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High prevalence of a globally disseminated hypervirulent clone, *Staphylococcus* aureus CC121, with reduced vancomycin susceptibility in community settings in China

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Objectives: Most vancomycin-intermediate *Staphylococcus aureus* (VISA) and heterogeneous VISA (hVISA) are derived from hospital-associated MRSA due to treatment failure; however, the prevalence of hVISA/VISA in community settings remains unclear.

Methods: Four hundred and seventy-six community-associated isolates were collected between 2010 and 2011 during national surveillance for antimicrobial resistance in 31 county hospitals across China. Drug susceptibility evaluation and *mecA* detection were performed by using broth microdilution and PCR analysis, respectively. hVISA/VISA were identified by using macro-Etest and a modified population analysis profile (PAP)-AUC method. The genetic features of all hVISA/VISA isolates were genotyped.

Results: Among 476 isolates, MRSA and MSSA accounted for 19.7% (n=94) and 80.3% (n=382), respectively. Two VISA and 36 hVISA isolates were identified by PAP-AUC testing. The VISA isolates and 29 of the hVISA isolates were MRSA. The proportion of hVISA/VISA was significantly higher in MRSA (30.9%) than in MSSA (1.8%). The hVISA/VISA isolates were assigned to 18 STs classified into seven clonal complexes (CCs). CC121 (n=12) followed by ST239 (n=11) was the most prevalent hVISA/VISA clone. All ST239-hVISA/VISA were MRSA, while 12 CC121-hVISA isolates included 6 MSSA and 6 MRSA isolates. SCC*mec* III was predominant among MRSA-hVISA/VISA isolates. *agr* I and *agr* IV were detected in ST239 and CC121, respectively. All except two strains were positive for Panton–Valentine leucocidin genes.

Conclusions: To the best of our knowledge, this is the first report of CC121 as a prevalent hVISA clone in community settings, highlighting the necessity of surveillance and stricter infection control measures for this globally disseminated lineage.

Introduction

MRSA has become a major cause of hospital-acquired (HA) and community-acquired (CA) infections.[1–3] The glycopeptide antibiotics vancomycin is regarded as one of the mainstays of treatment for MRSA infections. However, prolonged or inappropriate use of vancomycin may lead to the emergence of strains with reduced susceptibility, namely vancomycin-intermediate *Staphylococcus aureus* (VISA) and/or heterogeneous vancomycin-resistant *S. aureus* (hVISA). It is thought that hVISA is a precursor of VISA after a selective pressure by the use of glycopeptides for a prolonged period.[4] Currently, hVISA cannot be detected by standard susceptibility testing methods, since they are ordinarily present at low frequencies of 10^{-5} to 10^{-6} within the vancomycin-intermediate range and grow more slowly.[5] The gold standard for the identification of hVISA is population analysis profile (PAP)-AUC testing; however, it is a labour-intensive process not suitable for the clinical microbiology laboratory. An alternative method, the macro-Etest, has recently been reported to have, relative to population analysis, sensitivities of 80% and 94% and specificities of 87% and 96% for detection of hVISA at 24 h and 48 h, respectively.[6]hVISA/VISA infections have been reported since 1996 and have been associated with poor patient outcomes.[7–9] Of more concern, the prevalence of hVISA/VISA has been increasing

in recent years worldwide. A meta-analysis reveals that the prevalence of hVISA/VISA increased from 4.68%/2.05% before 2006 to 7.01%/7.93% in 2010–14.[10] Although identified predominantly in MRSA, hVISA/VISA are also present among MSSA.[10] This indicates that the prevalence might be underestimated since hVISA/VISA are screened for among the MRSA population in most studies. The dominant hVISA/VISA clone is ST239, followed by ST5. ST239 and ST5 are two epidemic HA-MRSA clones disseminating in Asia, South America and Eastern Europe.[10,11] These results support that most hVISA/VISA are derived from HA-MRSA.[12] Of note, hVISA/VISA have recently been sporadically detected in CA-MRSA, most of which are caused by treatment failure of CA-MRSA infections, suggesting an alarming risk that hVISA/VISA may disseminate in community settings.[13] To evaluate such a situation, understanding the prevalence and epidemiological characterization of hVISA/VISA in community settings would be necessary. However, the distribution of the hVISA/VISA population in community settings on a national scale in China is not clear. The aim of this study was to investigate the epidemiological and genetic characteristics of hVISA/VISA isolates causing community-onset infections in 31 county hospitals across China.

