ORIGINAL RESEARCH

# Molecular Epidemiology and Virulence Gene Analysis of Methicillin-Resistant *Staphylococcus aureus* Associated with Skin and Soft Tissue Infections in the Shaoxing Region

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## ABSTRACT

**Objective** • This study aimed to investigate the prevalence, molecular types, and virulence genes of methicillin-resistant *Staphylococcus aureus* (MRSA) causing skin and soft tissue infections (SSTIs) in the Shaoxing region.

**Methods** • MRSA strains were collected from patients with SSTIs in Shaoxing People's Hospital from January 2019 to December 2019. We conducted SCCmec typing, Staphylococcus protein A (SPA) typing, multilocus sequence typing (MLST), and virulence gene analysis using whole-genome sequencing on all MRSA strains.

**Results** • The detection rate of community-acquired MRSA (CA-MRSA) isolated from SSTI patients in our hospital was 33.3% (6/18). The primary SCCmec types of CA-MRSA strains were IV and V, with IVg(2B) and V(5C2&5) accounting for 16.7% each. Hospital-acquired MRSA (HA-MRSA) strains primarily exhibited SCCmec types IVa(2B) (25.0%), followed by II(2A) (16.7%), V(5C2) (16.7%), and V(5C2&5) (8.3%). SPA typing indicated that CA-MRSA strains causing SSTIs were predominantly t437 (14.3%), t034 (14.3%), t309 (14.3%), t4549 (14.3%), and t7637 (14.3%). The primary SPA type of HA-MRSA strains was t311 (16.7%). MLST typing revealed that the main sequence types (STs) of CA-MRSA strains causing SSTIs were ST22 (33.3%), followed by ST398, ST59, ST88, and ST630, each accounting for 16.7%. The principal STs of HA-MRSA strains were ST398 (16.7%), ST59 (16.7%), ST88 (16.7%), and ST5 (16.7%), followed by ST22, ST630, ST6, and ST188, each at 8.3%. The primary clones of CA-MRSA strains causing SSTIs were ST59-t437-IVg(2B) (16.7%) and ST630-t4549-V(5C2&5) (16.7%), while the primary clones of HA-MRSA strains were ST59-t437-IVa(2B), ST630-t4549-V(5C2&5), ST6-t304-IVa(2B), ST5-t311-II(2A), ST59-t172-IVa(2B), ST398-t571-V(5C2), ST398-t034-V(5C2), and ST5-t311-II(2A), each accounting for 8.3%. The detection rate of the lukSF-PV virulence gene was higher in CA-MRSA strains (50.0%) than in HA-MRSA strains (16.7%).

**Conclusions** • The isolation rate of CA-MRSA strains causing SSTIs was high in Shaoxing People's Hospital, with ST59-t437-IVg(2B) and ST630-t4549-V(5C2&5) being the predominant clones. MRSA strains exhibited multiple virulence genes, with the lukSF-PV gene having a higher detection rate in CA-MRSA strains, signifying its importance as a virulence factor in CA-MRSA. (*Altern Ther Health Med.* 2023;29(8):776-781).

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## INTRODUCTION

*Staphylococcus aureus* (*S. aureus*) is a common Gram-positive bacterium capable of colonizing various body parts, including the skin.[1-2] From 2005 to 2019, the China Antimicrobial Surveillance Network (CHINET) reported a total of 132 284 non-repetitive clinical isolates of *Staphylococcus aureus*. Among these, 41.15% (54438 isolates) were identified as methicillin-resistant *Staphylococcus aureus* (MRSA).[1] Notably, the annual detection rate of MRSA among clinical isolates of *Staphylococcus aureus* consistently exceeded 30%.[2]

Yueh et al.[2] conducted a retrospective analysis of patients with skin and soft tissue infections (SSTIs) admitted to a children's hospital in Taiwan between 2010 and 2019. In their results, *Staphylococcus aureus* emerged as the predominant pathogen in 639 confirmed cases of skin and soft tissue infections (SSTIs), with MRSA constituting more than half of these cases. MRSA significantly contributes to various conditions, including bacteremia, endocarditis, SSTIs, osteoarticular infections, and hospital-acquired infections.[3]

