

Antibiotic susceptibility of *Streptococcus pneumoniae* from Asia: 2008 – 2010

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Revised Abstract

Background: *Streptococcus pneumoniae* (SP) is the most prevalent pathogen in community-acquired pneumonia (CAP), which frequently progresses to invasive pneumococcal disease, causing significant morbidity and mortality worldwide. The increase in the rates of resistance of SP to frequently used antibiotics and the rapid global spread of multidrug-resistant strains requires comprehensive surveillance and monitoring. The Tigecycline Evaluation and Surveillance Trial (TEST) is an ongoing global surveillance program. In this study, we evaluate the susceptibility of SP from Asia from 2008-2010.

Methods: 223 SP isolates from various sources were collected from investigative sites in 7 Asian countries. Minimum inhibitory concentrations (MICs) were determined by broth microdilution panels and interpreted according to CLSI guidelines.

Results: Overall (2008-2010), *in vitro* penicillin susceptibility of SP from Asia was 40.8%, and erythromycin susceptibility was 31.0%. Additional overall summary data are shown in the following table:

Drug	MIC ₅₀	MIC ₉₀	%S	%I*	%R*
AmoxClav	1	8	73.1	10.8	16.1
Ceftriaxone	0.5	2	71.8	22.0	6.3
Clindamycin	32	>64	46.0	0	54.0
Erythromycin	64	>64	31.0	0	69.0
Levofloxacin	1	1	98.2	0.5	1.4
Linezolid	1	1	100	—	—
Meropenem	0.25	1	51.1	22.4	26.5
Penicillin	1	4	40.8	13.9	45.3
Tigecycline	0.015	0.06	95.1	—	—
Vancomycin	0.5	0.5	100	—	—

* — intermediate and resistant categories are undefined for these antimicrobial agents against *S. pneumoniae*

Conclusions: Linezolid, vancomycin, levofloxacin and tigecycline all showed potent *in vitro* activity against SP from Asia, with %S of >95%. The *in vitro* activity of amoxicillin-clavulanic acid, erythromycin, and ceftriaxone did not show potent activity against SP in this region. Continued surveillance of resistance in SP to new and established antimicrobials is warranted.

Introduction

Tigecycline is approved for the treatment of complicated skin and skin structure infections (cSSSI) and complicated intra-abdominal infections (cIAI) and has been approved in some markets for the treatment of community-acquired pneumonia (CAP). Infections due to *S. pneumoniae* continue to evolve worldwide and are a major cause of morbidity and mortality. Resistance in *S. pneumoniae* not only to penicillin but also to cephalosporins, macrolides, trimethoprim-sulfamethoxazole, fluoroquinolones and tetracycline is well documented. New guidelines for the management of in-patient and out-patient community-acquired pneumonia have recently been published [1]. This study describes the *in vitro* activity of tigecycline and comparators against *Streptococcus pneumoniae*, an important etiologic agent in CAP, in Asia from 2008-2010 as part of the larger ongoing global Tigecycline Evaluation and Surveillance Trial.

Materials & Methods

- ❖ **Clinical isolates:** Isolates were identified to the species level and tested at each participating laboratory. All organisms were deemed clinically significant by local participant criteria. Isolate inclusion was independent of medical history, antimicrobial use, age, or gender. All sites identified each study isolate utilizing local laboratory criteria. All isolates were from the period 2008 - 2010 and collected from 23 cumulative sites in 7 Asian countries.
- ❖ **Susceptibility testing:** Minimum inhibitory concentrations (MICs) were determined using broth microdilution plates manufactured by MicroScan (Siemens Medical Solutions Diagnostics, West Sacramento, CA, USA) or TREK Diagnostics (TREK Diagnostic Systems, Cleveland, OH, USA), following manufacturer and Clinical and Laboratory Standards Institute (CLSI) instructions for broth microdilution testing [2]. Susceptibility was determined using clinical breakpoints published by the CLSI [3] and the FDA (tigecycline) [4].
- ❖ **Quality Control:** QC of broth microdilution panels followed manufacturers' and CLSI guidelines using: *S. pneumoniae* ATCC 49619 [3].

