

## Revised Abstract

**Background:** The Tigecycline Evaluation and Surveillance Trial (TEST) monitors the activity of tigecycline and comparators against multiple pathogens collected worldwide. Such monitoring assists in investigating resistance rates either globally, regionally or by country. The current report describes the frequency of selected MDR gram-positive pathogens from Asia during 2009-2010 and their susceptibility to tigecycline and comparator agents. **Methods:** A total of 477 clinical isolates were collected from multiple infection sources in Asia during 2009-2010. Susceptibility testing was performed as per CLSI guidelines and interpreted using CLSI/FDA clinical breakpoints. **Results:** Frequency of MDR isolates and tigecycline susceptibility were as follows:

Species / Phenotype	All	MDR*	% MDR	%S TIG**
<i>E. faecalis</i>	131	1	0.7	100
<i>E. faecium</i>	102	43	42	100
<i>S. agalactiae</i>	134	0	0	100
<i>S. pneumoniae</i>	110	45	41	100
PSSP	55	2	3.6	100
PISP	13	3	23	100
PRSP	42	40	95	100

\* MDR, multi-drug resistance due to resistance to at least three antibiotic classes; \*\*Percent of isolates susceptible to tigecycline

**Conclusions:** The highest MDR rates were observed in pneumococci, especially PRSP (95%) and *E. faecium* (42%). On the contrary MDR rates in other gram-positives were all <1%. Tigecycline exhibited 100% susceptibility against all MDR isolates.

## Introduction

Since the introduction of the penicillins many decades ago, multiple species of bacteria have responded to the use of antimicrobial agents in their ability to develop and transmit antimicrobial resistance. Furthermore, examples of multi-drug resistant (MDR) gram-negative and gram-positive species have emerged and are further evolving. Increased consumption of antimicrobial agents and their misappropriate use amongst other factors have further catalyzed this resistance phenomenon. As bacterial resistance is a global healthcare issue, appropriate monitoring through governmental, institutional and industry or pharmaceutical lead surveillance programs is essential. The current report describes the frequency of MDR gram-positive pathogens isolated in Asia during 2009 – 2010 as part of the Tigecycline Evaluation and Surveillance Trial (TEST).

## Materials & Methods

- ❖ **Clinical isolates:** Isolates collected from multiple infection sources 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 2009 - 2010 and originated from various countries in Asia. Multi-drug resistance was defined as resistance to at least three antibiotic classes.
- ❖ **Susceptibility testing:** Minimum inhibitory concentrations (MICs) were determined using plates manufactured by TREK Diagnostics, following manufacturer and Clinical and Laboratory Standards Institute (CLSI) instructions for broth microdilution testing (1). Susceptibility was determined using clinical breakpoints published by the CLSI (2). FDA breakpoints were used for tigecycline. Tigecycline was supplied by Pfizer, Inc. (Collegeville, PA, USA). All other agents were supplied by the panel manufacturer TREK (TREK Diagnostic Systems, Cleveland, OH). The following antimicrobial agents were included on the panels with their dilution ranges (expressed in mcg/ml): amoxicillin-clavulanic acid (0.12/0.06-32/16); ampicillin (0.06-16); ceftriaxone (0.06-64); linezolid (0.5-8); meropenem (0.12-16); levofloxacin (0.008-8); minocycline (0.5-16); tigecycline (0.008-16); penicillin (0.06-8); piperacillin-tazobactam (0.06/4-128/4) and vancomycin (0.12-32). *S. aureus* ATCC 29213 and *E. faecalis* ATCC 29212 were tested as quality control organisms.

## References

- Clinical Laboratory Standards Institute. 2009. Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standards -- Eighth Edition. CLSI document M07-A8. Wayne, PA.
- Clinical and Laboratory Standards Institute. 2011. Performance Standards for Antimicrobial Susceptibility Testing; Twenty-First Informational Supplement. CLSI Document M100-S21. Wayne, PA.

## Acknowledgements

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## Results

Figure 1. Species distribution of all isolates (n = 477).