A study conducted by Millar et al.[4] highlighted a high degree of genomic similarity between infecting and colonizing isolates among military trainees who had developed skin and soft tissue infections attributed to MRSA. The colonization of MRSA strains can lead to skin and soft tissue infections, primarily due to compromised immune function and skin damage. MRSA strains exhibit heightened antibiotic resistance, harbor an array of toxin genes, can form biofilms, and significantly contribute to the pathogenesis of diverse skin disorders. Moreover, they possess the potential to disseminate to other body regions, instigating secondary infections.[5]

The elevated prevalence and mortality rates associated with MRSA infections present a significant concern in the field of clinical medicine.[3] In recent years, there has been a growing focus on Community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA). CA-MRSA has the capacity to colonize healthy individuals and propagate within the community. Given China's status as a populous nation with numerous densely populated cities, it provides an ideal environment for disseminating CA-MRSA. Furthermore, CA-MRSA strains linked to skin and soft tissue infections have been detected in intercontinental travelers to Europe, resulting in colonization and transmission within the host.[6]

CA-MRSA possesses unique characteristics that distinguish it from hospital-acquired methicillin-resistant *Staphylococcus aureus* (HA-MRSA). CA-MRSA frequently infects individuals in the community that lack known risk factors and demonstrates higher virulence compared to HA-MRSA.[7] HA-MRSA predominantly occurs within healthcare settings and can be managed through practices such as hand hygiene, disinfection, and isolation measures. In contrast, CA-MRSA represents a community-acquired infection for which effective prevention and control strategies are currently lacking, making it susceptible to outbreaks.

The recurrent infiltration of CA-MRSA clones into healthcare facilities can lead to transmissions and outbreaks, presenting a persistent and significant clinical concern.[8] There is a lack of comprehensive epidemiological data concerning CA-MRSA-related skin and soft tissue infections in China. Existing studies are primarily centered on hospitalized patients, potentially leading to an inaccurate or underestimated rate of CA-MRSA isolation. Consequently, further research in this domain is imperative.

In this study, we gathered MRSA strains from patients with skin and soft tissue infections, both in outpatient and hospitalized settings, at Shaoxing People's Hospital in 2019. We conducted molecular typing and detected virulence genes utilizing whole-genome sequencing. This approach aids in comprehending the prevailing trends, molecular variations, and virulence gene profiles of CA-MRSA in skin and soft tissue infections within our hospital. Furthermore, it furnishes valuable epidemiological evidence to guide the prevention and control of CA-MRSA in our region.

## PATIENTS AND METHODS

### Study Design

We conducted a retrospective analysis of MRSA strains collected from patients with skin and soft tissue infections, both in our hospital's outpatient and hospitalized settings, covering the period from January 2019 to December 2019. The study was focused on differentiating between CA-MRSA and HA-MRSA strains, contributing valuable insights into the region's epidemiology and characteristics of CA-MRSA. This study received approval from the Hospital Ethics Committee.

### Patient Selection Criteria for CA-MRSA and HA-MRSA Strains

The following inclusion criteria for CA-MRSA were employed: (1) the strain must have been isolated from an outpatient or within 48 hours of hospitalization; (2) the patient should have no prior history of MRSA infection or colonization; (3) no recent hospitalization or residency in a nursing home within the past year; (4) no record of dialysis or surgery; (5) no extended catheterization; (6) and no use of medical devices that puncture the skin.[9] Exclusion criteria: All other MRSA strains were classified as HA-MRSA. Duplicate strains were excluded, with only the initial isolated strain considered for inclusion.

### MRSA Strain Genome Analysis

Bacterial genomic DNA was extracted utilizing the DNA extraction kit (DP302) from TianGen Biotech Co., Ltd. Subsequently, the extracted genomic DNA was preserved at -80°C for future use. For second-generation sequencing, the genomic DNA was outsourced to Zhejiang Tianke Company. The obtained sequences underwent assembly through Unicycler. Mec typing was determined utilizing SCCmecFinder (https://cge.cbs.dtu.dk/services/SCCmecFinder/); the spa typing was determined using spaTyper (https://cge.cbs.dtu.dk/services/spaTyper/); the ST typing was determined using MLST 2.0 (https://cge.cbs.dtu.dk/services/MLST/); and the virulence genes were detected using VirulenceFinder (https://cge.cbs.dtu.dk/services/VirulenceFinder/).

