



hVISA are common among vancomycin susceptible methicillin-resistant *Staphylococcus aureus* (MRSA). Report from SENTRY Asia-Pacific Region.

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Introduction

Although the incidence of VISA or VRSA remains low in *Staphylococcus aureus* (SAUR), there are increasing reports of hetero-resistance to vancomycin (hVISA) including ones describing treatment failure. The prevalence of hetero-resistance in vancomycin susceptible strains is not known.

The aim of this study was to screen a large number of oxacillin-resistant *S. aureus* (MRSA) isolates from the Asia-Pacific Region for hVISA subpopulations, and examine the findings with the vancomycin and teicoplanin broth microdilution MICs.

Methods

Isolates

As part of the SENTRY Asia-Pacific region we examined SAUR from infected hospitalized patients in 9 countries (17 laboratory centres) collected since 1998. Isolates came from blood, LRTI, skin/skin structure, urine and intensive care specimens. All strains were referred to the Women's and Children's Hospital, Adelaide, Australia for testing.

Susceptibility testing

Isolates were tested using custom made broth microdilution panels (Trek Diagnostic Systems) against a wide range of antimicrobials including vancomycin (VAN) and teicoplanin (TEI) according to CLSI standards.¹ Breakpoints for resistance were those recommended by the CLSI.²

Screening methods

A range of VAN and TEI MICs were screened for hVISA subpopulations using the macro ETest method.³ A VAN MIC ≥ 8 and TEI ≥ 8 mg/L; or TEI ≥ 12 mg/L were recorded as screen positive.

Population Analysis Profiles (PAP)

A subset of possible hVISA isolates were confirmed using vancomycin PAP-area under the curve ratio method⁴

Table 1. Glycopeptide resistance vs country and oxacillin resistance

	AUS	HKK	CHI	PHL	SIN	TWN	KOR	JPN	SAF	Total
<i>S. aureus</i>	2347	564	54	122	527	443	94	1140	424	5715
Oxacillin -resistant	558	316	15	15	258	287	41	778	186	2454
VAN ≥ 2 and TEI ≥ 2	41	4	3	0	9	26	9	33	34	159
% overall	1.7%	0.7%	5.6%	0.0%	1.7%	5.9%	9.6%	2.9%	8.0%	2.8%
% MRSA	7.3%	1.3%	20.0%	0.0%	3.5%	9.1%	22.0%	4.2%	18.3%	6.5%

Figure 1. Vancomycin MIC Distribution

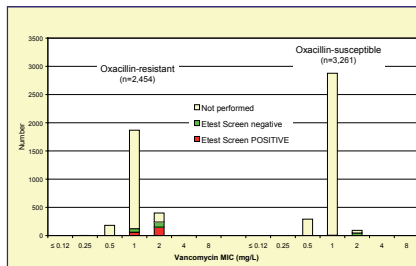
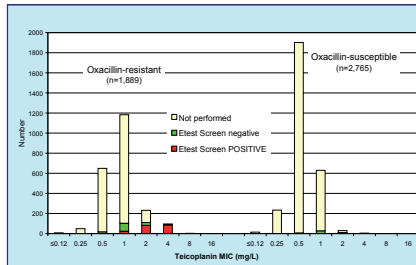


Figure 2. Teicoplanin MIC Distribution



References

1. CLSI. 2003. Approved Standard M7-A6
2. CLSI. 2005. M100-S15
3. Etest Technical Guide 14. 20000. AB BIODISK
4. Walsh et al. 2001 JCM 39:2439-244

Figure 3. Proportion of MRSA hVISA screen Positive

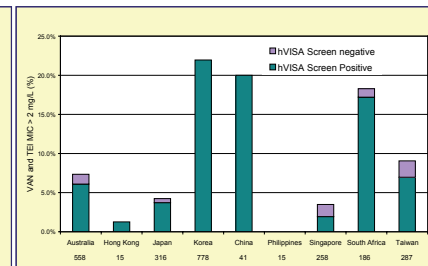
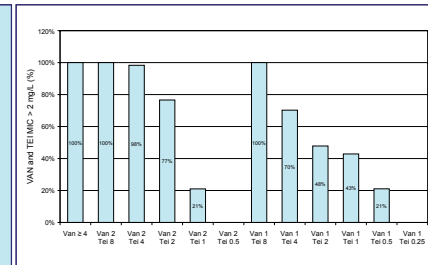