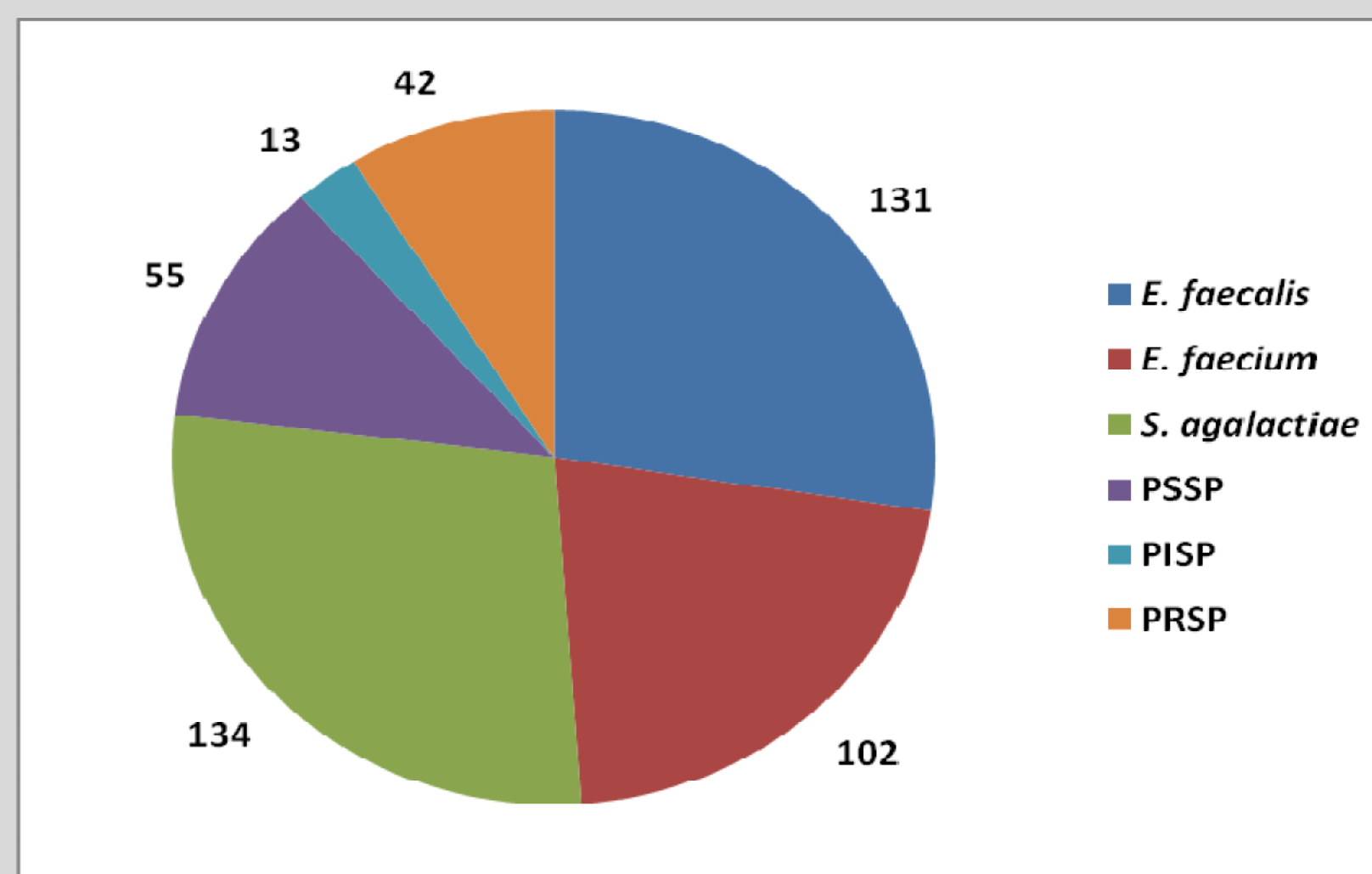


Figure 2. Percentage of MDR phenotypes by species (n = 89).

