Journal of Microbiology, Immunology and Infection 55 (2022) 880—887

Available online at www.sciencedirect.com

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Original Article

A longitudinal molecular surveillance of clinical methicillin-resistant *Staphylococcus aureus* isolates in neonatal units in a teaching hospital, 2003—2018

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Received 7 June 2021; received in revised form 11 October 2021; accepted 26 October 2021
Available online 4 November 2021

KEYWORDS
Methicillin-resistant *Staphylococcus aureus*;
Neonatal care units;
Molecular analysis

Abstract *Background:* Methicillin-resistant *Staphylococcus aureus* (MRSA) has been an important nosocomial pathogen in our neonatal units since 1990s. To understand the longitudinal changing molecular epidemiology of these MRSA isolates, we conducted this study.
Materials: From 2003 to 2018, we collected clinical MRSA isolates from 536 infants hospitalized at neonatal units of a medical center in northern Taiwan. First isolate from each infant was characterized.
Results: The case/isolate number ranged from 7 cases/isolates (the lowest) in 2010 to 71 cases/isolates (the highest) in 2004. Of the 536 isolates, a total of 15 pulsotypes were identified. Three major clones were identified and characterized as sequence type (ST) 239/pulsotype A/staphylococcal chromosomal cassette (SCC) *mec* III/Panton-Valentine leukocidin (PVL)-negative, accounting for 22.2% of the isolates, ST59/pulsotype C/SCC*mec* IV/PVL-negative, accounting for 34.3% and ST59/pulsotype D/SCC*mec* V_T/PVL-positive, accounting for 30.0%. The first clone (hospital strains) dominated in the first two years, and became weakened from 2005 through 2016. Clonal complex (CC) 59 (combined the second and third clones) dominated (>50% of the isolates) from 2005 through 2018. One community clone (ST573) demonstrated a marked increase since 2007 and vanished abruptly since 2010. Several minor MRSA clones emerged after 2010.
Conclusion: The molecular epidemiology of MRSA isolates in our neonatal units from 2003 to 2018 revealed that an epidemic as well as endemic hospital clone of ST239 dominated before

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https://doi.org/10.1016/j.jmii.2021.10.007

2005 and was replaced by the local community clone of CC59 thereafter.

Introduction

Methicillin-resistant *Staphylococcus aureus* (MRSA) was an important cause of nosocomial infections worldwide and was first reported in the United Kingdom in 1961.[1] In Taiwan, MRSA was first recorded in the 1980s and nosocomial MRSA infection incidence increased remarkably in the 1990s.[2,3]

In our neonatal units, including neonatal intensive care units (NICUs) and special care nurseries (SCNs), *S. aureus* is the leading pathogen of hospital-acquired infections (HAIs) and MRSA represented majority of all the *S. aureus* isolates since 1997. During 1997 and 1999, *S. aureus* is responsible for 43% of the HAIs and MRSA represents more than 90% of the *S. aureus* isolates.[4] MRSA was an endemically prevalent pathogen in our neonatal units.[5] We then implemented a series of infection control interventions stepwise in our NICUs and successfully controlled MRSA after a 7-year campaign[6] and MRSA healthcare-associated infection (HAI) density reduced by 92%, from 5.47 episodes per 1000 patient-days in 1999 to 0.45 episodes per 1000 patient-days in 2006; MRSA bloodstream infection reduced from 40 cases in 1999 to only one case in 2006. However, after we discontinued the "search and destroy" strategy (active surveillance of MRSA colonization and decolonization if colonization identified), MRSA activity came back and fluctuated thereafter.

Changing molecular epidemiology of MRSA in a hospital setting, region and even a country was not infrequently reported. However, a long-term molecular surveillance of MRSA in a specific unit was not frequently documented. To understand the longitudinal changing molecular epidemiology of MRSA isolates in a specific unit, we conducted this study to characterize MRSA isolates collected in our neonatal units over a 16-year interval from 2003 to 2018.

