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Antibiotic resistance and molecular characteristics of methicillin-resistant *Staphylococcus epidermidis* recovered from hospital personnel in China

Zhen Xu[1], Rory Cave[2], Liqin Chen[1], Tsetan Yangkyi[3], Yan Liu [4], Ke Li[1], Ge Meng[1], Kaijun Niu[1], Wanqi Zhang[1], Naijun Tang[1], Jun Shen[1], Hermine V Mkrtchyan[2]*

1．Tianjin Key Laboratory of Environment, Nutrition and Public Health，Department of Toxicology and Sanitary Chemistry, School of Public Health, Tianjin Medical University, Qixiang Road No. 22, Tianjin, China, 300070

2．School of Health, Sport and Biosciences, University of East London, London, UK. E15 4LZ,

3．CDC of Biru County.Tibet, China, 850000

4．Tianjin Central hospital of Gynecology, Obstetrics, Tianjin, China, 300110

Corresponding author

*Hermine V Mkrtchyan: School of Health, Sport and Biosciences, University of East London, London, UK. E1 4NS, London, E1 4NS; E-mail: h.mkrtchyan@uel.ac.uk

Highlights

- The colonization rate of MRSE (91%) was unusually high among hospital personnel from two hospitals in Tianjin, China, who were carriers of *S. epidermidis*.
- The MRSE isolates had high resistance rates towards β-lactam antibiotics, but low resistance rates against non-β-lactam antibiotics.

- The majority of MRSE in this study belonged to cluster II domain of CC2. ST59-IV was the predominant clone among isolates recovered from hospital personnel, a sequence type that was reportedly associated with clinical infections.
- New MLST types were determined, thus confirming the genetic diversity of these isolates.
- The hospital personnel may well act as a reservoir of antimicrobial resistant pathogens.

Abstract

Objectives

Staphylococcus epidermidis is a major nosocomial pathogen predominantly associated with indwelling medical device infections. Studies reporting on *S. epidermidis* recovered from hospital personnel in China are scarce. The aim of this study was to evaluate the carriage and antibiotic resistance of *S. epidermidis* among the hospital personnel in Tianjin, China and provide insights into their genetic diversity.

Methods

107 *S. epidermidis* isolates were recovered from 68 hospital personnel in two public hospitals in Tianjin between March 2018 and May 2018. SCC*mec* types were determined by the combination of *mec* and *ccr* complexes. Multi-locus sequence typing was used to determine the sequence types (ST) of *S. epidermidis* isolates.

Results

62 (76.5%) isolates were determined to be methicillin-resistant *S. epidermidis* (MRSE). 35 (51%) out of 68 hospital personnel carried *S. epidermidis*, of which 32 (91%) were carriers of MRSE. All 62 MRSE isolates had high levels of resistance to penicillin (90%) and cefoxitin (100%). 37 (60%) isolates carried

SCC*mec* type IV, followed by 15 (24%) carrying SCC*mec* V, and 4 (6%) SCC*mec* II. Novel sequence types were assigned to four *S. epidermidis* isolates (ST832, ST833, ST834 and ST835).

Conclusions

In this study, the majority of MRSE belonged to cluster II domain of CC2. The ST59-IV was a dominant clone among isolates recovered from hospital personnel. Determination of new MLST types confirmed the genetic diversity of these isolates. These observations highlight the need to review the infection control strategies to reduce the carriage of MRSE among hospital personnel.

Keywords: *Staphylococcus epidermidis*, hospital personnel, *mecA*, SCC*mec*, MLST, sequence type

1. Introduction

Staphylococcus epidermidis is a common colonizer of the human skin [1], but also one of the major opportunistic pathogens responsible for medical device associated infections (MDAI). However, the role of *S. epidermidis* as a nosocomial pathogen has been underestimated until late 1980s [2]. Recently, several studies reported that the distribution of *S. epidermidis* in human clinical samples was higher than infections caused by *S. aureus* in Greece and India [1,3]. The ever increasing antibiotic resistance aggravates the problem, and poses a greater challenge for the control of hospital acquired infections [4]. Methicillin resistance is mediated by the *mecA* gene, which encodes penicillin binding protein 2a that has low affinity to β-lactam antibiotics, and thus confers methicillin resistance [5]. The *mecA* gene is located on a mobile genetic island named staphylococcal cassette chromosome *mec* (SCC*mec*). Up to date eleven SCC*mec* types have been assigned based on combinations of *mec* and *ccr* complexes [6]. Molecular typing methods, including multi-locus sequence typing have been instrumental to identify

highly diverse genetic lineages of *S. epidermidis* [7]. *S. epidermidis* species have been assigned onto one major clonal complex (CC2), 8 minor clonal complexes and 13 singletons [8].

While there are many studies reporting the molecular epidemiology of *S. aureus*, studies reporting the molecular characteristics of *S. epidermidis* are fragmentary. It has been documented that hospital personnel are often carriers of methicillin-resistant staphylococci and aid the dissemination of hospital –acquired infections [9]. However, little is known about the genotypic diversity of methicillin-resistant *S. epidermidis* (MRSE) among hospital personnel in China. To our knowledge, only two studies have reported acquisition of MRSE among hospital personnel with 89% of hospital personnel carrying MRSE in Sweden [10] and 30% in Shanghai, China [11].