### Statistical Analysis

Statistical analysis was conducted using IBM SPSS Statistics version 25.0 software (IBM, Armonk, NY, USA). Continuous variables were reported as mean ± standard deviation ($\bar{x} \pm s$), while categorical variables were expressed as percentages (%). Fisher's exact test was employed for statistical analysis, with a significance threshold set at $P < .05$ to determine statistical significance.

## RESULTS

### Clinical Characteristics of CA-MRSA and HA-MRSA Strains

A total of 18 MRSA strains were isolated from patients with skin and soft tissue infections, comprising 6 CA-MRSA strains (33.3%) and 12 HA-MRSA strains (66.7%). The average age of patients diagnosed with CA-MRSA-related skin and soft tissue infections was 73.8 ± 33.5 years, involving 4 male and 2 female patients. Meanwhile, patients with HA-MRSA-related skin and soft tissue infections had an average age of 52.9 ± 15.2 years, with an equal distribution of 6 male and 6 female patients.

### Molecular Typing of CA-MRSA and HA-MRSA Strains

**SCCmec Typing.** The SCCmec typing of MRSA strains was conducted using SCCmecFinder. The findings revealed that CA-MRSA strains predominantly exhibited SCCmec types IV and V, with IVg(2B) and V(5C2&5) each accounting for 16.7%. Untypeable strains constituted 66.7% of the CA-MRSA strains. In contrast, HA-MRSA strains primarily possessed SCCmec type IVa(2B) (25.0%), followed by types II(2A) (16.7%), V(5C2) (16.7%), and V(5C2&5) (8.3%). Untypeable strains represented 33.3% of the HA-MRSA strains. Detailed results are provided in Table 1.

**Spa Typing.** The spa typing of MRSA strains was carried out using spaTyper 1.0. The outcomes revealed that the most prevalent spa types in CA-MRSA strains included t437, t034, t309, t4549, and t7637, each accounting for 14.3%. The predominant spa type in HA-MRSA strains was t311 (16.7%). Detailed results are presented in Table 2.

**MLST Typing.** MLST typing of MRSA strains was conducted using MLST 2.0. The findings revealed that the most prevalent MLST type among CA-MRSA strains was ST22 (33.3%), followed by ST398, ST59, ST88, and ST630, each accounting for 16.7%. Within HA-MRSA strains, the dominant MLST types were ST398 (16.7%), ST59 (16.7%), ST88 (16.7%), and ST5 (16.7%), with ST22, ST630, ST6, and ST188 each representing 8.3%. Detailed results are presented in Table 3.

### Virulence Genes in CA-MRSA and HA-MRSA Strains

Virulence genes within MRSA strains were identified utilizing VirulenceFinder-2.0. The findings revealed that CA-MRSA strains carried 22 distinct virulence genes, whereas HA-MRSA strains carried 27 virulence genes. Notably, all MRSA strains exhibited the presence of virulent genes aur, hlgA, hlgB, and hlgC. Within the CA-MRSA strains, the detection rates of sak and scn virulence genes were 83.3%, while those of lukF-PV and lukS-PV virulence genes stood at 50.0%.

Conversely, among HA-MRSA strains, the scn virulence gene was detected in 91.7% of cases, sak virulence genes in 83.3%, and lukD, lukE, splA, and splB virulence genes in 50.0%. Notably, the detection rates of lukF-PV and lukS-PV virulence genes were higher in CA-MRSA strains than in HA-MRSA strains ($P = .268$). Additionally, the MRSA strains exhibited a relatively high prevalence of superantigen enterotoxin genes. Detailed results are provided in Table 4.