Methods

Hospital setting

This study was conducted in Chang Gung Children's Hospital, which is a university-affiliated teaching hospital in northern Taiwan and is a part of Chang Gung Memorial Hospital (CGMH). There are five neonatal units, including three NICUs and two SCNs, distributed on 2 floors, in this children's Hospital. Currently, there are 16, 24 and 10 beds in NICU-1 (3L), NICU-2 (5L), and NICU-3 (3L) respectively. For SCNs, there are 24 beds in SCN-1 (3L) and 30 beds in SCN-2 (5L).

Bacterial isolates

From the microbiology laboratory logbook, there were 1443 MRSA clinical isolates identified from 823 infants hospitalized at the neonatal units between 2003 and 2018. Though

Table 1 Distribution of the first methicillin-resistant *Staphylococcus aureus* clinical isolates from 536 infants in neonatal units stratified by origin of specimens, 2003–2018.

Year	No. of collected/all isolates	No. (%) of enrolled/all infants	No. (% in each year) of the first isolates from enrolled infants								
			Pus	Sputum	Blood	Urine	Eye	CVC	CSF	Ascites	OTH*
2003	101/260	59/113(52.2)	10(16.9)	20(33.9)	8(13.6)	6(10.2)	6(10)	7(11.9)	1(1.7)	0	1(1.7)
2004	116/197	71/97(73.2)	22(31.0)	26(36.6)	7(9.9)	4(5.6)	1(1.4)	10(14.1)	0	0	1(1.4)
2005	43/87	29/47(61.7)	11(37.9)	10(34.5)	2(6.9)	4(13.8)	0	2(6.9)	0	0	0
2006	24/52	17/32(53.1)	9(52.9)	5(29.4)	0	1(5.9)	0	0	0	1(5.9)	1(5.9)
2007	43/102	33/55(60.0)	5(15.2)	16(48.5)	5(15.2)	5(15.2)	1(3)	1(3.0)	0	0	0
2008	57/119	36/72(50.0)	9(25.0)	12(33.3)	5(13.9)	5(13.9)	0	2(5.6)	1(2.8)	0	2(5.6)
2009	12/42	10/27(37.0)	0(0.0)	5(50.0)	3(30.0)	2(20.0)	0	0	0	0	0
2010	8/37	7/29(24.1)	2(28.6)	1(14.3)	3(42.9)	0	0	1(14.3)	0	0	0
2011	29/70	22/40(55.0)	6(27.3)	15(68.2)	0	0	0	0	0	0	1(4.5)
2012	107/127	64/75(85.3)	19(29.7)	34(53.1)	5(7.8)	5(7.8)	0	0	1(1.6)	0	0
2013	50/64	34/44(77.3)	11(32.4)	18(52.9)	1(2.9)	2(5.9)	0	2(5.9)	0	0	0
2014	52/56	36/38(94.7)	17(47.2)	14(38.9)	1(2.8)	2(5.6)	0	2(5.6)	0	0	0
2015	58/67	42/50(84.0)	17(40.5)	16(38.1)	4(9.5)	2(4.8)	0	3(7.1)	0	0	0
2016	42/52	28/36(77.8)	9(32.1)	11(39.3)	6(21.4)	2(7.1)	0	0	0	0	0
2017	48/72	30/43(69.8)	8(26.7)	19(63.3)	0	1(3.3)	0	2(6.7)	0	0	0
2018	30/39	18/25(72.0)	7(38.9)	7(38.9)	3(16.7)	0	0	1(5.6)	0	0	0
Total	820/1443	536/823(65.1)	162(30.2)	229(42.7)	53(9.9)	41(7.6)	8(1.5)	33(6.2)	3(0.6)	1(0.2)	6(1.1)

OTH*, others: ear discharge, nasal discharge, umbilical discharge.
Abbreviations: CVC, central venous catheter; CSF, cerebrospinal fluid.

we requested for reservation of all clinical MRSA isolates, a total of 820 MRSA clinical isolates from 536 infants were prospectively collected and stored by the microbiology laboratory technicians and available for characterization. First isolate from each infant was retrieved from the stocks of our microbiology laboratory. A total of 536 MRSA isolates were characterized. Specimens were assorted into nine different categories according to their sources: pus, sputum, blood, urine, eye, CVC (central venous catheter), CSF (cerebrospinal fluid), ascites, and other discharges (including ear discharge, nasal discharge, and umbilical discharge).