Materials and methods

Bacterial isolates

During national surveillance for antibiotic resistance among outpatients in county hospitals, *S. aureus* isolates responsible for community-associated infections were continuously collected from 31 county hospitals located in 12 provinces, representing seven geographical regions of China (east, south, north, middle south, north-east, north-west and south-west), between August 2010 and December 2011.[14] Patients were selected for this study using the criteria as previous described.[15] Species identification was performed using MALDI-TOF MS (Bruker Diagnostics, Bremen, Germany).

Antimicrobial susceptibility testing

Susceptibility was assessed according to the instructions of the CLSI (Twenty-First Edition: M100). *S. aureus* ATCC 25923 and ATCC 29213 were used for quality control. *mecA* was screened for by PCR.

Macro-Etest

Macro-Etest was used for hVISA screening as previously described.[16] Briefly, colonies were picked and suspended in saline (turbidity equivalent to that of a 2.0 McFarland standard). A 100 μL aliquot of this suspension was evenly spread onto a 90 mm brain heart infusion (BHI) agar plate and allowed to dry. Vancomycin and teicoplanin Etest strips (bioMérieux, Marcy-l'Étoile, France) were applied to the surface of the BHI agar and the plates were incubated at 35°C for 48 h. The results were recorded at 24 and 48 h. Zones were read at complete inhibition carefully observing for visual hazy growth and microcolonies. Strains Mu3 (hVISA), Mu50 (VISA) and ATCC 29213 were used as controls. A strain was considered positive for hVISA by macro-Etest if microcolonies were detected at ≥8 mg/L for both vancomycin and teicoplanin or at ≥12 mg/L for teicoplanin alone. The results were independently interpreted by two investigators.

PAP-AUC testing

PAP-AUC testing was performed using a microdilution method as previously described, with slight modifications.[17] Briefly, serial dilutions (10^{-1} to 10^{-6}) of a 0.5 McFarland suspension were prepared in sterile saline. Spiral platings of 100 μL of 10^{-1}, 10^{-3} and 10^{-6} dilutions were dropped onto 11 different BHI agar plates with different concentrations of vancomycin (0, 0.5, 1.0, 2.0, 2.5, 4.0 and 8.0 mg/L). After air drying, the plates were incubated at 35°C. After 24 and 48 h of incubation, colony counts ($\log_{10}$ cfu/mL) were determined and plotted against the vancomycin concentration. The AUC was calculated using GraphPad Prism 7 (GraphPad Software Inc., San Diego, CA, USA). Isolates with an AUC ratio of 0.90–1.30 (AUC of test isolate divided by AUC of hVISA control strain Mu3) are defined as hVISA and those with a PAP-AUC ratio of ≥1.3 are defined as VISA.

Genotype characterization of hVISA/VISA

SCCmec typing

Multiplex PCR was used to determine the SCC*mec* type (I–V) according to the method published by Milheirico *et al.*[18] Non-typeable strains were defined as those showing unexpected fragments or lacking some fragments in the multiplex PCR. International clones of SCC*mec* types I–V were used as positive controls, and strain ATCC 29213 (*mecA* negative) was used as the negative control.

spa typing

spa typing was performed as previously described,[19] and short sequence repeats were assigned by the *spa* database (http://www.spaserver.ridom.de/). The *spa* complex was defined by visual analysis, whereby *spa* types with similar short sequence repeats were clustered into a complex as previously described.[20] *agr* typing was performed as previously described by Gilot *et al.*[21]

MLST. MLST was performed as previously described.[22] STs were assigned by the *S. aureus* MLST database (http://saureus.mlst.net). A minimum spanning tree (MST) was generated by BioNumerics (Applied Maths NV, Sint-Martens-Latem, Belgium) using the categorical coefficient.