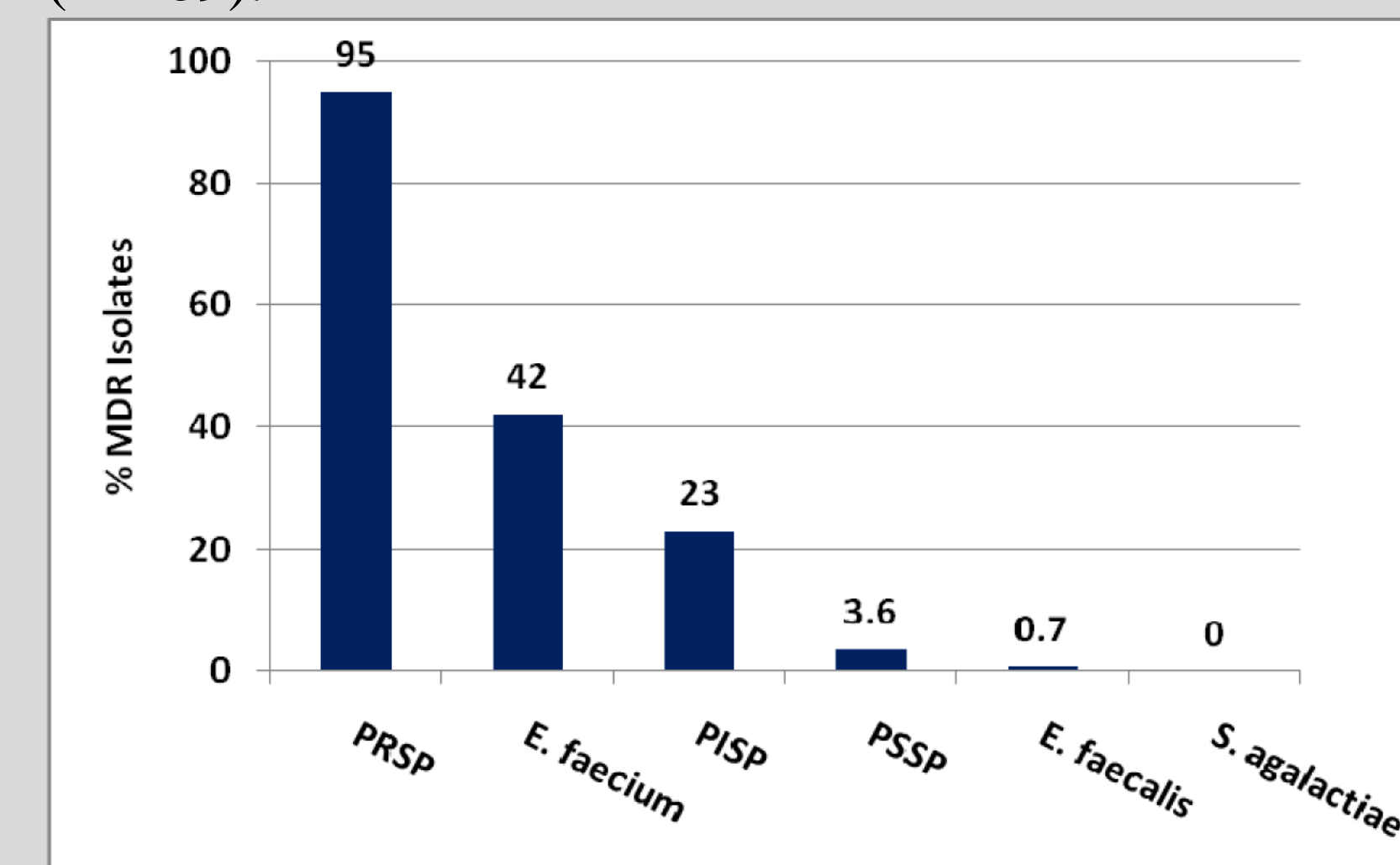


Figure 3. Number of all isolates (n = 477) and MDR isolates (n = 89) by country.