Molecular characterization of MRSA isolates

Identification of MRSA was confirmed according to the guidelines of the Clinical and Laboratory Standards Institute.[7] Briefly, *S. aureus* was identified by morphology, Gram stain, and coagulase tests of strains grown on agar plates. To identify MRSA, cefoxitin disk was used by disk-diffusion method according to the recommendation of Clinical and Laboratory Standard Institute.

All of the retrieved MRSA isolates were characterized by pulsed-field gel electrophoresis (PFGE), staphylococcal chromosome cassette *mec* (SCC*mec*) type and the detection of Panton-Valentine leukocidin (PVL) gene. Some strains of representative PFGE patterns were selected for multilocus sequence typing (MLST) and *spa* typing. PFGE was performed according to the procedure described previously.[8–11] The genotypes were designated in alphabetical order following previous studies; strains with banding patterns identical in the size and number of bands were considered genetically indistinguishable and assigned to an individual type; strains with banding patterns that differed by only three or fewer bands from an existing genotype were considered closely related and described as subtypes of a given pulsotype; and strains with banding patterns that differed by four or more bands were considered different and assigned to a separate type.

Staphylococcal chromosome cassette *mec* (SCC*mec*) type was determined by a multiplex polymerase chain reaction (PCR) strategy described previously.[12,13] The presence of the Panton-Valentine leukocidin (PVL) genes was determined by a PCR assay described elsewhere.[13] According to our previous experiences on molecular characterizations of MRSA, that isolates of the same pulsotype shared the same clonal complex (same sequence type or its single locus variants; same *spa* type or its variants), multilocus sequence typing (MLST) and *spa* typing were performed for selective strains of each PFGE patterns in this study and the methods were described elsewhere.[13]

Results

The numbers of clinical isolates identified from each lesion site by year are summarized in Table 1. The majority of MRSA clinical isolates were identified from sputum (n = 229, 42.7%). Pus specimens were the second most common source (n = 162, 30.2%) followed by blood specimen (n = 53, 9.9%), urine (n = 41, 7.6%), and CVC (n = 33, 6.2%). Sputum and pus constituted the overwhelming majority of specimen sources throughout the study period. The annual numbers of MRSA positive cases are also presented in Table 1.

Table 2 Resolution and distribution of pulsed-field gel electrophoresis patterns of first methicillin-resistant *Staphylococcus aureus* clinical isolates from 536 infants in neonatal units, 2003–2018.