In this study, we evaluate the carriage and susceptibility patterns of MRSE among the hospital personnel recovered from two hospitals in Tianjin, China and provide insights into their genetic diversity.

2. Material and Methods

2.1 Study protocol

As a part of a small surveillance study to assess the carriage of MRSE among the hospital personnel, one hundred and seven samples were recovered from the hospital personnel (n=68) in two public hospitals in Tianjin city, North China, between March 2018 and May 2018. Samples were taken from doctors and nurses' hands (n=68) and nasal cavity (n=39).

The research protocol and informed consent was approved by the Ethics committee of Tianjin Science and Technology Commission (approval No TMUaMEC2017017). All research was performed in accordance with the relevant guidelines and regulations. Informed consent was obtained from all participants.

All specimens were inoculated onto mannitol salt agar (MSA, Oxoid, Basingstoke, UK) and incubated aerobically at 37 ℃ for 24-48 h.

2.2 Identification

S. epidermidis isolates were subjected to partial 16S rRNA gene sequencing using the primers and PCR conditions as described previously [12]. Amplified PCR products were sequenced by Sangon Biotech (Shanghai, China). Homology searches were carried out using BLAST tool (NCBI: https://www.ncbi.nlm.nih.gov/) [13].

2.3 Antimicrobial susceptibility test

Susceptibility to ten antibiotics was tested for all isolates using standard disk diffusion method. The antibiotics tested included: CN: gentamicin (10 µg), E: erythromycin (15 µg), FOX: cefoxitin (30 µg), P: penicillin (10 units), T: tetracycline (30 µg), TEC: teicoplanin (30 µg), DA: clindamycin (2 µg), CHL: chloramphenicol (30 µg), LZD: linezolid (30 µg), and RD: rifampin (5 µg). The isolates were categorized as susceptible, intermediate resistant, or resistant according to the recommendations of Clinical and Laboratory Standard Institute (CLSI) [14].

2.4 *mecA* gene determination and SCC*mec* typing

The *mecA* gene was determined for all isolates using PCR method as described previously [15]. SCC*mec* types were determined for all *mecA* positive isolates by evaluating the *mec* and *ccr* complexes [15].

2.5 Multi locus sequence typing of *S. epidermidis*

The *mecA* positive isolates (n=60) were analysed for seven housekeeping genes using multi locus sequence typing (MLST) as described previously [16]. In brief, seven house-keeping genes of each isolate were amplified by using *arcC*, *aroE*, *gtr*, *mutS*, *pyr*, *tpi*, and *yqil* primers and then sequenced by

Sangon Biotech (Shanghai, China). The sequence type for each isolate was assigned using the *S. epidermidis* MLST database (https://pubmlst.org/).

2.6 Statistics

The goeBURST algorithm (http://www.phyloviz.net/goeburst/) was used to build goeBURST diagram tree [11] . A hierarchy clustering heatmap was constructed using the MLST sequence type data, isolation source and SCC*mec* type and resistance profile of the *mecA* positive isolates using the r. package "Heatmap.plus" (https://www.rdocumentation.org/packages/heatmap.plus/versions/1.3/topics/heatmap.plus.package).Principal component analysis was performed to distinguish between antibiotic resistance profiles by site using the r packages "FactorMineR" (https://cran.r-project.org/web/packages/Facto MineR/index.html) and "factoextra" (https://cran.r-project.org/package_=facto extra).

The χ^2 test was used to analyze the quantitative variables. A P-value < 0.05 was considered statistically significant.

3. Results

3.1 Study protocol and identification of isolates

Samples were taken from hands of hospital personnel (n=68) and nasal cavity (n=39). 35 out of 68 (51%) hospital personnel were identified as carriers of *S. epidermidis*, including 24 of 68 (35%) carried *S. epidermidis* on their hands. 19 out of 39 (49%) hospital personnel were nasal carriers. In addition, 8 out of 68 (12%) carried *S. epidermidis* both on their hands and nasal cavity. A total of 165 isolates were recovered from the hands or nasal cavity samples of the hospital personnel working in two public hospitals in Tianjin city, China between March 2018 and May of 2018. 81 (81/165, 49%) isolates were

identified as *S. epidermidis*, including 40 isolates recovered from hands and 41 *S. epidermidis* isolated from nasal cavity.

3.2 *mecA* gene determination of *S. epidermidis*

The *mecA* gene was determined in 62 (62/81; 76.5%) isolates, including 30 (30/40; 75%) recovered from hospital personnel hands, and 32 (32/41; 78%) from nasal cavity. In addition, 33 (33/68; 49%) hospital personnel were carriers of MRSE, including 19 (19/68; 28%) carried MRSE on their hands and 19 (19/68; 28%) carried MRSE in their nasal cavity. Moreover, 5 (5/68; 7%) of the hospital personnel were carriers of MRSE both on their hands and in the nasal cavities (**Table 1**).