References

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- Tygacil®, 2010 Federal Drug Administration (FDA) product information. Pfizer, Inc. Collegeville, PA, USA.

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Results

Figure 1. Distribution of 223 *S. pneumoniae* isolates from 7 Asian countries, 2008-2010.

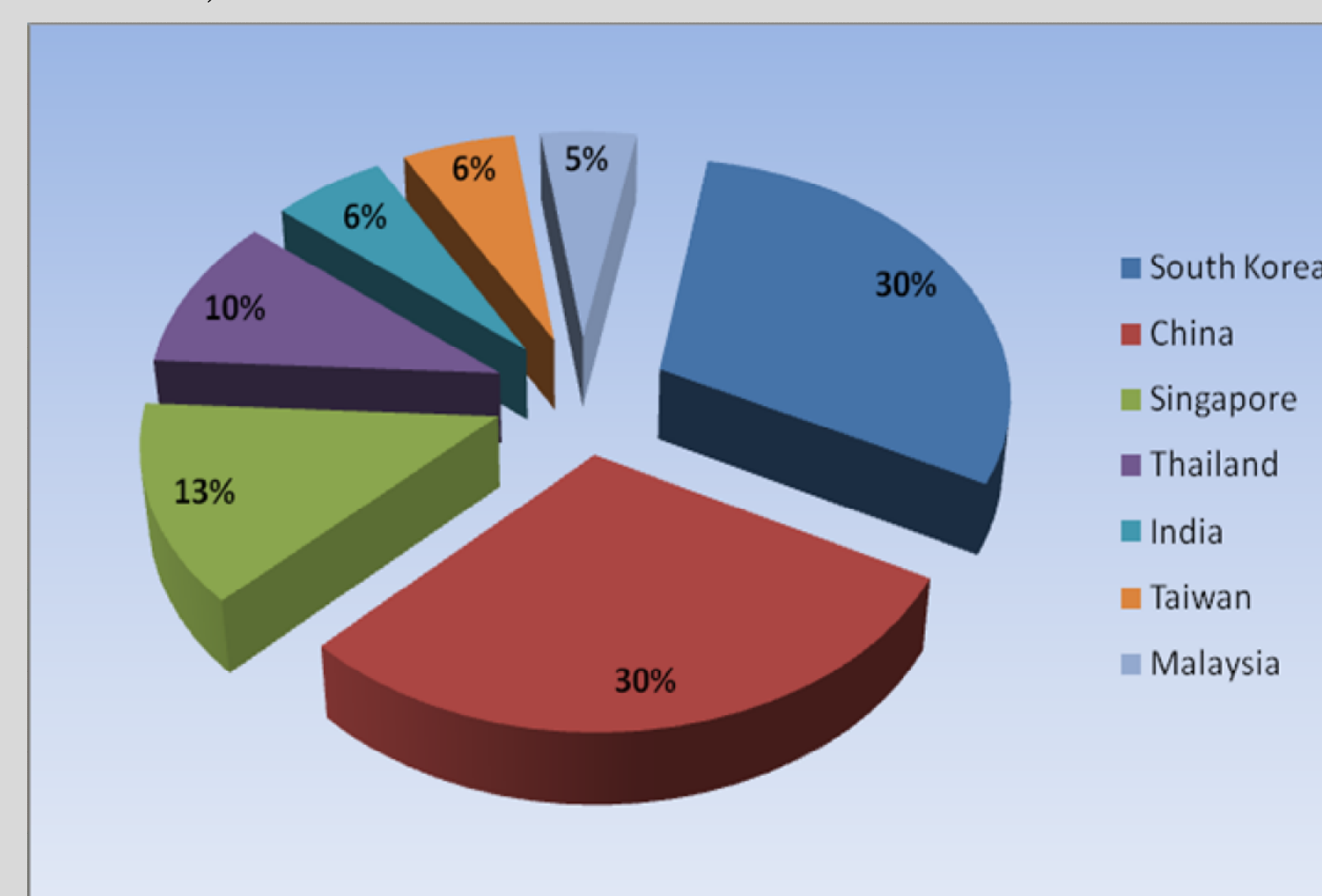


Figure 2. Distribution of 223 *S. pneumoniae* isolates from Asia by source, 2008-2010.