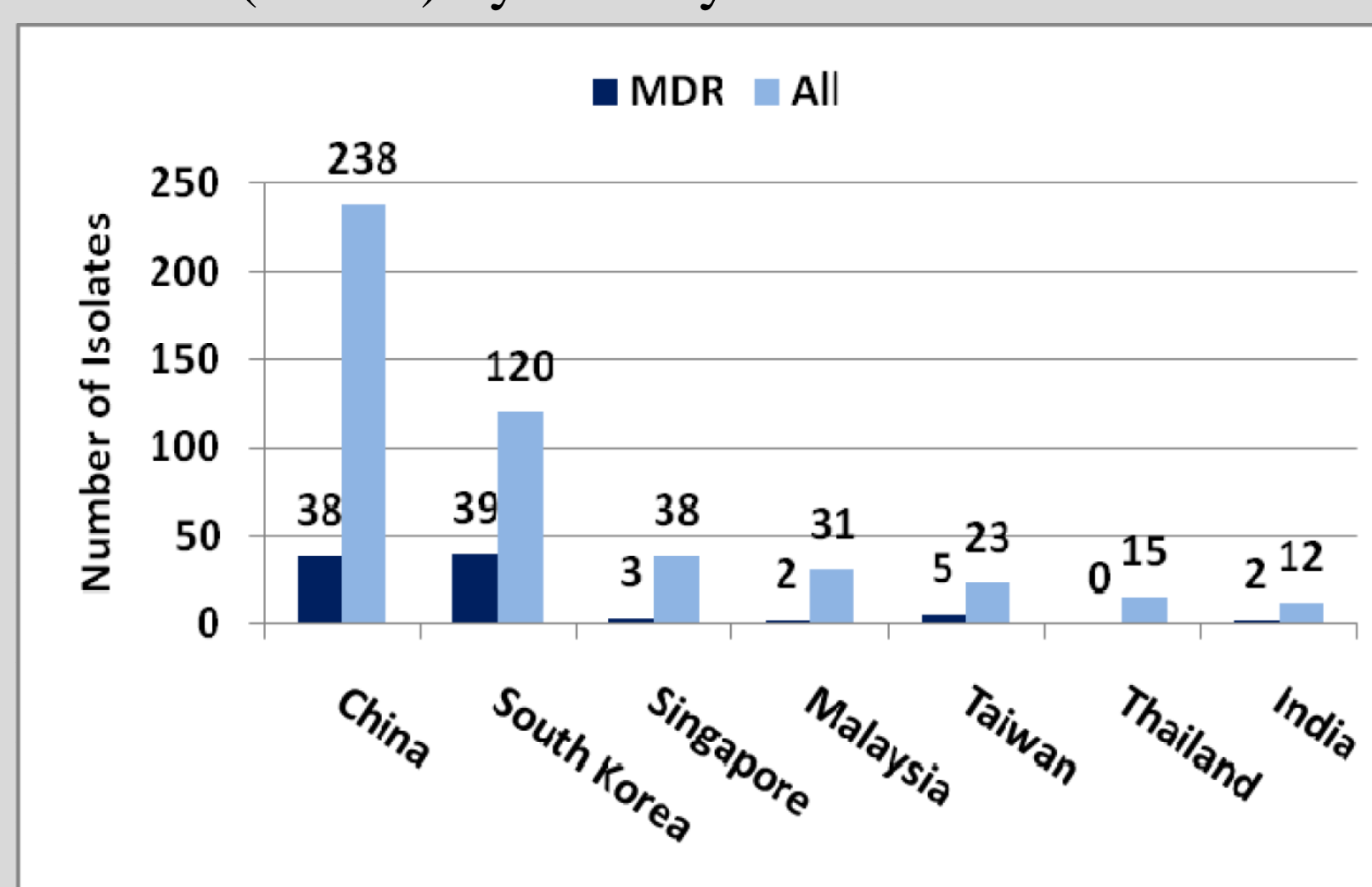


Figure 4. Percentage of MDR isolates (n = 89) by country.