3.3 Antimicrobial susceptibility of MRSE

The disc diffusion method was used to test the susceptibility of all *S. epidermidis* isolates (n=81) against 10 antibiotics. Eighty-one (100%) isolates were resistant to at least one antibiotic. Resistance to penicillin and cefoxitin was observed in 70 out of 81 (86%) and 62 out of 81(77%) isolates respectively. Thirty-four (42%) isolates were resistant to erythromycin (R≦1.3 cm), whereas 18 (26%) isolates showed intermediate resistance (I=1.4-2.2 cm) towards erythromycin. Five (8%) isolates were resistant to gentamicin (R≦ 1.2 cm), and 4 (5%) to tetracycline (R≦1.4 cm). (**Table 1**). Thirty-one (38%) isolates were resistant to teicoplanin (R≦ 1.0 cm), thirty-four (42%) isolates to clindamycin (R≦1.4 cm), six (7%) to chloramphenicol (R≦1.2 cm), six (7%) to linezolid (R≦ 2.0 cm), and thirteen (16%) to rifampin (R≦1.6 cm). All the *mecA*-negative *S. epidermidis* isolates were susceptible to cefoxitin. The majority of *mecA*-negative isolates were susceptible to gentamicin, chloramphenicol, linezolid and rifampin. Fourteen (14/19; 73.7%) *mecA*-negative isolates were resistant to penicillin, followed by 13 (13/19;

68.4%) to clindamycin, 12 (12/19; 63.2%) to erythromycin, and 6 (6/19; 31.6%) to teicoplanin (**Table 2**).

3.4 SCC*mec* typing of MRSE

SCC*mec* types were determined for all 62 MRSE isolates. Thirty-seven (60%) isolates (from hands n=21; from nasal cavity n=16) harboured SCC*mec* type IV, followed by 15 (24%) SCC*mec* type V, and 4 (6%) SCC*mec* type II. In addition to this, 6 isolates were non-typeable, including 3 (5%) isolates harboured a combination of class C *mec* complex and the *ccr* type 3 complex, and 2 (3%) isolates carried class C *mec* complex and *ccr* type 2, whereas 1 (2%) isolate lacked *mec* complex but carried *ccr* type 3 complex (**Table 1**).

3.5 Multi locus sequence typing of MRSE

Multi locus sequence typing was performed to determine the sequence types of 60 MRSE, including 29 recovered from hospital personnel hands (n=18) and 31 from nasal samples (n=18). The ST59 (n=19) was the most common sequence type, followed by ST35 (n=4), ST14 (n=3), ST57 (n=3), ST218 (n=3), ST20 (n=3), ST49 (n=2), ST69 (n=2), ST110 (n=2), ST152 (n=2), ST227 (n=2), ST466 (n=2), ST5 (n=1), ST6 (n=1), ST17(n=1), ST50 (n=1), ST84 (n=1), ST130 (n=1), ST190 (n=1), ST192 (n=1), and ST234 (n=1). In addition, four isolates contained novel sequence types that were assigned as: ST832. ST833, ST834 and ST835. All 60 MRSE isolates were clustered into clonal complex 2 (CC2) by the goeBURST algorithm. In addition, no singleton was detected (**Fig 1**).

3.6 Hierarchical clustering Heatmap and PCA analysis

A hierarchical cluster heatmap was performed on 60 MRSE isolates based on their site of isolation, SCC*mec* and MLST types (**Fig 2A**) to their antibiotic resistant profile. These analyses showed that there

was no obvious clustering based on the site of isolation, SCC*mec* and MLST types. This was further showed by PCA analysis on site isolates as the confidence ellipse overlapped each other (**Fig 2B**).

3.7 Statistical analysis

The χ^2 test was used to analyse the quantitative variables. A *P*-value < 0.05 was considered statistically significant.

4. Discussion

S. epidermidis is a major nosocomial pathogen responsible for device associated infections [1]. Hospital personnel have an important role of being in direct contact with patients and subsequently play a key role in cross-transmission of MRSE [9]. In this study, we report the antimicrobial resistance patterns and genetic diversity of MRSE among the hospital personnel in Tianjin, China.

The resistance of MRSE towards penicillin is well documented. Xin et al [11] reported that 90.4% of *S. epidermidis* isolates recovered from hospital environments were resistant to penicillin. Consistent with their results we have shown that 90% of MRSE isolates in our study were phenotypically resistant to penicillin. In addition, we have previously reported high levels of antibiotic resistance towards penicillin in environmental *S. epidermidis* (70%) isolates recovered from London [12]. Interestingly, in this study the resistance rates towards gentamicin (8%), and erythromycin (35%) were relatively low compared with others that demonstrated resistance towards gentamicin and erythromycin as 20% and 50% respectively [10,11]. Previously, it was shown that cefoxitin disk diffusion method was preferable for routine methicillin resistance screening of *S. aureus*, *S. epidermidis* and other CoNS isolates [17,18]. In this study, 62 (62/81, 77%) *S. epidermidis* isolates were resistant to cefoxitin, all of which carried the *mecA* gene. Li M et al, reported that resistance of clinical *S. epidermidis* isolates towards penicillin,