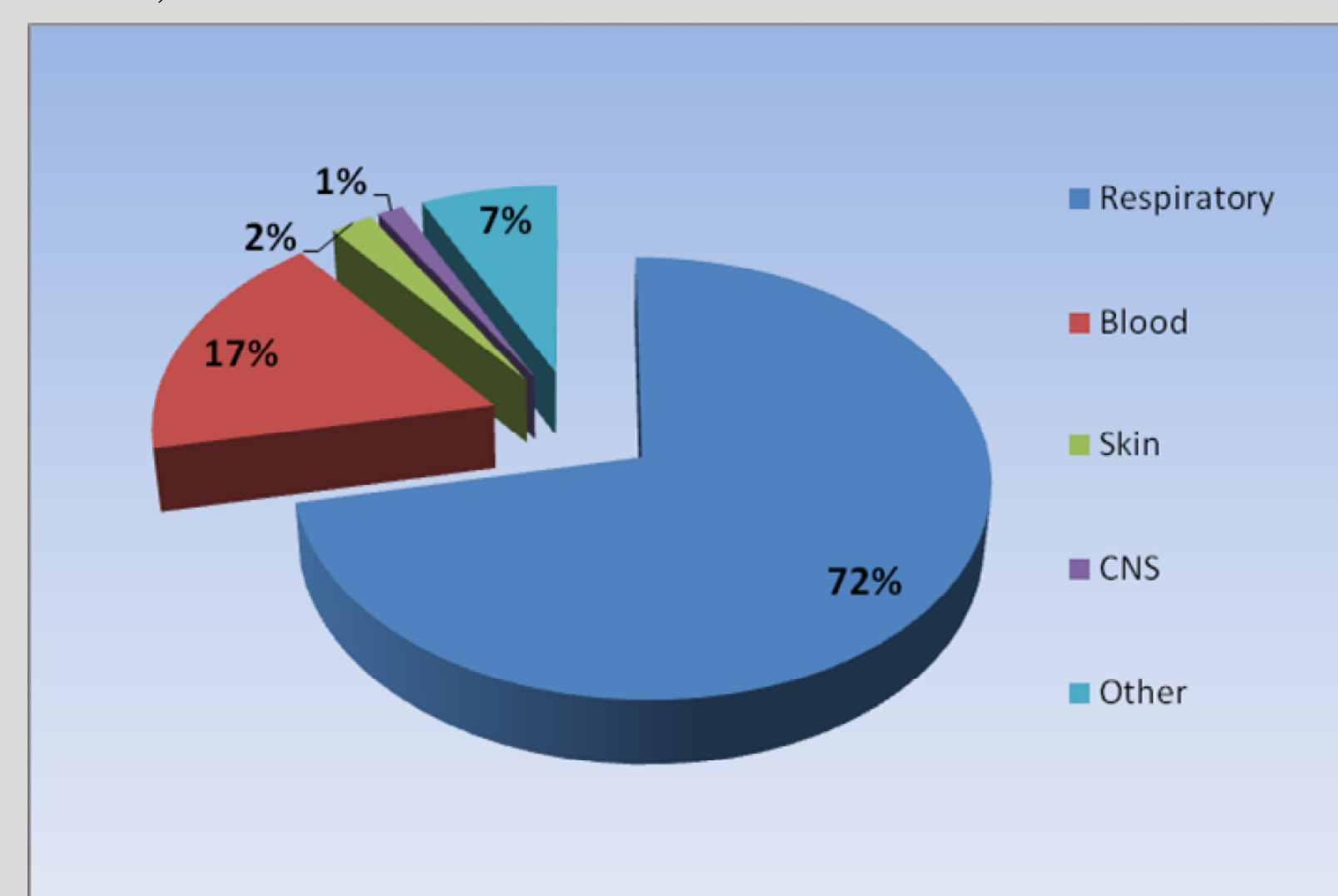
