsusceptibility and poorer patient outcome.^{30,31} In the current study we found no significant difference in the mortality of patients infected by PSSP-M and PNSP-M or between PSSP-NM and PNSP-NM isolates but shock at presentation was significantly associated with in-hospital mortality in infected patients. The overall in-hospital mortality rate of pneumococcal disease in our study was 6%, a rate lower than those reported in previous studies, which ranged from 14% to 23%.^{31–33} The mortality rates among the patients age 65 years and older and age 5 years and younger (12.9% and 2.4%, respectively) were also lower than previous reports.^{34,35} Our study encompassed isolates from different sources and the proportion of patients with invasive pneumococcal disease was less than previous studies, which likely contributed to the lower mortality rate found in the current study. However, we did find 60% of

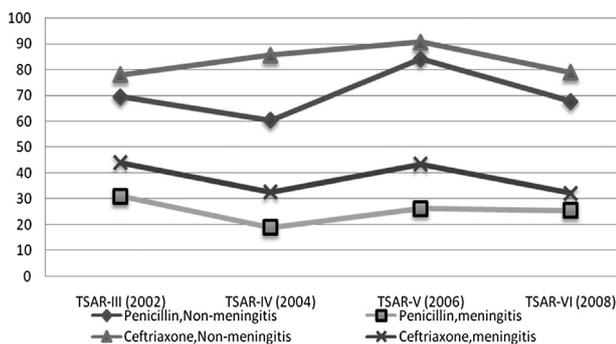


Figure 1. Trends of penicillin and ceftriaxone susceptibility in Taiwan Surveillance of Antimicrobial Resistance (TSAR) periods.

Table 3 Factors significantly associated with carriage or infection by PNSP-M or PNSP-NM; results by univariate analysis

Parameters	Nonmeningitis criteria			Meningitis criteria				
	Odds ratio	95% CI	<i>p</i>	Odds ratio	95% CI	<i>p</i>		
TSAR III (2002)	1.404	0.718	2.748	0.3214	1.912	0.913	4.006	0.086
TSAR IV (2004)	0.405	0.178	0.921	0.0310	1.260	0.592	2.681	0.549
TSAR V (2006)	1.026	0.509	2.068	0.9430	1.311	0.631	2.722	0.468
Antibiotic use within prior 15 days	1.852	1.062	3.2320	0.0299	3.088	1.396	6.831	0.005

TSAR = Taiwan Surveillance of Antimicrobial Resistance; PNSP-M = penicillin-nonsusceptible *S. pneumoniae* meningitis; PNSP-NM = penicillin-nonsusceptible *S. pneumoniae* nonmeningitis.

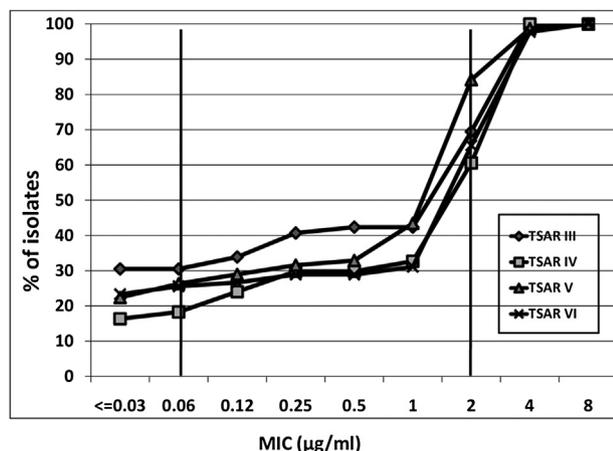


Figure 2. Cumulative distribution of minimum inhibitory concentrations (MICs) of *S. pneumoniae* to penicillin from Taiwan Surveillance of Antimicrobial Resistance (TSAR) III to TSAR VI.

the mortality cases in our study occurred in patients age 65 years and older, which is compatible to the previous finding that older age (≥ 65 years) is significantly associated with case-fatality of invasive pneumococcal disease.³⁴

In conclusion, we found that penicillin nonsusceptibility of *S. pneumoniae* in Taiwan remained high, albeit a transient decrease was noted during the study period. Although we did not find significant difference in mortality in patients infected with penicillin-nonsusceptible and -susceptible isolates, we did show that previous antibiotic exposure was an independent factor associated with subsequent acquisition of penicillin-nonsusceptible pneumococci. Therefore, judicious antibiotic use is an important measure to control the spread of penicillin-nonsusceptible pneumococci. Continued surveillance is needed to monitor changes in pneumococcal resistance as vaccination programs change in Taiwan.

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