Detection of Panton–Valentine leucocidin (PVL) genes

Genomic DNA was extracted by the QIAamp DNA Mini Kit (QIAGEN, Hilden, Germany) and used as the template for PVL PCR. The PCR primers were obtained from a previous study.[23] DNA fragments with the size of 433 bp were considered as being positive for the PVL genes.

Statistical analysis

Pearson's χ^2 test and Fisher's exact test were used as appropriate to test associations between qualitative variables. Significance was assumed at $P < 0.05$.

Results

We collected 476 community-associated *S. aureus* strains obtained from 31 county hospitals distributed in seven geographical regions (east, south, north, middle south, north-east, north-west and south-west) in China. The strains were isolated from abscess (*n*=153, 32.1%), secretion (*n*=145, 30.5%), sputum (*n*=83, 17.4%), blood (*n*=28, 5.88%), throat swab (*n*=20, 4.2%), fine-needle (*n*=13, 2.73%), urine (*n*=5, 1.05%) and other (*n*=29, 6.09%).[14] The prevalence of MRSA and MSSA was 19.7% (94/476) and 80.3% (382/476), respectively. The highest proportion of MRSA was found in the other specimens (12/29, 41.4%), followed by sputum (26/83, 31.3%), fine-needle (4/13, 30.8%), secretion (31/145, 21.4%) and abscess (18/94, 19.1%). Regarding geographical distribution, the highest ratio of MRSA was found in the north (26/80,

32.5%), followed by the south (17/63, 27%), middle south (14/60, 23.3%) and north-east (4/19, 21.1%). Details are shown in Table 1.

Screening of the 476 isolates for hVISA by macro-Etest resulted in 48 positive isolates, and 38 isolates were further confirmed by using the PAP-AUC approach, comprising 36 hVISA and 2 VISA isolates. The prevalence of hVISA and VISA was 7.6% (36/476) and 0.4% (2/476), respectively. The two VISA isolates and 29 of 36 hVISA isolates were MRSA. The proportion of hVISA/VISA was significantly higher in MRSA (31/94, 33%) than in MSSA (7/382, 1.8%) ($P < 0.001$). The hVISA/VISA isolates were mainly obtained from abscess (12/38, 31.6%), secretion (10/38, 26.3%) and sputum (9/38, 23.7%). The prevalence ratio of hVISA/VISA was <10% in most regions, except for the south (8/63, 12.7%), north-west (10/96, 10.4%) and north-east (2/19, 10.5%). This is not consistent with the geographical distribution of MRSA. Details are shown in Table 1.

The MICs of nine antimicrobial agents were determined for the isolates (Table 2). All isolates were susceptible to vancomycin, teicoplanin, linezolid and fosfomycin. The vancomycin MIC value for the two VISA isolates was 1 and 2 mg/L, respectively. Such inconsistency between broth microdilution and PAP-AUC methods has previously been reported.[24] Compared with MSSA isolates, MRSA were significantly more resistant to gentamicin, ciprofloxacin, tetracycline, clindamycin and erythromycin ($P < 0.05$). Most of the isolates showed an MIC value of 0.5–1.0 mg/L for vancomycin and an MIC value of 1.0–2.0 mg/L for teicoplanin. The MIC values of vancomycin and teicoplanin for MRSA were higher than those for MSSA (Table 2).