Year	No. of isolates	No. of first isolates from infants	No. (% in each year) of isolates											
			Type A	Type B	Type C	Type D	Type F	Type U	Type AI	Type AN	Type AJ	Type AK	Type AF	OTH*
2003	101	59	44(74.6)	1(1.7)	6(10.2)	8(13.6)	0	0	0	0	0	0	0	0
2004	116	71	35(49.3)	1(1.4)	27(38.0)	7(9.9)	1(1.4)	0	0	0	0	0	0	0
2005	43	29	10(34.5)	0	14(48.3)	3(10.3)	1(3.4)	1(3.4)	0	0	0	0	0	0
2006	24	17	0	0	7(41.2)	10(58.8)	0	0	0	0	0	0	0	0
2007	43	33	7(21.2)	0	8(24.2)	7(21.2)	0	2(6.1)	0	9(27.3)	0	0	0	0
2008	57	36	4(11.1)	1(2.8)	18(50.0)	7(19.4)	0	5(14)	0	1(2.8)	0	0	0	0
2009	12	10	1(10)	0	3(30.0)	3(30.0)	0	3(30)	0	0	0	0	0	0
2010	8	7	0	0	1(14.3)	4(57.1)	0	2(29)	0	0	0	0	0	0
2011	29	22	0	0	13(59.1)	8(35.3)	0	0	1(4.5)	0	0	0	0	0
2012	107	64	2(3.1)	0	31(48.4)	18(28.1)	0	0	0	0	6(9.4)	3(4.7)	4(6.3)	0
2013	50	34	0	0	17(50.0)	12(35.3)	0	0	0	0	5(14.7)	0	0	0
2014	52	36	0	0	8(22.2)	20(55.6)	0	0	0	0	0	7(19.4)	0	1(2.8)
2015	58	42	1(2.4)	0	6(14.3)	30(71.4)	1(2.4)	0	0	0	0	1(2.4)	0	3(7.1)
2016	42	28	0	1(3.6)	12(42.9)	12(42.9)	0	0	2(7.1)	0	0	0	0	1(3.6)
2017	48	30	12(40.0)	1(3.3)	10(33.3)	6(20.0)	0	0	1(3.3)	0	0	0	0	0
2018	30	18	3(16.7)	0	3(16.7)	6(33.3)	1(5.6)	0	2(11)	0	0	1(5.6)	0	2(11.1)
Total	820	536	119(22.2)	5(0.9)	184(34.3)	161(30.0)	4(0.7)	13(2.4)	6(1.1)	10(1.9)	11(2.1)	12(2.2)	4(0.7)	7(1.3)

OTH*: 2014 (AX, 1) , 2015 (BM, 2, AG, 1) , 2016 (AG, 1) , 2018 (AG, 1, CR, 1).

Table 3 Distribution of pulsed-field gel electrophoresis patterns of 536 methicillin-resistant *Staphylococcus aureus* clinical isolates, stratified by identified sources of the isolates, 2003—2018.

Source	No. of isolates	No. (% in each year) of isolates											
		Type A	Type B	Type C	Type D	Type F	Type U	Type AI	Type AN	Type AJ	Type AK	Type AF	OTH*
Pus	162	16	0	48	84	0	3	1	2	2	2	0	4
Sputum	229	60	2	91	42	3	1	1	6	9	9	4	1
Blood	53	13	1	21	9	1	1	3	1	0	1	0	2
urine	41	5	0	14	15	0	6	0	1	0	0	0	0
Eye	8	6	0	2	0	0	0	0	0	0	0	0	0
CVC	33	17	1	6	7	0	1	1	0	0	0	0	0
CSF	3	0	1	1	1	0	0	0	0	0	0	0	0
Ascites	1	0	0	0	1	0	0	0	0	0	0	0	0
OTH	6	2	0	1	2	0	1	0	0	0	0	0	0
Total	536	119(22.2)	5(0.9)	184 (34.3)	161 (30.0)	4 (0.7)	13 (2.4)	6 (1.1)	10 (1.9)	11(2.1)	12 (2.2)	4 (0.7)	7 (1.3)

OTH*, others: Pus (AX, BM, AG, CR), Sputum (BM), Blood (AG).
Abbreviations: CVC, central venous catheter; CSF, cerebrospinal fluid.