cefoxitin, gentamicin and erythromycin were 100%, 100%, 77.8% and 72.2% respectively [19]. In this study, the resistance towards non-β-lactam antibiotics in *S. epidermidis* isolates recovered from hospital personnel was significantly lower than that of clinical *S. epidermidis* isolates, whereas the resistance towards β-lactam antibiotics was similar to clinical *S. epidermidis* isolates.–In this study, 100% *S. epidermidis* isolates were phenotypically resistant to at least 1 antibiotic. 22 out of 81 (27%) *S. epidermidis* isolates were resistant to 2 antibiotics, 27 isolates (33%) were resistant to 3 antibiotics, 18 isolates (22%) were resistant to 4 antibiotics, 5 (6%) isolates were resistant to 5 antibiotics, 5 (6%)isolates were resistant to 6 antibiotics and 1 (1.2%) isolate was resistant to 9 antibiotics.

In this study 32 (91%) out of 35 *S. epidermidis* carriers were identified to carry MRSE.-Although, in this study the carriage of MRSE among the hospital personnel was significantly higher than among the hospital personnel in Shanghai, China [11], our findings were consistent with the MRSE rates (89%) among the hospital personnel in Intensive Care Unit in Sweden [10]. Previously, it was reported that the rate of MRSE carriage among the volunteers and in the environment was 11% [20], which was significantly lower than the rate of MRSE carriage among the hospital personnel.

The size of SCC*mec* IV and V is smaller than those of SCC*mec* types I, II and III, and thus conferring SCC*mec* IV and V increased mobility and dissemination ability [21]. Li et al reported that 35% of clinical MRSE harboured SCC*mec* types IV and V in China [19]. In this study, 60% of MRSE harboured SCC*mec* type IV, followed by 24% harbouring SCC*mec* type V. We determined that 6% of MRSE that carried SCC*mec* type II were recovered from nasal samples. SCC*mec* II was reportedly identified in clinical *S. aureus*, *S. epidermidis* and other coagulase negative staphylococci [19]. Interestingly, we did not identify SCC*mec* types I, and III, which in contrast have been identified by Xin D. et al in isolates recovered from

hospital personnel in Shanghai [11]. Six previously un-classified SCC*mec* types were determined in this study, including 3 carrying class C *mec* complex and *ccr* 3, and 2 had a combination of class C *mec* complex and *ccr* 2. In addition, one MRSE was classified as SCC*mec*12263 since it lacked *mec* complex. For *S. epidermidis*, one major clonal complex (CC2), 8 minor clonal complexes and 13 singletons have been categorized [16]. In this study, all MLST types were classified into one major CC2 clonal complex, hence we did not detect isolates belonging to minor clonal complexes or singletons (**Fig 1**). However, although belonging to one CC group, in our study, we detected a diversity of MLST types (n=25). Miragaia et al summarized the sequence types of CC2 that accounted for 74% of the *S. epidermidis* population, and divided them into 2 clusters: cluster I: included the predicted ancestor (ST2) and cluster II: included several subgroup founders (ST5, -6, -57, -85, and -89) [16]. In this study, the majority of sequence types were categorized into cluster II, including those identified as subgroup founders: ST5, 49, 57, 110, 152, and 835 (**Fig 1**). In addition, two isolates belonged to ST35. Miragaia et al reported that ST2 of cluster I is the most widely disseminated sequence type that has been identified in thirteen different countries [16]. In this study, no ST2 was determined among the *S. epidermidis* isolates recovered from two hospital personnel in Tianjin, China. However, the ST59 of cluster II was the most frequently identified sequence type. Isolates belonging to ST59 sequence type were reported to be only the second to the ST2, a prominent cause of clinical infections in China [11]. Thus, the prevalence of ST59 among the hospital personnel is rather worrying.

Previously, whole genome sequencing studies revealed that environmental *S. epidermidis* ST59 isolate carried SCC*mec* type IV mobile genetic element [22]. To the best of our knowledge, this is the first study reporting that isolates belonging to ST59 harboured unclassified SCC*mec* types (C/2 and C/3) (**Fig 1**).

S. epidermidis ST5 has been associated with clinical and animal infections [23], whereas *S. epidermidis* ST6, ST20, ST110, ST130 and ST152 were associated with clinical infections [8,24,25]. It is largely known that the main transmission route of staphylococci is person to person and hospital personnel play a major role in such transmission [1]. Thus, our study provides further insights on the colonization of the hospital personnel with *S. epidermidis*. In addition, Xin et al reported a variety of *S. epidermidis* sequence types identified among hospital personnel (ST14, ST16, ST54, ST88, ST153, ST171, ST184, ST190, ST192, ST193, ST194, ST203, ST204, ST210, ST218, ST219, ST220, ST226, ST233, ST237, ST262, ST267, ST291, ST327, ST362, ST387, ST406, and ST466) [11]. Some of the sequence types (ST14, ST190, ST218, and ST466) identified in this study were consistent with their findings. However, in addition to this we also report sequence types (ST35, ST57, ST69, ST84, ST227, and ST234) that were not identified by Xin et al. [11]. In addition, four new MLST types were determined in this study.