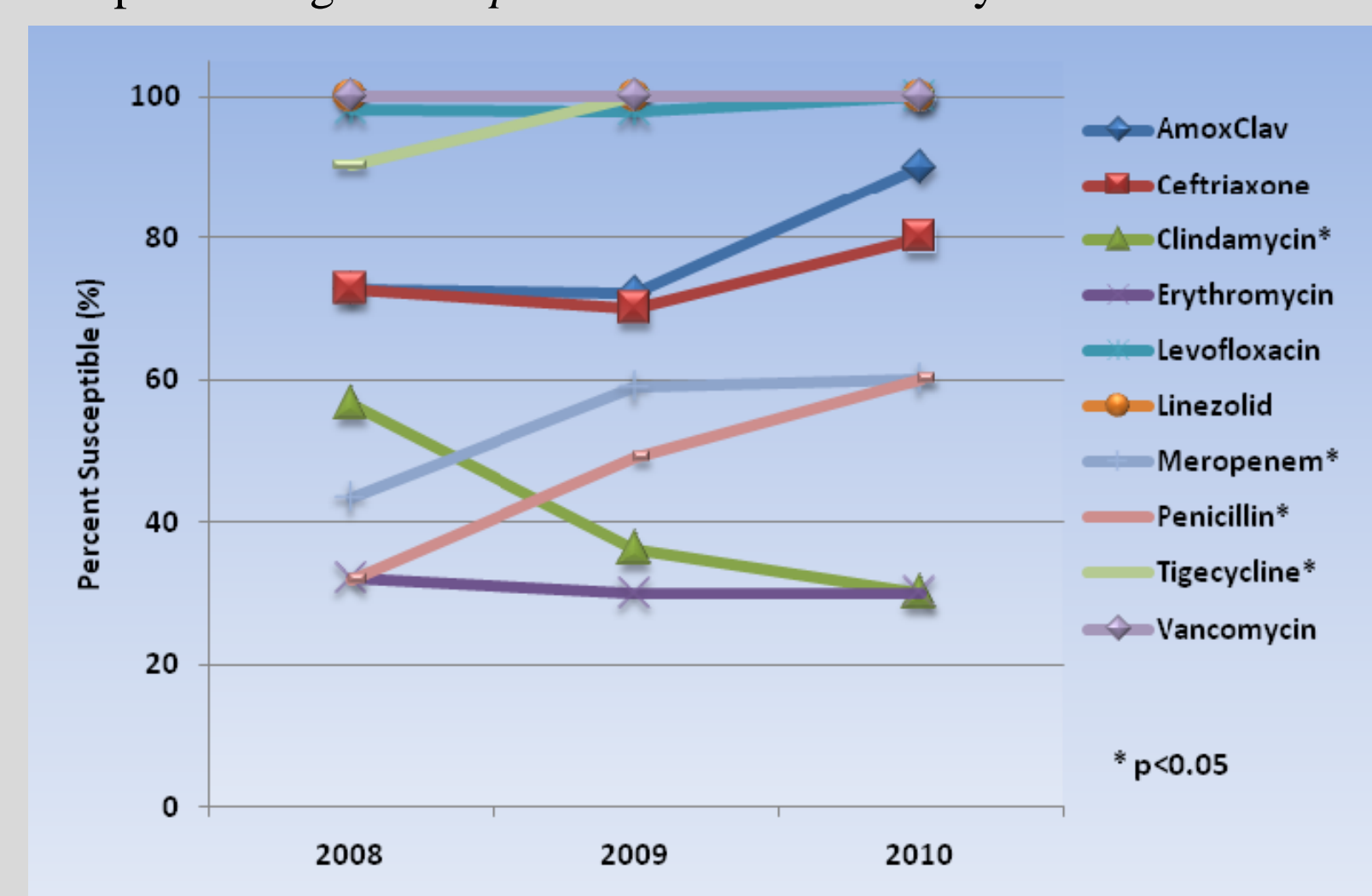