**Table 1.** SCCmec Typing Results of CA-MRSA and HA-MRSA Strains

| SCCmec Typing | CA-MRSA (n = 6) | | HA-MRSA (n = 12) | | *P* value |
|---|---|---|---|---|---|
| | Detected Strains | Detection Rate (%) | Detected Strains | Detection Rate (%) | |
| IVa(2B) | 0 | 0.0 | 3 | 25.0 | .515 |
| IVg(2B) | 1 | 16.7 | 0 | 0.0 | .333 |
| V(5C2&5) | 1 | 16.7 | 1 | 8.3 | 1.000 |
| II(2A) | 0 | 0.0 | 2 | 16.7 | .529 |
| V(5C2) | 0 | 0.0 | 2 | 16.7 | .529 |
| Untypeable | 4 | 66.7 | 4 | 33.3 | .321 |

Note: Table 1 provides the SCCmec typing results for CA-MRSA and HA-MRSA strains. SCCmec Typing: *Staphylococcal* Chromosomal Cassette mec Typing; CA-MRSA: Community-Acquired Methicillin-Resistant *Staphylococcus aureus;* HA-MRSA: Hospital-Acquired Methicillin-Resistant *Staphylococcus aureus;* n: Number of strains; Detection Rate: Percentage of strains with detected SCCmec types; IVa(2B): SCCmec type IVa, which belongs to the 2B subtype; IVg(2B): SCCmec type IVg, a subtype of 2B; V(5C2&5): SCCmec type V, encompassing 5C2 and 5 subtypes; II(2A): SCCmec type II, belonging to the 2A subtype; V(5C2): SCCmec type V, specifically the 5C2 subtype; Untypeable: Strains for which SCCmec typing could not be determined.

**Table 2.** Spa Typing Results of CA-MRSA and HA-MRSA Strains

| Spa Typing | CA-MRSA (n = 6) | | HA-MRSA (n = 12) | | *P* value |
|---|---|---|---|---|---|
| | Detected Strains | Detection Rate (%) | Detected Strains | Detection Rate (%) | |
| t437 | 1 | 16.7 | 1 | 8.3 | 1.000 |
| t034 | 1 | 16.7 | 1 | 8.3 | 1.000 |
| t309 | 1 | 16.7 | 1 | 8.3 | 1.000 |
| t4549 | 1 | 16.7 | 1 | 8.3 | 1.000 |
| t7637 | 1 | 16.7 | 0 | 0.0 | .333 |
| t311 | 0 | 0.0 | 2 | 16.7 | .529 |
| t571 | 0 | 0.0 | 1 | 8.3 | 1.000 |
| t172 | 0 | 0.0 | 1 | 8.3 | 1.000 |
| t189 | 0 | 0.0 | 1 | 8.3 | 1.000 |
| t304 | 0 | 0.0 | 1 | 8.3 | 1.000 |
| Untypeable | 1 | 16.7 | 2 | 16.7 | 1.000 |

Note: Table 2 presents the Spa typing results for CA-MRSA and HA-MRSA strains. Spa Typing: *Staphylococcus* Protein A Typing; CA-MRSA: Community-Acquired Methicillin-Resistant *Staphylococcus aureus;* HA-MRSA: Hospital-Acquired Methicillin-Resistant *Staphylococcus aureus;* n: Number of strains; Detection Rate: Percentage of strains with detected Spa types; t437, t034, t309, t4549, t7637, t311, t571, t172, t189, t304: Spa types identified in the strains; Untypeable: Strains for which Spa typing could not be determined.

**Table 3.** MLST Typing Results of CA-MRSA and HA-MRSA Strains

| MLST Typing | CA-MRSA (n = 6) | | HA-MRSA (n = 12) | | *P* value |
|---|---|---|---|---|---|
| | Detected Strains | Detection Rate (%) | Detected Strains | Detection Rate (%) | |
| ST22 | 2 | 33.3 | 1 | 8.3 | .245 |
| ST398 | 1 | 16.7 | 2 | 16.7 | 1.000 |
| ST59 | 1 | 16.7 | 2 | 16.7 | 1.000 |
| ST88 | 1 | 16.7 | 2 | 16.7 | 1.000 |
| ST630 | 1 | 16.7 | 1 | 8.3 | 1.000 |
| ST5 | 0 | 0.0 | 2 | 16.7 | .529 |
| ST6 | 0 | 0.0 | 1 | 8.3 | 1.000 |
| ST188 | 0 | 0.0 | 1 | 8.3 | 1.000 |

Note: Table 3 displays the MLST Typing results for CA-MRSA and HA-MRSA strains. MLST Typing: Multi-Locus Sequence Typing; CA-MRSA: Community-Acquired Methicillin-Resistant *Staphylococcus aureus*; HA-MRSA: Hospital-Acquired Methicillin-Resistant *Staphylococcus aureus;* n: Number of strains; Detection Rate: Percentage of strains with detected MLST types; ST22, ST398, ST59, ST88, ST630, ST5, ST6, ST188: MLST types identified in the strains.