The 38 hVISA/VISA strains showed a polyclonal structure and were assigned to 18 STs, including four new STs (ST3293–ST3296) (Table 3 and Figure 1). ST239 was the most prevalent clone (11/38; 28.9%), followed by ST121 (5/38; 13.2%). The 18 STs were assigned to seven clonal complexes (CCs) by eBURST analysis, i.e. CC8 (ST239), CC121 (ST121, ST837, ST2160, ST3293 and ST3295), CC398 (ST398), CC59 (ST59 and ST338), CC6 (ST6), CC15 (ST15) and CC1 (ST1 and ST3296). As shown in Figure 1, CC121 constitutes the largest group (n=12). Mutations occurring in *aroE*, *pta* and *yqil* were found among the CC121 members (Table S1, available as Supplementary data at *JAC* Online). All ST239 strains were MRSA and two of them were VISA. MSSA were exclusively identified in CC121 (n=6) and ST945 (n=1). Regarding geographical distribution, ST239 has disseminated in six geographical regions and ST121 and ST398 in three regions (Table 3). Like ST239, CC121 has also been detected in six geographical regions.

Nineteen *spa* types were identified in the hVISA/VISA strains. The ST239 clone consisted of two *spa* types (t030 and t037), of which 81.8% were t030 (9/11). Five *spa* types, including two new types, were identified in the CC121 population, and t435 was the predominant type (5/11) (Table 3 and Table S1). Two and three types of SCC*mec* and *agr* were detected in the hVISA/VISA strains, and the predominant types were SCC*mec* III (90.3%; 28/31) and *agr* I (50%; 19/38), followed by SCC*mec* IV (9.7%; 3/31) and *agr* IV (44.7%; 17/38). All ST239 isolates carried *agr* I, while all CC121 strains carried *agr* IV. All except two strains (ST964 and ST707)

Table 1. Origins and phenotypes of 476 *S. aureus* isolates collected in this study

Location	Number of isolates MRSAhVISA/VISA	Specimens							
		blood	secretion	throat swab	abscess	fine-needle	sputum	urine	other
North	80	3	32	6	6	3	22	1	7
	26 (32.5%)	0	9	1	0	1	13	1	1
	4 (5%)	0	1	0	0	0	2	1	0
South	63	3	12	1	37	0	9	1	0
	17 (27%)	0	5	0	6	0	6	0	0
	8 (12.7%)	0	3	0	2	0	3	0	0
Middle south	60	4	8	0	5	6	20	0	17
	14 (23.3%)	0	0	0	1	2	5	0	6
	2 (3.33%)	0	0	0	0	0	2	0	0
North-west	96	4	47	4	38	0	2	0	1
	14 (14.6%)	2	8	1	3	0	0	0	0
	10 (10.4%)	2	3	0	5	0	0	0	0
East	52	0	20	0	8	3	19	2	0
	10 (19.2%)	0	3	0	3	1	2	1	0
	4 (7.69%)	0	0	0	1	0	2	1	0
South-west	106	12	25	9	47	1	9	1	2
	9 (8.49%)	0	5	0	4	0	0	0	0
	8 (7.55%)	0	3	2	3	0	0	0	0
North-east	19	2	1	0	12	0	2	0	2
	4 (21.1%)	1	1	0	1	0	0	0	1
	2 (10.5%)	1	0	0	1	0	0	0	0
Total	476	28 (5.88%)	145 (30.5%)	20 (4.2%)	153 (32.1%)	13 (2.73%)	83 (17.4%)	5 (1.05%)	29 (6.09%)
	94 (19.7%)	3 (10.7%)	31 (21.4%)	2 (10%)	18 (11.8%)	4 (30.8%)	26 (31.3%)	2 (40%)	12 (41.4%)
	38 (8.0%)	3 (10.7%)	10 (6.9%)	2 (10%)	12 (7.84%)	0 (0%)	9 (10.8%)	2 (40%)	0 (0%)