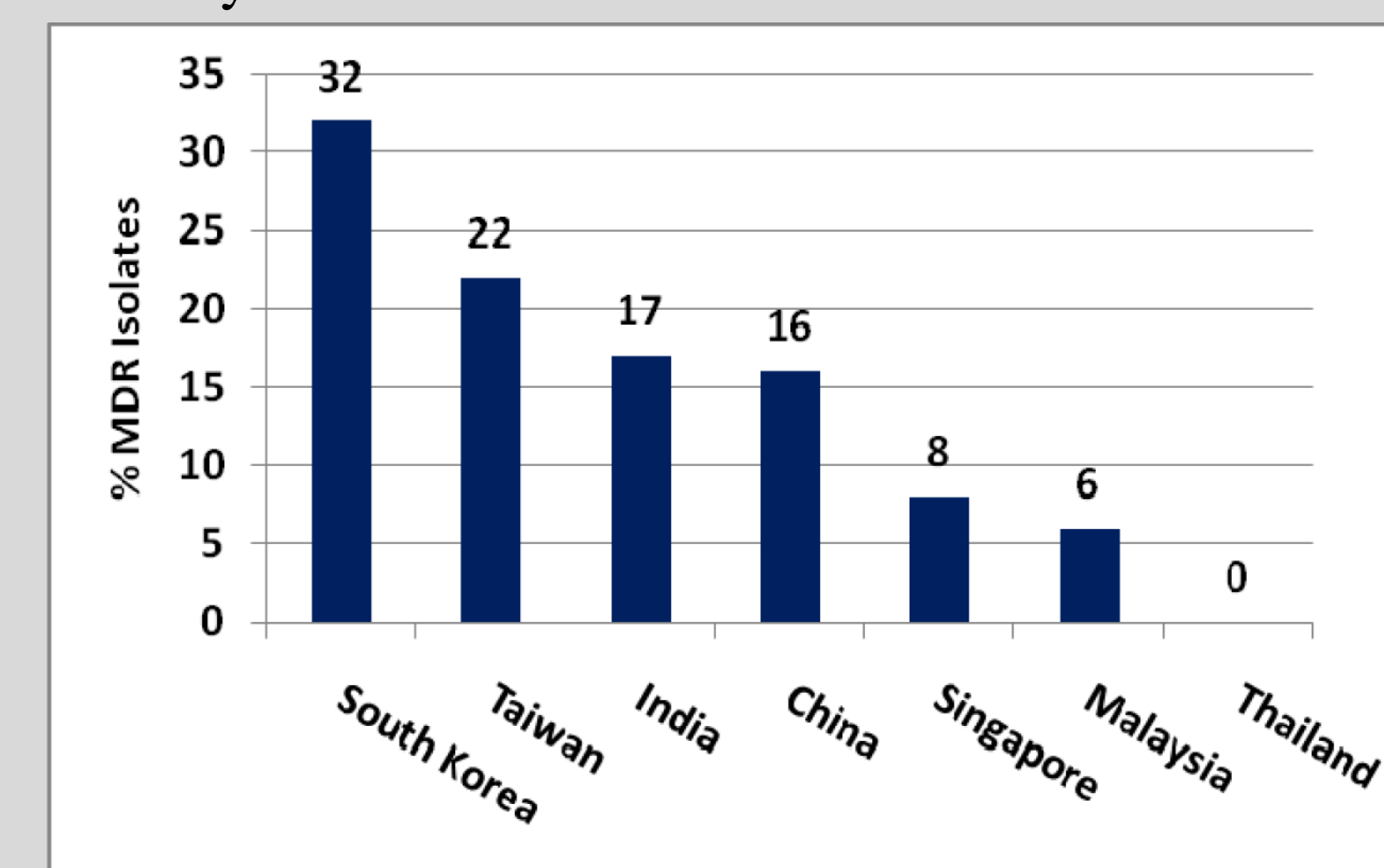


Table 1. Activity of selected antimicrobial agents against all isolates (n = 477) and MDR isolates (n = 89).

Organism	All isolates (n = 477)			Organism	MDR isolates (n = 89)	
	Drug	%Susc			Drug	%Susc
<i>E. faecalis</i> (n=131)	Linezolid	100		<i>E. faecalis</i> (n=1)	Linezolid	100
	Tigecycline	100			Tigecycline	100
	Vancomycin	99			Vancomycin	100
<i>E. faecium</i> (n=102)	Linezolid	100		<i>E. faecium</i> (n=43)	Linezolid	100
	Tigecycline	100			Tigecycline	100
	Vancomycin	76			Vancomycin	47
<i>S. agalactiae</i> (n=134)	Linezolid	100		PSSP (n=2)	Linezolid	100
	Tigecycline	100			Tigecycline	100
	Vancomycin	100			Vancomycin	100
PSSP (n=55)	Linezolid	100		PISP (n=3)	Linezolid	100
	Tigecycline	100			Tigecycline	100
	Vancomycin	100			Vancomycin	100
PISP (n=13)	Linezolid	100		PRSP (n=40)	Linezolid	100
	Tigecycline	100			Tigecycline	100
	Vancomycin	100			Vancomycin	100
PRSP (n=42)	Linezolid	100				
	Tigecycline	100				
	Vancomycin	100				

## Conclusions

- ❖ Of the 477 isolates tested, 89 (19%) were MDR isolates. The highest MDR rates were observed in pneumococci, especially PRSP (95%) and *E. faecium* (42%). On the contrary MDR rates in other gram-positives were all <1%.
- ❖ By country, the highest MDR rates were observed in South Korea (32%) and Taiwan (22%) and the lowest in Thailand (0%) and Malaysia (6%).
- ❖ Tigecycline exhibited 100% susceptibility against all MDR isolates as was the case for linezolid and vancomycin, with the exception of *E. faecium* for which a significant proportion were resistant to vancomycin.