We did not detect any obvious clustering based on site of isolation, SCC*mec* types and MLST types (**Fig 2A**). This was further demonstrated by PCA analysis on site isolates as the confidence ellipse overlapped each other (**Fig 2B**). Other authors reported discrepancies between the antibiotic resistance profile and different types of SCC*mec* elements [26]. This report shows that SCC*mec* type III and IV in *S. epidermidis* were more likely to be resistant to a larger number of antibiotics.

5. Conclusion

The main limitation of this study is that only samples recovered from the hospital personnel were included. The carriage of MRSE (91%) was unusually high among hospital personnel who were carriers of *S. epidermidis*. We also observed different MRSE colonization rate in hospital personnel in two hospitals. The MRSE isolates had high resistance rates towards β-lactam antibiotics, but low resistance

rates against non-β-lactam antibiotics. Moreover, the majority of MRSE in this study belonged to cluster II domain of CC2. ST59-IV was the predominant clone among isolates recovered from hospital personnel, a sequence type that was reportedly associated with clinical infections. Moreover, new MLST types were determined, thus further confirming the genetic variability of these isolates. Our data demonstrate that the hospital personnel may well act as a reservoir of antimicrobial resistance pathogens. Undoubtably, there is a need to review the infection control strategies and implement appropriate screening and monitoring measures to identify the high carriage of MRSE among hospital personnel on timely manner.

Abbreviations

CoNS: Coagulase-negative staphylococci

MRSE: Methicillin-resistant *Staphylococcus epidermidis*

SCC*mec*: Staphylococcal cassette chromosome *mec*

E: erythromycin; CN: gentamicin; FOX: cefoxitin; P: penicillin; T: tetracycline

MLST: Multi-locus sequence typing

ST: sequence types

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Competing interests

The authors declare they have no competing interests

Ethics approval

The research protocol and informed consent was approved by the Ethics committee of Tianjin science and technology commission (approval No TMUaMEC2017017).

Consent for publication

Not applicable

Authors' contributions

ZX: conception and design of the study, samples collection, data analysis, manuscript preparation. study design, laboratory work. TY, RC: Data analysis, manuscript preparation. LC, RC: Data analysis, critically reviewing the paper. TYL, GM, KN: sample collection, critically reviewing the paper. YL, WZ, NT, JS: critically reviewing the paper, HVM: conception and design of the study, data analysis, manuscript preparation, critically reviewing the paper. All authors read and approved the final manuscript.

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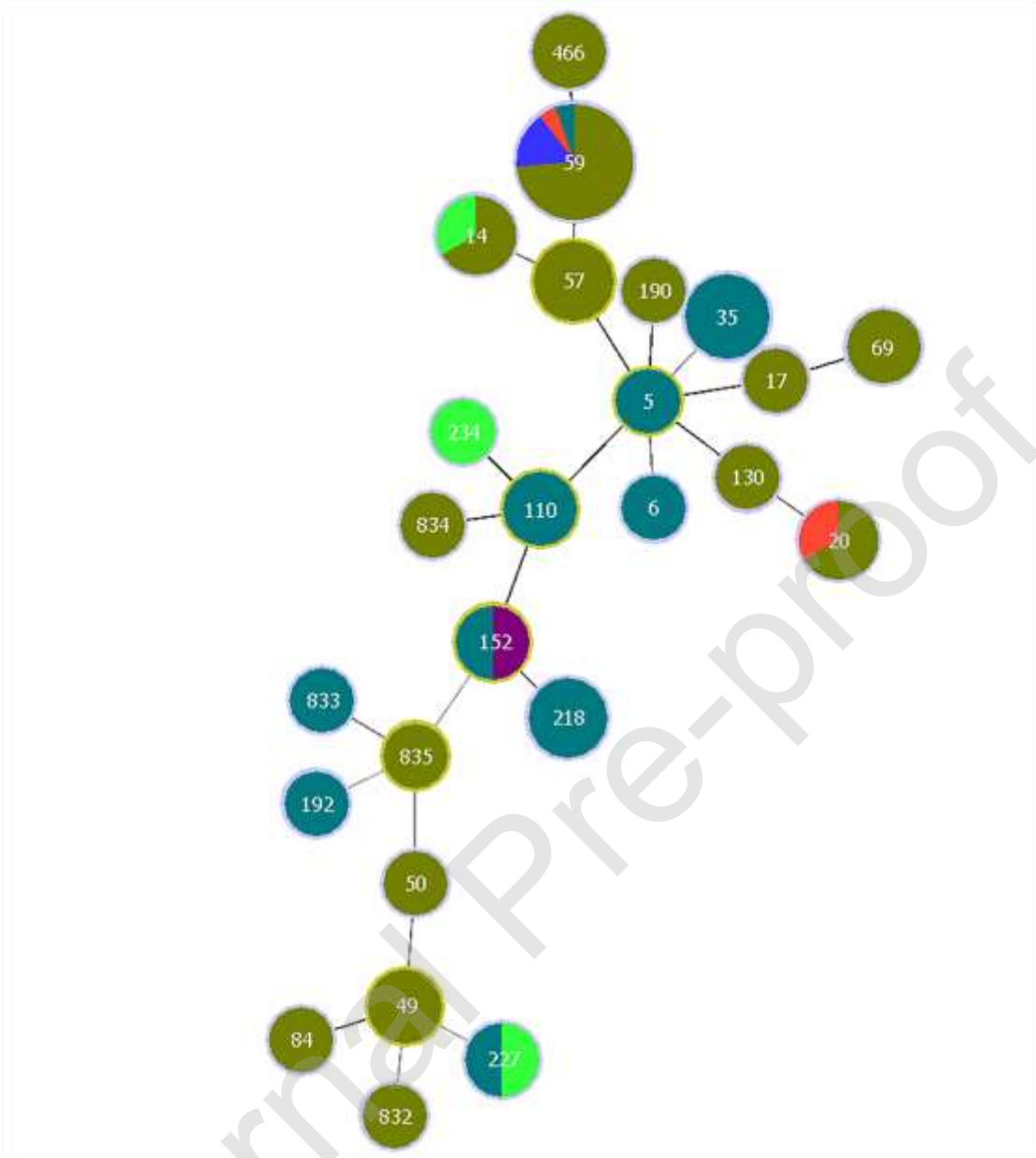
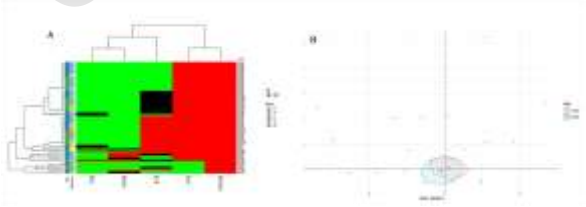
Figure 1 goeBURST analysis of 60 MRSE isolates recovered from hospital personnel in China