Table 2. Antimicrobial susceptibility profiles of 476 *S. aureus* isolates

	Percentage resistant (*n*)			
Drug	MRSA (*N*=94)	MSSA (*N*=382)	hVISA/VISA (*N*=38)	VSSA (*N*=438)
Gentamicin	52.1 (49)	18.1 (69)	36.8 (14)	23.7 (104)
Ciprofloxacin	44.7 (42)	5.0 (19)	31.6 (12)	11.2 (49)
Tetracycline	47.9 (45)	23.8 (91)	47.4 (18)	26.9 (118)
Clindamycin	69.1 (65)	43.7 (167)	42.1 (16)	49.3 (216)
Erythromycin	77.7 (73)	61.0 (233)	63.2 (24)	64.4 (282)
Linezolid	0 (0)	0 (0)	0 (0)	0 (0)
Fosfomycin	0 (0)	0 (0)	0 (0)	0 (0)
Vancomycin[a]				
0.5 mg/L	52.1 (49)	62.0 (237)	47.4 (18)	61.2 (268)
1.0 mg/L	40.4 (38)	33.5 (128)	42.1 (16)	34.2 (150)
2.0 mg/L	5.3 (5)	1.0 (4)	7.89 (3)	1.37 (6)
Teicoplanin[a]				
1.0 mg/L	40.4 (38)	51.3 (196)	39.5 (15)	50.0 (219)
2.0 mg/L	29.8 (28)	18.6 (71)	31.6 (12)	19.9 (87)
4.0 mg/L	14.9 (14)	1.6 (6)	18.4 (7)	2.97 (13)
8.0 mg/L	1.1 (1)	0 (0)	2.63 (1)	0 (0)

VSSA, vancomycin-susceptible *S. aureus*.
[a]All isolates are susceptible to vancomycin and teicoplanin. Three MIC values (0.5–2.0 mg/L) for vancomycin and four MIC values (1.0–8.0 mg/L) for teicoplanin are shown here, which cover >90% of isolates of this study.

Table 3. Genotypes of 38 hVISA/VISA isolates detected in this study

Phenotype	*spa* type	MLST ST	CC	*agr*	SCC*mec*	*mecA*	PVL	No. of isolates	Geographical location
hVISA	t030	ST239	CC8	I	III	+	+	9	SW, MS, NW, N, E, S
VISA	t037	ST239	CC8	I	III	+	+	2	S, E
hVISA	t435	ST121	CC121	IV	III	+	+	3	NW
hVISA	new	ST3293	CC121	IV	/	−	+	3	SW
hVISA	t435	ST3295	CC121	IV	III	+	+	2	NW
hVISA	new	ST2160	CC121	IV	/	−	+	1	S
hVISA	t7065	ST837	CC121	IV	/	−	+	1	NW
hVISA	new	ST121	CC121	IV	/	−	+	1	N
hVISA	t2019	ST121	CC121	IV	III	+	+	1	E
hVISA	t034	ST398	CC398	I	III	+	+	3	NE, N, SW
hVISA	new	ST946	/	IV	/	−	−	1	N
hVISA	t435	ST88	CC88	IV	III	+	+	1	NE
hVISA	t437	ST59	CC59	I	IV	+	+	1	S
hVISA	t441	ST59	CC59	I	IV	+	+	1	S
hVISA	t437	ST338	CC59	I	III	+	+	1	SW
hVISA	t664	ST72	/	I	III	+	+	1	SW
hVISA	t701	ST6	CC6	I	III	+	+	1	MS
hVISA	t084	ST15	CC15	II	III	+	+	1	NW
hVISA	t002	ST3294	/	II	IV	+	+	1	NW
hVISA	t6980	ST3296	CC1	IV	III	+	+	1	NW
hVISA	new	ST707	CC707	IV	III	+	−	1	SW
hVISA	t127	ST1	CC1	IV	III	+	+	1	E

E; east, S; south, N; north, MS; middle south, NE; north-east, NW; north-west, SW; south-west.