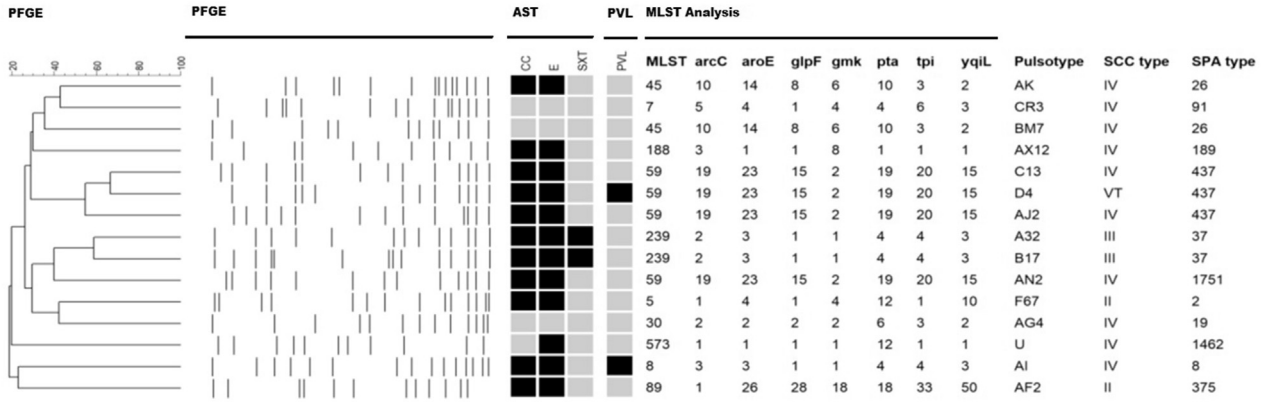

Figure 1. The molecular characteristics of 15 MRSA pulsotypes in neonatal units in a medical center. For the antimicrobial susceptibility test (AST), the black and grey bars represent resistance and susceptibility to the antibiotic, respectively. Abbreviations: PFGE, pulsed-field gel electrophoresis; CC, clindamycin; E, erythromycin; SXT, trimethoprim/sulfamethoxazole; PVL, Panton-Valentine leucocidin; SCC, Staphylococcal chromosome cassette.

Molecular characteristics of MRSA clinical and colonized isolates

The detailed distributions of PFGE patterns in each year are shown in Tables 2 and 3. Of the 536 isolates, a total of 15 PFGE patterns were identified. PVL genes were identified in 164 isolates (30%) and harbored by 0.5% (1/184) of PFGE type C isolates, 97.5% (157/161) of PFGE type D isolates, 83.3% (5/6) of PFGE type AI isolates, and 33.3% (1/3) of PFGE type AG isolates. Four types (types II, III, IV, and V_T) of SCC*mec* elements were identified among the isolates, with type IV (47.7%) being the predominant type, followed by type V_T (27.0%).

MLST analysis were performed for 47 isolates with 15 different pulsotypes and revealed 15 different sequence types (ST). Clonal complex (CC) 59, comprising ST59 and its single-locus variants of ST3205 and ST5225, was the most common clone and accounted for the isolates of pulsotypes C, D, AN, and AJ. ST239 and its single locus variants of ST1310 and ST3053 comprised CC239 and accounted for the isolates of pulsotypes A and B. *Spa* typing was performed for 61 isolates and 21 *spa* types were identified. Fig. 1 and Table 4 illustrate the 15 PFGE patterns as well as other detailed associated molecular characteristics of these isolates.

Overall, there were three major clones. The first clone was characterized as ST239/pulsotype A/SCC*mec* III or IIIA/PVL-negative accounting for 22.2% of the isolates, the second clone was characterized as ST59/pulsotype C/SCC*mec* IV/PVL-negative accounting for 34.3%, and the third clone was characterized as ST59/pulsotype D/SCC*mec* V_T/PVL-positive accounting for 30.0% of the isolates.

Changes in the molecular epidemiology between 2003 and 2018

We evaluated the temporal trend for each genotype (Table 2, Fig. 2). MRSA isolates once were dominated by ST239/pulsotype A/SCC*mec* III or IIIA/PVL-negative in 2003 but exhibited a dramatic decline from 74.6% in 2003 to 0% in

Table 4 Molecular characteristics of 536 methicillin-resistant *Staphylococcus aureus* clinical isolates, stratified by pulsed-field gel electrophoresis (PFGE) patterns.

