P0203

Community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) is associated with low level resistance against oxacillin, cefoxitin, and vancomycin

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Background: *Staphylococcus aureus*, especially MRSA, is a leading pathogen responsible for community- and hospital-associated infections with increasing resistance to existing antibiotics. *mecA*+ *S. aureus* with oxacillin and cefoxitin susceptibility phenotypes has been reported in Taiwan and elsewhere [1], but its impact on clinical practice is not clear. We aim at delineating the molecular distribution and prevalence of low level resistance to oxacillin and cefoxitin, and vancomycin susceptibility pattern among clinicical *S. aureus* isolates.

Materials & Methods: *S. aureus* isolates were collected from clinical specimens discovered in a medical center in central Taiwan (Chung-Shan Medical University Hospital) between July, 2011 and June, 2014, and they were identified by morphologic and biochemistry standards with minimal inhibitory concentrations (MIC) against oxacillin (OX), cefoxitin (FOS), and vancomycin (VA) being determined with agar dilution with according to Clinical and Laboratory Standards Institute (CLSI) [2]. MRSA was confirmed with *mecA* gene existence by polymerase chain reaction (PCR). The molecular types of staphylococcal cassette chromosome *mec* (SCC*mec*) was determinated by PCR [3].

Results: Totally 427 non-duplicate *S. aureus* were collected, which most were isolated from pus (233, 54.6%), sputum (139, 32.6%), and urine (32, 7.5%) (Table 1). Most were cultivated from non-sterile sites. There were 188 (44%) methicillin-susceptible *S. aureus* (MSSA) and 239 (56%) MRSA identified (Table 1). Five SCC*mec* types, including II (14, 5.8%), III (85, 35.6%), IV (77, 32.2%), V (17, 7.1%), and V_T (46, 19.2%), were found (Table 4), and their molecular distribution among different sites were listed in Table 2.

Table 1. Source of 427 clinical *Staphylococcus aureus* isolates

Source	MSSA no. (%)	MRSA no. (%)	*S. aureus* no. (%)
Pus (skin and soft tissue)	113 (60.1)	120 (50.2)	233 (54.6)
Sputum	57 (30.3)	82 (34.3)	139 (32.6)
Urine	12 (6.4)	20 (8.4)	32 (8.2)
Bronchoalveolar lavage (BAL)	1 (0.5)	7 (2.9)	8 (1.9)
Ascites	1 (0.5)	3 (1.2)	4 (0.9)
Synovial fluid	2 (1.1)	1 (0.4)	3 (0.7)
Pleural effusion	1 (0.5)	2 (0.8)	3 (0.7)
Stool	1 (0.5)	2 (0.8)	3 (0.7)
Blood	0 (0)	1 (0.4)	1 (0.2)
Cerebrospinal fluid (CSF)	0 (0)	1 (0.4)	1 (0.2)
Total	188 (100.0)	239 (100.0)	427 (100.0)

Table 2. Distribution of SCC*mec* types among 239 *mecA*+ MRSA isolates

Source/SCC*mec* type	I	II	III	IV	V	V_T	Total
Pus[1]	0	2	27	49	4	38	120
Sputum	0	9	41	18	8	6	82
Urine	0	1	9	5	5	0	20
BAL[2]	0	1	3	2	0	1	7
Ascites	0	1	2	0	0	0	3
Synovial fluid	0	0	1	1	0	0	2
Pleural effusion	0	0	0	0	0	1	1
Stool	0	0	1	1	0	0	2
Blood	0	0	1	0	0	0	1
CSF[3]	0	0	0	1	0	0	1
Total	0	14	85	77	17	46	239

[1]: isolated from skin and soft tissue; [2]: bronchoalveolar lavage; [3]: cerebrospinal fluid.

The mean VA MIC for *S. aureus*, MSSA, and MRSA were 1.06 ± 0.45, 1.02 ± 0.41, and 1.09 ± 0.48 mg/L, respectively (p = 0.08), Higher mean VA MIC was noted in isolates from sputum than pus (Fig. 1, $p < 0.001$), especially in *S. aureus* and MRSA (Table 3).

Table 3. Mean MIC against vancomycin of 404 *S. aureus* isolated from major sources

Strain/MIC[1]/Source	pus	sputum	urine
S. aureus	0.99 ± 0.40	1.18 ± 0.49[4]	1.00 ± 0.43
MSSA[2]	1.00 ± 0.47	1.05 ± 0.39	0.92 ± 0.40
MRSA[3]	0.98 ± 0.40	1.26 ± 0.52[5]	1.05 ± 0.44

[1]: minimal inhibitory concentration; [2]: methicillin-susceptible *S. aureus*; [3]: methicillin-resistant *S. aureus*; [4]: $p < 0.001$ when compared MIC of pus with sputum; [5]: $p < 0.001$ when compared MIC of pus with sputum.