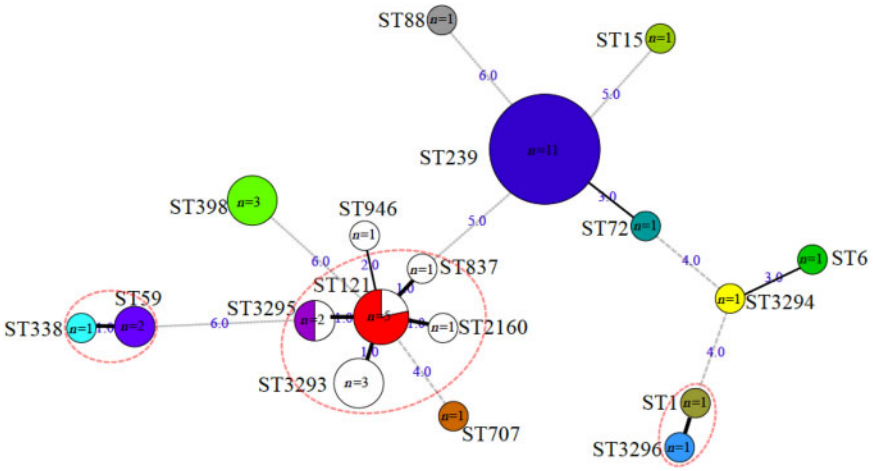

Figure 1. MST of hVISA/VISA isolates. The 38 hVISA/VISA isolates detected in this study were assigned to 18 STs and their relationship is estimated by the MST. A CC is indicated by a red dashed circle. The thickness of lines represents the number of mutations detected in the seven housekeeping genes used by MLST as shown on the lines. Filled circles, MRSA; open circles, MSSA. This figure appears in colour in the online version of *JAC* and in black and white in the print version of *JAC*.

were PVL positive. Overall, the predominant genotype of hVISA/VISA isolates was ST239-SCC*mec* III-t030-*agr* I (23.7%, 9/38), followed by CC121-SCC*mec* III-t435-*agr* IV (13.2%, 5/38).

Discussion

The emergence of hVISA/VISA has become a new concern since their first report in 1996, because such strains are potentially associated with the treatment failure of vancomycin.[25] Of more concern, hVISA/VISA are disseminating worldwide with an increasing trend, and are sporadically detected in CA-MRSA, suggesting an alarming risk that hVISA/VISA may disseminate in community settings. To evaluate this hypothesis, we here investigated the prevalence of hVISA/VISA among *S. aureus* isolates responsible for community-associated infections in county hospitals in China.

In this surveillance, community-associated *S. aureus* isolates collected from 31 county hospitals distributed in 12 provinces in China were surveyed.[14] The proportion of hVISA/VISA was ∼8% among the community-associated isolates. This is relatively lower than the prevalence ratio detected in the HA population (including MRSA and MSSA) in China.[8,26] However, the proportion of hVISA/VISA was high in CA-MRSA (29/94, 30.9%). This ratio is much higher than that (13%–16%) detected in 1012 MRSA isolates obtained between 2005 and 2007 in 14 cities in China.[27] Although this extraordinarily high proportion of hVISA/VISA among CA-MRSA might be caused by the small scale of MRSA collection obtained in this study, it highlights the severe situation for the infection control of hVISA/VISA in community settings. The high proportion of community-associated hVISA/VISA would greatly challenge the empirical treatments, especially in the county hospitals, and re-emphasizes the need for a rational antibiotic policy. The lack of antibiotic-use records does not allow us to elucidate the emergence of hVISA/VISA in community settings.