Molecular characteristics	PFGE patterns												
	Type A	Type B	Type C	Type D	Type F	Type U	Type AI	Type AN	Type AJ	Type AK	Type AF	Type AG	Type AX	Type BM	Type CR
No. isolates	119	5	184	161	4	13	6	10	11	12	4	3	1	2	1
MLST	239, 1310[a], 3053[a]	239	59, 3205[b], 5225[b]	59	5	573	8	59	59	45, 508[c]	89	30	188	45	7
Spa type	37, 297	37	437,441,1751	437, 441, 1751, 4135, 4145	2, 214	1462,3525	8	1751	437	15, 26	375	19	189	26, 1081	91
PVL-positive	0	0	1	157	0	0	5	0	0	0	0	1	0	0	0
SCC*mec*	III (18), IIIA(101),	III(3), IIIA(2)	IV	V_T(145), IV(11), V(5)	II	IV	IV	IV	IV	IV	II	IV	IV	IV, V	IV

[a] A single locus variant of ST 239.
[b] A single locus variant of ST 59.
[c] A single locus variant of ST 45.
Abbreviations: MLST, multilocus sequence type; PVL, Panton-Valentine leucocidin; SCC, staphylococcal cassette chromosome.

2006. The proportion of this clone once rose to 21.2% in 2007, then declined gradually and remained low (0%—3.1%) throughout 2016 and a sudden surge was observed in 2017, which accounted for 40.0% of the MRSA cases.

Two clones, characterized as ST59/pulsotype C and ST59/pulsotype D, were progressively replacing ST239/pulsotype A. The proportion of PFGE types C and D were similar, which accounted for 34.3% and 30.0% of MRSA isolates, respectively. Both clones made up more than half of the MRSA isolates since 2005 and throughout the study period, except in 2007 (accounted for 45.5% of MRSA isolates). However, in 2017 the combined proportion of PFGE types C and D dropped from 85.7% in 2016 to 53.3%, while PFGE type A increased from 0% to 40%.

The MRSA clone characterized as ST573/PFGE type U was first detected in 2005 in this study. The clone demonstrated a marked increase since 2007 and accounted for 30.0% of all isolates in 2009. However, it vanished abruptly in 2010 and remained undetected during the rest of the study period.

Several minor clones emerged after 2010 and their rates fluctuated over time.

Discussion

Here we described a longitudinal study, which include all MRSA clinical isolates identified from neonates in the neonatal units of a university-affiliated teaching hospital over a 16-year period from 2003 to 2018. One of the strengths of this study is its long duration that allows us to delineate the changes in the local epidemiology. Most infants in the neonatal units were hospitalized within three days of birth, and only a few of the neonates were transferred from nearby clinics or local hospitals (estimated to be less than one quarter). In other words, most of the infants didn't had prior exposure to the community. According to previous studies, MRSA infections are largely considered to be horizontally transmitted due to the low risk of vertical transmission.[14] Taken together, most of the MRSA isolates included in this study can be regarded as hospital acquired. Healthcare workers and environmental objects have traditionally been considered reservoirs for MRSA transmission among hospitalized neonates.[15,16] Family members and other visitors were also possible vectors for MRSA transmission since MRSA is now disseminated in the community.

Our NICUs were once endemic for MRSA since 1990s.[4] A series of infection control interventions were then implemented in our NICUs since 2000 and MRSA was controlled successfully, with the MRSA healthcare-associated-infection density reduced by 92% from 1999 to 2006.[6] These interventions included augmenting hand washing before and after contact with patients, revision of standardized operation procedures for the insertion and continuous care of PICC (percutaneously inserted central catheter), institution of alcohol-based hand rubs, and active surveillance culture for MRSA with subsequent decolonization with mupirocin. The active surveillance culture for MRSA was discontinued since 2007 and a slight rebound of MRSA cases was found during 2007 and 2008. Other infection control interventions were sustained, and the number of MRSA cases declined in 2009 and in 2010.