ST nodes: Dark green circles: sub-group founder; Light blue circles: common nodes
Light green: SCC*mec* II; Dark yellow: SCC*mec* IV; Turquoise: SCC*mec* V; Red: SCC*mec* C/2; Blue: SCC*mec* C/3; Purple: non-typable SCC*mec*

Figure 2 Hierarchy cluster heatmap and PCA analysis of MRSE isolates antibiotic resistance profile



(A) Hierarchy clustered heatmap. Red tile resistant, Black tile intermediate, green tile sensitive. **(B)** PCA analysis. 95% confidence ellips

Table 1 Antibiotic resistance and molecular characterization of *mecA* gene positive *S. epidermidis*

ID	Hospital	Personnel	Sites	Species	*mecA*	*mec*	*ccr*	SCC*mec*	FOX_{30}	Other antibiotics								
										CHL_{30}	CN_{10}	DA_2	E_{15}	LZD_{30}	P_{10}	RD_5	TEC_{30}	T_{30}
1	A	A1	H	*S.epidermidis*	+	B	2	IV	R	S	S	R	S	S	R	S	I	S
2	A	A12	H	*S.epidermidis*	+	B	2	IV	R	R	S	I	R	S	R	S	I	S
3	A	A2	H	*S.epidermidis*	+	B	2	IV	R	S	S	I	I	S	R	S	R	S
4	A	A3	H	*S.epidermidis*	+	B	2	IV	R	S	S	S	S	S	S	S	R	S
5	A	A1	H	*S.epidermidis*	+	B	2	IV	R	S	S	I	S	R	R	S	I	S
6	A	A1	H	*S.epidermidis*	+	B	2	IV	R	S	S	S	S	S	R	R	R	I
7	A	A2	H	*S.epidermidis*	+	B	2	IV	R	S	S	I	S	S	R	S	R	S
8	A	A4	H	*S.epidermidis*	+	B	2	IV	R	S	S	S	I	R	R	S	R	S
9	A	A12	H	*S.epidermidis*	+	B	2	IV	R	R	S	I	R	S	R	S	I	S
10	A	A13	H	*S.epidermidis*	+	B	2	IV	R	S	S	I	R	S	R	S	R	S
11	A	A1	H	*S.epidermidis*	+	B	2	IV	R	S	S	I	S	S	R	S	R	S
12	B	B2	H	*S.epidermidis*	+	B	2	IV	R	R	R	R	R	R	R	R	R	S
13	B	B3	H	*S.epidermidis*	+	B	2	IV	R	R	R	R	I	S	R	S	R	S