Figure 3. Percents susceptible trends for tigecycline and comparators against *S. pneumoniae* in Asia for years 2008-2010.



* Cochran-Armitage trend test (asymptotic p-value) / two-tailed test.

Table 1. *In vitro* activity of tigecycline and comparators against 223 *S. pneumoniae* isolates from Asia, 2008-2010.

Drug	MIC ₅₀	MIC ₉₀	%Sus	%Int	%Res
<i>S. pneumoniae</i> (n=223)					
AmoxClav	1	8	73.1	10.8	16.1
Ceftriaxone	0.5	2	71.8	22	6.3
Clindamycin	32	>64	46	0	54
Erythromycin	64	>64	31	0	69
Levofloxacin	1	1	98.2	0.5	1.4
Linezolid	1	1	100	—	—
Penicillin	1	4	40.8	13.9	45.3
Tigecycline	0.015	0.06	95.1	—	—
Vancomycin	0.5	0.5	100	—	—
<i>S. pneumoniae</i>, Pen-Sus (n=91)					
AmoxClav	≤0.03	0.06	100	0	0
Ceftriaxone	≤0.03	0.06	100	0	0
Clindamycin	0.06	>64	67.9	0	32.1
Erythromycin	0.12	64	64.3	0	35.7
Levofloxacin	1	1	96.7	1.1	2.2
Linezolid	1	1	100	—	—
Penicillin	≤0.06	≤0.06	100	0	0
Tigecycline	0.015	0.06	93.4	—	—
Vancomycin	0.25	0.5	100	—	—
<i>S. pneumoniae</i>, Pen-Int (n=31)					
AmoxClav	0.5	4	87.1	3.2	9.7
Ceftriaxone	0.25	1	93.6	6.5	0
Clindamycin	64	>64	40	0	60
Erythromycin	64	>64	23.3	0	76.7
Levofloxacin	1	1	100	0	0
Linezolid	≤0.5	1	100	—	—
Penicillin	0.5	1	0	100	0
Tigecycline	0.015	0.03	93.6	—	—
Vancomycin	0.25	0.5	100	—	—
<i>S. pneumoniae</i>, Pen-Res (n=101)					
AmoxClav	4	>8	44.6	22.8	32.7
Ceftriaxone	2	4	39.6	46.5	13.9
Clindamycin	>64	>64	29.3	0	70.7
Erythromycin	64	>64	5.1	0	95
Levofloxacin	1	1	99	0	1
Linezolid	1	2	100	—	—
Penicillin	4	8	0	0	100
Tigecycline	0.015	0.03	97	—	—
Vancomycin	0.5	0.5	100	—	—

* Interpretive criteria defined in CLSI document M100-S21 (2011), where available. Tigecycline breakpoints are defined by FDA (Tygacil®, 2010).

Conclusions

- ❖ Penicillin and macrolide resistance in *S. pneumoniae* has been increasing in Asia for over a decade. In the last three years, however, macrolide resistance has remained level at 69% while penicillin resistance has decreased with a concomitant rise in penicillin-susceptible rates from 32% in 2008, 49% in 2009, and 60% in 2010 (p=0.005) and an average percent susceptible of 40.8% over the three year period. Significant increases in susceptibility rates against *S. pneumoniae* are also seen for meropenem and tigecycline. Clindamycin was the only antimicrobial agent to demonstrate a decrease in susceptibility in the same time frame (57% to 30%; p=0.003).
- ❖ Linezolid, levofloxacin, vancomycin, and tigecycline were consistently the most active antimicrobial agents *in vitro* against *S. pneumoniae* with overall percents susceptible of 100%, 100%, 98%, and 95%, respectively, without regard to penicillin phenotype.