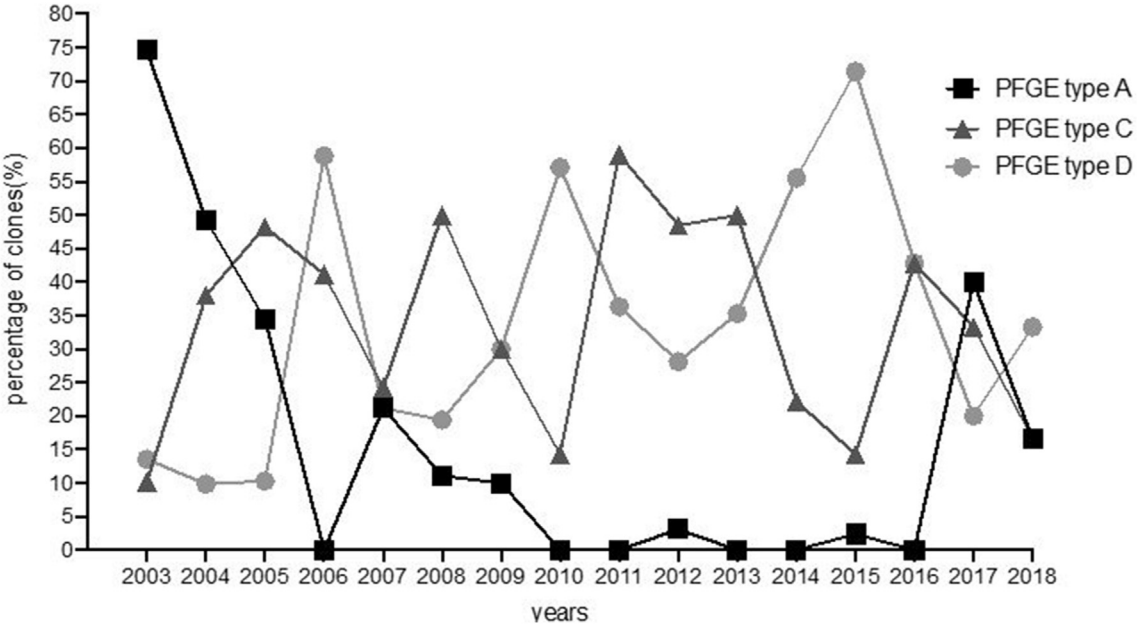

Figure 2. The dynamic changes of the proportion of MRSA among three major MRSA clones. PFGE A was characterized as ST239/pulsotype A/SCC*mec* III or IIIA/PVL-negative, PFGE C as ST59/pulsotype C/SCC*mec* IV/PVL-negative, and PFGE D as ST59/pulsotype D/SCC*mec* V_T/PVL-positive. Abbreviations: PFGE, pulsed-field gel electrophoresis; ST, sequence type; PVL, Panton-Valentine leucocidin; SCC, Staphylococcal chromosome cassette.

However, the MRSA cases increased again since 2011 and resurged its peak in 2012. Continued surveillance is needed.

From the molecular analysis of MRSA isolates, three major clones characterized as ST 239/pulsotype A/SCC *mec* III or IIIA/PVL-negative, ST 59/pulsotype C/SCC*mec* IV/PVL-negative, and ST 59/pulsotype D/SCCmec V_T/PVL-positive were found. ST239 was considered a healthcare-associated MRSA (HA-MRSA) and was prevalent worldwide.[8] ST239 has prevailed in Taiwanese hospitals since 1990s and accounted for 54%—93% of clinical isolates from different hospitals islandwide.[8,17,18] In our NICUs, this clone was recognized as endemically prevalent pathogen and accounted for over 90% of the MRSA clinical isolates in certain years between 1998 and 2003.[6] ST59 is recognized as a predominant strain of community-associated MRSA (CA-MRSA) in Taiwan.[19] Previous studies have shown ST59 lineage includes two major clones: the clone characterized as ST59/PFGE type D/SCCmec VT/PVL-positive ("Taiwan" clone), which was dominant among the clinical isolates, and the clone characterized as ST59/PFGE type C/SCC*mec* IV/PVL-negative ("Asian-Pacific" clone), which was dominant among the colonizing isolates.[20—22] The former was reported to have a greater virulence than the latter in both humans and an animal infection model.[22] However, the proportion of PFGE type C and D were similar in our NICU. As we know, the immunity of premature babies is not yet mature and thus these babies are vulnerable to getting infection, even from low-virulence pathogens. Under the high population colonization pressure, certain proportion of ST59/PFGE type C-colonizing infants would subsequently develop MRSA infection. These might explain the scenario seen in our neonatal units.