14	B	B3	H	*S.epidermidis*	+	B	2	IV	R	R	I	I	S	R	R	R	R	S
15	B	B4	H	*S.epidermidis*	+	B	2	IV	R	S	S	I	S	S	R	S	I	S
16*	B	B4	H	*S.epidermidis*	+	B	2	IV	R	S	S	S	S	S	R	S	I	S
17	B	B8	H	*S.epidermidis*	+	B	2	IV	R	S	S	I	I	R	R	S	R	I
18	B	B11	H	*S.epidermidis*	+	B	2	IV	R	S	S	S	R	S	R	S	I	S
19	B	B9	H	*S.epidermidis*	+	B	2	IV	R	S	S	S	S	S	R	S	I	S
20	B	B16	H	*S.epidermidis*	+	B	2	IV	R	S	S	S	I	S	R	S	I	S
21	B	B18	H	*S.epidermidis*	+	B	2	IV	R	S	R	S	S	S	S	S	I	S
22	B	B15	H	*S.epidermidis*	+	C	5	V	R	S	S	I	R	S	R	S	I	S
23	B	B5	H	*S.epidermidis*	+	C	5	V	R	S	S	S	R	S	R	S	R	I
24	B	B1	H	*S.epidermidis*	+	C	5	V	R	S	S	I	R	S	R	S	R	S
25	A	A5	H	*S.epidermidis*	+	C	5	V	R	S	S	S	R	S	R	R	I	I
26	A	A3	H	*S.epidermidis*	+	C	5	V	R	R	S	R	R	S	R	S	R	S
27	A	A4	H	*S.epidermidis*	+	C	5	V	R	S	S	R	R	S	R	R	I	S
28	A	A3	H	*S.epidermidis*	+	C	5	V	R	S	S	R	I	S	R	S	I	S
29	A	A5	H	*S.epidermidis*	+	C	2	C/2	R	S	I	R	R	S	R	R	I	S

30	B	B17	H	*S.epidermidis*	+	C	2	C/2	R	S	S	R	S	S	R	S	I	S
31	A	A11	NC	*S.epidermidis*	+	A	2	II	R	S	S	R	R	S	R	S	I	S
32	A	A11	NC	*S.epidermidis*	+	A	2	II	R	S	S	R	R	S	R	S	I	S
33	B	B19	NC	*S.epidermidis*	+	A	2	II	R	S	S	I	R	S	S	S	I	S
34	B	B20	NC	*S.epidermidis*	+	A	2	II	R	S	S	S	R	S	R	S	R	S
35	A	A8	NC	*S.epidermidis*	+	B	2	IV	R	S	S	I	S	S	R	S	R	S
36	A	A8	NC	*S.epidermidis*	+	B	2	IV	R	S	S	R	R	S	R	S	R	S
37	A	A12	NC	*S.epidermidis*	+	B	2	IV	R	S	S	S	R	S	R	S	R	S
38	A	A10	NC	*S.epidermidis*	+	B	2	IV	R	S	S	S	I	S	R	S	I	S
39	B	B6	NC	*S.epidermidis*	+	B	2	IV	R	S	R	S	S	S	R	S	I	S
40	B	B7	NC	*S.epidermidis*	+	B	2	IV	R	S	S	R	S	S	R	S	R	S
41	A	A6	NC	*S.epidermidis*	+	B	2	IV	R	S	S	I	S	R	R	S	I	S
42	A	A6	NC	*S.epidermidis*	+	B	2	IV	R	S	S	R	I	S	R	S	I	S
43	A	A10	NC	*S.epidermidis*	+	B	2	IV	R	S	S	S	I	S	R	S	R	S
44	B	B17	NC	*S.epidermidis*	+	B	2	IV	R	S	S	I	S	S	R	R	I	S
45*	B	B16	NC	*S.epidermidis*	+	B	2	IV	R	S	S	I	S	S	R	S	I	S

46	B	B12	NC	*S.epidermidis*	+	B	2	IV	R	S	S	R	S	S	S	S	I	S
47	B	B12	NC	*S.epidermidis*	+	B	2	IV	R	S	S	R	I	S	S	S	S	S
48	B	B10	NC	*S.epidermidis*	+	B	2	IV	R	S	S	R	I	S	R	R	R	S
49	B	B16	NC	*S.epidermidis*	+	B	2	IV	R	S	S	I	S	S	R	S	I	S
50	B	B18	NC	*S.epidermidis*	+	B	2	IV	R	S	S	I	S	S	R	S	R	S
51	A	A7	NC	*S.epidermidis*	+	C	5	V	R	S	S	R	I	S	R	S	I	S
52	A	A7	NC	*S.epidermidis*	+	C	5	V	R	S	S	I	I	S	R	R	I	S
53	B	B13	NC	*S.epidermidis*	+	C	5	V	R	S	S	R	R	S	R	S	R	S
54	B	B13	NC	*S.epidermidis*	+	C	5	V	R	S	S	R	R	S	R	R	R	S
55	B	B10	NC	*S.epidermidis*	+	C	5	V	R	S	S	R	R	S	R	R	I	R
56	B	B10	NC	*S.epidermidis*	+	C	5	V	R	S	S	I	R	S	R	R	I	S
57	B	B14	NC	*S.epidermidis*	+	C	5	V	R	S	S	R	I	S	R	S	I	S
58	B	B18	NC	*S.epidermidis*	+	C	5	V	R	S	S	I	I	S	R	S	R	S
59	B	B1	NC	*S.epidermidis*	+	C	3	C/3	R	S	R	I	I	S	R	S	I	R
60	B	B6	NC	*S.epidermidis*	+	C	3	C/3	R	S	S	I	S	S	R	S	I	S
61	B	B6	NC	*S.epidermidis*	+	C	3	C/3	R	S	S	S	S	S	R	S	I	S