Figure 4. Proportion of MRSA hVISA screen Positive



SAMR

Etest Screen	PAP		
	positive	negative	
Positive	102	11	113
negative	1	15	16
	103	26	129
	99.0%	42.3%	

Results

A total of 2,454 MRSA and 3,261 oxacillin-susceptible isolates were collected over the 7-year period (Table 1).

The proportion of MRSA isolates with VAN ≥ 2 and TEI ≥ 2 mg/L varied significantly by country. These isolates were common in Korea, Mainland China and South Africa.

Figures 1 and 2 show the VAN and TEI MICs distributions vs hVISA Etest screen. The modal TEI MIC was one dilution higher for MRSA isolates.

Three strains had VAN MIC of ≥ 4 mg/L, all were hetero-resistant. A further 156 isolates had VAN MIC of 2 mg/L but TEI MIC 2-8 mg/L (Table 2).

The proportion of hVISA detected among MRSA ranged from 49%, 63%, 100%, as VAN MIC increased from 1, 2, ≥ 4 mg/L; likewise for TEI, 29%, 71%, 88% and 100% of isolates were hVISA by Etest as TEI increased from 1, 2, 4, ≥ 8 mg/L respectively (Figure 3)

Eighty-five percent of MRSA with VAN MIC ≥ 2 mg/L and TEI ≥ 2 mg/L were hVISA.

As the proportion of both VAN and TEI MICs increased the incidence of hVISA increased; 70% of MRSA with VAN MIC 1 and TEI MIC 4 mg/L were hVISA.

95% of all isolates that were possible hVISA by ET were confirmed by PAP.

Figure 4 shows the proportion of MRSA isolates with both VAN and TEI MICs ≥ 2 mg/L that were hVISA ETest screen positive. This profile was highly indicative of the strain being a hVISA.

Three strains from Korea and one from Japan with VAN MIC of 1 mg/L and TEI MIC 0.5 mg/L were screen positive; PAP studies are still to be done

Nine of the 11 screen-positive, PAP negative strains were from Japan.

Table 2. MRSA Glycopeptide Profile vs hVISA Etest Screen

VanTeiProfile	hVISA Screen		Total	%Pos
	POS	neg		
Van ≥ 4	3	3	100%	
Van 2 Tei 8	2	2	100%	
Van 2 Tei 4	59	1	60	98%
Van 2 Tei 2	72	22	94	77%
Van 2 Tei 1	17	64	81	21%
Van 2 Tei 0.5		3	3	0%
Van 1 Tei 8	1	1	100%	
Van 1 Tei 4	26	11	37	70%
Van 1 Tei 2	11	12	23	48%
Van 1 Tei 1	18	24	42	43%
Van 1 Tei 0.5	4	15	19	21%
Van 1 Tei 0.25	1	1	0%	
Total	213	153	366	
Tei 0.25 Van 1		1	1	0%
Tei 0.5 Van 1	4	15	19	21%
Tei 0.5 Van 2		3	3	0%
Tei 1 Van 1	18	24	42	43%
Tei 1 Van 2	18	64	82	22%
Tei 2 Van 1	11	12	23	48%
Tei 2 Van 2	71	22	93	76%
Tei 4 Van 1	26	11	37	70%
Tei 4 Van 2	59	1	60	98%
Tei 8 Van 1	1	1	100%	
Tei 8 Van2	2	2	100%	

Conclusions

- The prevalence of hetero-resistance to vancomycin in MRSA from the Asia Pacific whose conventional vancomycin MICs are 1-2 mg/L is high, suggesting that hetero-resistance may be much more common than previously described.
- Detection of these strains remains problematic