An apparent shift in clonal distribution among MRSA isolates were observed in our neonatal units during the study period. ST239, once dominated among all MRSA isolates in neonatal units, exhibited a descending trend from 2003 to 2010. This period coincided with the decreasing prevalence of total MRSA isolates, implying that ST239 may attribute the initial decreasing trend of overall MRSA isolates, due to the serial infection control measures implemented since 2000s. Starting in the early 2000s, ST59 lineage increased in the prevalence and later became the dominant clones throughout the study period. A positive correlation between the rise in ST59- MRSA clones and the increasing prevalence of MRSA during 2010—2012 was indicated. Likewise, the gradual decline of MRSA cases was, to some extent, attributed to the decrease of ST59-MRSA clones since 2012. In the late study period, ST59- MRSA clones, though still the predominant clone, the proportion decreased from 85.7% in 2016 to 50% in 2018. Noticeably, the ST239 clones, which were once disappeared in our NICU, returned and identified from clinical isolates again and reached 43.3% among MRSA isolates in 2017. These findings suggest that if we can control the major clone of MRSA in a healthcare setting, the prevalence of MRSA cases will be reduced, though a small replacement by other minor clones might occur. Further surveillances are essential for monitoring the changing epidemiological trends.

From its emergence in late 1990s, CA-MRSA infections appear to be an emerging phenomenon worldwide. CA-MRSA strains are distinct from HA-MRSA strains in their molecular characteristics. The former usually carries SCC*mec* IV or V, has higher susceptibility to non-β-lactam antibiotics, and harbors multiple virulence and colonizing factors, such as Panton-Valentine Leukocidin (PVL) genes.[23,24] CA- MRSA infection was first documented in Taiwan in 1997. The proportion of CA- MRSA isolates increased rapidly and was over 50% in the 2000s.[25] The

replacement of traditional HA-MRSA strains with CA-MRSA strains in health care settings has been frequently reported. Some studies proposed that CA-MRSA clones possessed ecological advantages due to smaller SCC*mec*, shorter doubling times, high transmission rates in congregate environments, as well as higher virulence factors.[23,26]

The clone characterized as ST 573/pulsotype U/SCC*mec* IV/PVL-negative demonstrated a dramatically increase soon after its emergence in 2005 and accounted for 30% of MRSA isolates in 2009—2010, disappeared abruptly since 2011. This clone was reported to be a dominant colonizing clone in our two previous studies among infants and children aged between 2 months and 5 years conducted during 2009—2011 and 2005—2010, respectively, in northern Taiwan.[27,28] The clinical significance and impact of the wax and wane of this clone in Taiwan needs further studies and observation.

Our study has several limitations. First, this was an observational study performed in a university-affiliated children's hospital, and thus the results may not be generalized. Second, sputum was the most common site of MRSA identified in this study and thus colonization, rather than infection, could not be excluded. However, most of these infants had clinical symptoms/signs of respiratory tract infection and antimicrobial agents were administered by clinical physicians. Third, there were only approximately two-thirds of the patient isolates identified in these neonatal units available for characterization, so a full scope of MRSA molecular epidemiology in these units could not be reached. However, more than 500 isolates were characterized in this study and the number, we thought, is powerful.

Conclusions

We demonstrated the changing molecular epidemiology of MRSA in neonatal units of a medical center during a 16 - year period from 2003 to 2018. An epidemic as well as endemic hospital clone, ST239, dominated in the first years and then was replaced by the local endemic community clone, clonal complex 59, since 2005 and throughout the study period to 2018. Further investigation is warranted to monitor the changing epidemiological trends and to figure out the impact of CA-MRSA in hospital-acquired infections.

Funding

This study was supported by grants from Chang Gung Memorial Hospital at Linkou, Taiwan (CMRPG3F1852, CMRPG3J1601).

Declaration of competing interest

The authors have no conflicts of interest to declare.

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