62	A	A9	NC	*S.epidermidis*	+	NT	3	NT	R	S	I	I	S	S	S	S	I	S

A: hospital 1, B: hospital 2; H: hand, NC: nasal cavity. NT: non-typeable, E: erythromycin; CN: gentamicin; FOX: cefoxitin; P: penicillin; T: tetracycline, TEC: teicoplanin, DA: clindamycin, CHL: chloramphenicol, LZD: linezolid, and RD: rifampin. NT non-typeable; * MLST type not determined.

penicillin: (S≥2.9 cm, R≤2.8 cm), erythromycin(S≥2.3 cm, I=1.4-2.2 cm, R≤1.3 cm), cefoxitin (S≥2.5 cm, R≤2.4 cm), gentamicin (S≥1.5 cm, I=1.3-1.4 cm, R≤1.2 cm), tetracycline (S≥1.9 cm, I=1.5-1.8 cm, R≤1.4 cm), teicoplanin (S≥1.4 cm, I=1.1-1.3 cm, R≦ 1.0 cm), clindamycin (S≥2.1 cm, I=15-20 cm, R≦1.4 cm), chloramphenicol (S≥1.8 cm, I=1.3-1.7 cm, R≦1.2 cm), linezolid (S≥2.1 cm, R≦ 2.0 cm), rifampin (S≥20 cm, I=1.7-1.9 cm, R≦1.6 cm)

Table 2 Antibiotic resistance of *mecA* gene negative *S. epidermidis*

ID	Hospital	Personnel	Species	*mecA*	CHL_{30}	CN_{10}	DA_{2}	E_{15}	FOX_{30}	LZD_{30}	P_{10}	RD_{5}	TEC_{30}	T_{30}
63	A	A1	*S.epidermidis*	–	S	S	R	I	S	S	R	S	R	S
64	A	A1	*S.epidermidis*	–	S	S	I	R	S	S	S	S	R	S
65	A	A1	*S.epidermidis*	–	S	S	R	R	S	S	S	S	I	S
66	A	A5	*S.epidermidis*	–	S	S	R	S	S	S	S	S	I	S
67	A	A6	*S.epidermidis*	–	S	S	R	R	S	S	R	S	I	S
68	A	A7	*S.epidermidis*	–	S	S	R	I	S	S	R	S	I	R
69	A	A8	*S.epidermidis*	–	S	S	R	R	S	S	R	S	I	S
70	A	A8	*S.epidermidis*	–	S	S	R	R	S	S	R	S	I	S
71	A	A9	*S.epidermidis*	–	S	S	I	R	S	S	R	R	R	S
72	A	A10	*S.epidermidis*	–	S	S	I	S	S	S	R	S	I	S
73	A	A10	*S.epidermidis*	–	S	S	I	S	S	S	R	S	R	S
74	A	A11	*S.epidermidis*	–	S	S	R	R	S	S	R	S	I	S
75	A	A11	*S.epidermidis*	–	S	S	R	S	S	S	R	S	I	S
76	A	A11	*S.epidermidis*	–	S	S	R	R	S	S	R	S	I	S
77	A	A13	*S.epidermidis*	–	S	S	S	R	S	S	R	S	I	S
78	A	A14	*S.epidermidis*	–	S	S	R	S	S	S	R	S	R	R
79	A	A15	*S.epidermidis*	–	S	S	I	R	S	S	R	S	R	S
80	A	A15	*S.epidermidis*	–	S	S	R	R	S	S	S	S	I	S
81	B	B20	*S.epidermidis*	–	S	I	R	R	S	S	S	S	I	I

A: hospital 1, B: hospital 2; H: hand, N: nose. NT: non-typeable, E: erythromycin; CN: gentamicin; FOX: cefoxitin; P: penicillin; T: tetracycline, TEC: teicoplanin, DA: clindamycin, CHL: chloramphenicol, LZD: linezolid, and RD: rifampin. NT non-typeable; * MLST type not determined.

penicillin: (S≥2.9 cm, R≤2.8 cm), erythromycin(S≥2.3 cm, I=1.4-2.2 cm, R≤1.4-2.2 cefoxitin (S≥2.5 cm, R≤2.4 cm), gentamicin (S≥1.5 cm, I=1.3-1.4 cm, R≤1.2 cm), tetracycline (S≥1.9 cm, I=1.5-1.8 cm, R≤1.4 cm), teicoplanin (S≥1.4 cm, I=1.1-1.3 cm, R≦ 1.0 cm), clindamycin (S≥2.1 cm, I=15-20 cm, R≦1.4 cm), chloramphenicol (S≥1.8 cm, I=1.3-1.7 cm, R≦1.2 cm), linezolid (S≥2.1 cm, R≦ 2.0 cm), rifampin (S≥20 cm, I=1.7-1.9 cm, R≦1.6 cm)