The mean VA MIC of HA-MRSA (SCC*mec* II and III) was higher than CA-MRSA (SCC*mec* IV, V, and V_T) (1.25 ± 0.54 vs. 0.98 ± 0.39 mg/L, $p < 0.001$) (Fig. 3), and the difference was significant between SCC*mec* III (1.26 ± 0.54 mg/L) and SCC*mec* IV (0.98 ± 0.39 mg/L) and SCC*mec* V_T (0.97 ± 0.40 mg/L) (p = 0.001 and p = 0.003, respectively) (Table 4 and Fig. 2).

Table 4. Mean MIC against vancomycin in different categories of *S. aureus*

Variants/no./MIC (mg/L)	no.	mean MIC ± S.D.	*p* value
Resistance			
MSSA	188	1.02 ± 0.40	0.075
MRSA	239	1.09 ± 0.48	
SCC*mec* type			
II	14	1.14 ± 0.50	
III	85	1.26 ± 0.54	
IV	77	0.98 ± 0.39	0.001[1]
V	17	1.03 ± 0.41	
V_T	46	0.97 ± 0.40	0.003[2]
Molecular clones			
CA-MRSA[3]	140	0.98 ± 0.39	< 0.001
HA-MRSA[4]	99	1.25 ± 0.54	

[1]: SCC*mec* IV vs. SCC*mec* III; [2]: SCC*mec* V_T vs. SCC*mec* III; [3]: including SCC*mec* IV, SCC*mec* V, and SCC*mec* V_T; [4]: including SCC*mec* II and SCC*mec* III

Extremely high sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were noted for oxacillin (98.7%/99.5%/99.6%/98.4%) and cefoxitin (95.8%/99.5%/99.6%/94.9%), respectively (Table 5).

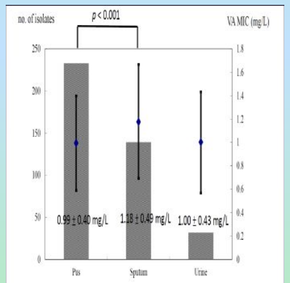

Figure 1. Distribution of major specimen sources from pus (233 isolates), sputum (139 isolates), and urine (32 isolates) and their vancomycin (VA) minimal inhibitory concentrations (MIC) among 404 clinical *Staphylococcus aureus* isolates.

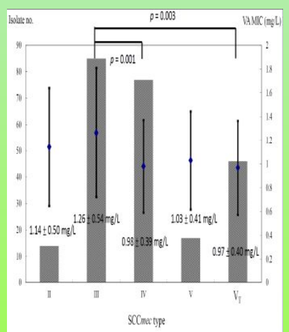

Figure 2. Distribution of SCC*mec* types and their vancomycin (VA) minimal inhibitory concentrations (MIC) among 239 clinical methicillin-resistant *Staphylococcus aureus* (MRSA) isolates.

Table 5. Sensitivity, specificity, positive predictive value, and negative predictive value of oxacillin and cefoxitin agar dilution in detecting *mecA*+ MRSA among 427 clinical *S. aureus* isolates

Methods/Results	Sensitivity	Specificity	Positive predictive value	Negative predictive value
oxacillin agar dilution	95.8%	99.5%	99.6%	94.9%
cefoxitin agar dilution	98.7%	99.5%	99.6%	98.4%

Ten MRSA (2.3%) with phenotypes of oxacillin susceptibility and 3 (0.7%) with cefoxitin susceptibility were exclusively noted in molecularly CA-MRSA (SCC*mec* IV, V, an V_T).

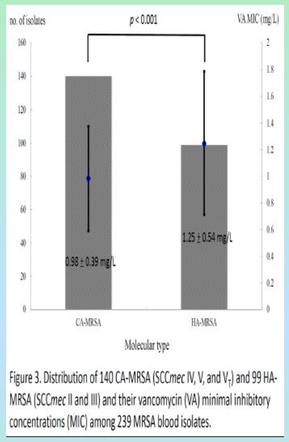

Figure 3. Distribution of 140 CA-MRSA (SCC*mec* IV, V, and V_T) and 99 HA-MRSA (SCC*mec* II and III) and their vancomycin (VA) minimal inhibitory concentrations (MIC) among 239 MRSA blood isolates.

Conclusion: Low level resistance againt oxacillin, cefoxitin, and vancomycin are mostly found among CA-MRSA. MRSA does not harbor higher vancomycin resistance than MSSA. Cefoxitin and oxacillin agar dilution could be used as excellent tools in screening MRSA isolates mostly from nonsterile site.

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