The hVISA/VISA isolates detected in this study showed a different population structure compared with the hospital-associated isolates reported previously. Numerous studies identified that the majority of hVISA/VISA isolates were from ST239 and CC5, in particular ST5.[8,26] Here, CC121 (followed by ST239) was the most prevalent population among hVISA/VISA isolates, and no CC5 isolates were found. To the best of our knowledge, this is the first report that identified CC121 as a prevalent clone among the hVISA/VISA population. CC121, especially ST121, is a globally disseminated clone.[28] This clone colonizes the anterior nares of asymptomatic subjects, but is also a common cause of infections, varying from mild and superficial to invasive and life-threatening diseases.[28,29] CC121 isolates are commonly susceptible to methicillin (∼90%)[28] and are widely distributed as major MSSA clones in the Americas, Asia and Europe, but have also been found in Africa.[30] However, methicillin resistance has recently been found in CC121 among CA-MRSA from Cambodia and China.[31,32] In particular, a recent study revealed that ST121 (37.3%) was the most prevalent ST among the CA-MRSA collected in six geographical regions (north-east, north, north-west, east, middle south and south-west) in China.[31] This is consistent with our findings and further raises the concern that the prevalence of CA-MRSA-CC121 promotes the emergence of hVISA/VISA-CC121. Indeed, a more severe situation was identified in this study in which half of hVISA-CC121 (6/12) were CA-MRSA. Together, these data highlight the rapid evolution of drug resistance among the CC121 population in community settings, although it was previously suggested that the CC121 genome was not suitable for the maintenance of SCC*mec*. Emergence of hVISA-CC121 greatly challenges public health efforts on drug resistance control, due to its wide dissemination, and surveillance for the emerging hVISA population thus becomes necessary.

Of note, it is suggested that CA-MRSA can be distinguished from HA-MRSA by the type of SCC*mec* element present. The most common SCC*mec* types in CA-MRSA strains are SCC*mec* IV and V, whereas HA-MRSA strains traditionally carry SCC*mec* I, II and III.[33] Our study showed that SCC*mec* III was predominant among the hVISA/VISA isolates. This is consistent with the finding that SCC*mec* III is the most prevalent type in HA-MRSA in China.[27] We thus suppose that some of the CA-MRSA strains collected in this study might obtain SCC*mec* from HA-MRSA and/or be derived from HA-MRSA escaping to the community. Additionally, we found few hVISA strains harbouring SCC*mec* IV, suggesting that hVISA is not limited to typical hospital clones of *S. aureus*. We further noted

that our CA-MRSA-CC121 strains exclusively carried SCC*mec* III, while SCC*mec* IV and V were found to be predominant in CA-MRSA-CC121 in previous studies.[31] Such differences indicate that CC121 has evolved to be MRSA through multiple pathways.

Of more concern, the ST121 lineage is a hypervirulent clone for humans. Numerous mobile genetic elements encoding the potent toxins involved in human disease pathogenesis, such as PVL and toxic shock syndrome toxin-1 (TSST-1), have been identified in the clone.[28] All CC121 isolates of this study carried *agr* IV, which is in agreement with previous studies that almost all CC121 strains are *agr* IV (98.6%, 137/139).[28] It is suggested that the distinctive carriage of *agr* IV in CC121 strains may contribute to their characterized pathogenesis. Another important toxin of *S. aureus* is PVL, a bicomponent pore-forming cytotoxin assembled by LukS–PV and LukF–PV. PVL closely relates to the development of *S. aureus* infection,[34] and a high frequency of PVL is detected among most MSSA strains and successful MRSA clones.[35] It is suggested that PVL is a characteristic feature of prevalent CA-MRSA clones. Previous studies also identified that CC121 is a predominant clone among PVL-positive MSSA. In accordance, all hVISA-CC121 isolates in this study harboured PVL. It is suggested that the high frequency of carriage of PVL in CC121 strains may contribute to the hypervirulent features of the clone and favour its successful spread.[36,37]

Additionally, *S. aureus* CC121 has a multi-host tropism and it has been reported that a prevalent clone ST121 caused a majority of chronic staphylococcal infections in rabbits.[38] Abuse of vancomycin in breeding animals could stimulate the emergence of hVISA/VISA-CC121. Therefore, CC121 dissemination between human and animals greatly challenges the public health efforts on controlling the dissemination of the emerging hVISA clone.

In summary, to the best of our knowledge, we are the first to report a globally disseminated lineage, CC121, being prevalent among the hVISA/VISA population in community settings. This clone with hypervirulent potential greatly threatens public health and highlights the necessity of tailor-made surveillance to prevent its further dissemination.

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Transparency declarations

None to declare.

Supplementary data

Table S1 is available as Supplementary data at *JAC* Online.

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