## DISCUSSION

MRSA is a highly pathogenic Gram-positive bacterium that frequently colonizes healthy human skin. When the immune system is compromised, it can lead to skin and soft tissue infections.[10] MRSA strains are characterized by the presence of multiple virulence genes, high antibiotic resistance, and the potential to trigger infection outbreaks. It increases challenges in treatment, raises mortality rates, and elevates the societal and medical burden. Notably, skin and soft tissue infections represent the most prevalent clinical manifestation of community-acquired *Staphylococcus aureus* infections.[5]

In Japan, the detection rate of MRSA was 24.9% among 1455 isolates of *S. aureus* from skin and soft tissue infections in 30 outpatient clinics from 2013 to 2017.[11] In recent years, there has been a notable increase in the detection rate of community-acquired MRSA, which has garnered significant attention. Nichol et al.[12] reported that the proportion of CA-MRSA genotypes among 1963 MRSA strains isolated from outpatient and inpatient populations in tertiary hospitals across Canada surged from 20.8% in 2007 to 56.3%

**Table 4.** Virulence Gene Detection Results of CA-MRSA and HA-MRSA Strains

| Virulence Genes | CA-MRSA (n = 6) | | HA-MRSA (n = 12) | | *P* value |
|---|---|---|---|---|---|
| | Detected Strains | Detection Rate (%) | Detected Strains | Detection Rate (%) | |
| aur | 6 | 100.0 | 12 | 100.0 | — |
| hlgA | 6 | 100.0 | 12 | 100.0 | — |
| hlgB | 6 | 100.0 | 12 | 100.0 | — |
| hlgC | 6 | 100.0 | 12 | 100.0 | — |
| sak | 5 | 83.3 | 10 | 83.3 | 1.000 |
| scn | 5 | 83.3 | 11 | 91.7 | 1.000 |
| lukF-PV | 3 | 50.0 | 2 | 16.7 | .268 |
| lukS-PV | 3 | 50.0 | 2 | 16.7 | .268 |
| sea | 0 | 0.0 | 4 | 33.3 | .245 |
| seb | 1 | 16.7 | 1 | 8.3 | 1.000 |
| sec | 0 | 0.0 | 3 | 25.0 | .515 |
| seg | 2 | 33.3 | 3 | 25.0 | 1.000 |
| sei | 2 | 33.3 | 3 | 25.0 | 1.000 |
| sek | 1 | 16.7 | 1 | 8.3 | 1.000 |
| sel | 0 | 0.0 | 3 | 25.0 | .515 |
| sem | 2 | 33.3 | 2 | 16.7 | .569 |
| sen | 2 | 33.3 | 3 | 25.0 | 1.000 |
| seo | 2 | 33.3 | 3 | 25.0 | 1.000 |
| sep | 2 | 33.3 | 2 | 16.7 | .569 |
| seq | 1 | 16.7 | 1 | 8.3 | 1.000 |
| seu | 2 | 33.3 | 3 | 25.0 | 1.000 |
| lukD | 1 | 16.7 | 6 | 50.0 | .316 |
| lukE | 1 | 16.7 | 6 | 50.0 | .316 |
| splA | 1 | 16.7 | 6 | 50.0 | .316 |
| splB | 1 | 16.7 | 6 | 50.0 | .316 |
| splE | 0 | 0.0 | 2 | 16.7 | .529 |
| tst | 0 | 0.0 | 2 | 16.7 | .529 |

Note: Table 4 provides the Virulence Gene Detection results for CA-MRSA and HA-MRSA strains. Virulence Genes: Specific genes asssignificance. virulence factors; CA-MRSA: Community-Acquired Methicillin-Resistant *Staphylococcus aureus;* HA-MRSA: Hospital-Acquired Methicillin-Resistant *Staphylococcus aureus;* n: Number of strains; Detection Rate: Percentage of strains with detected virulence genes; aur: Metalloproteinase; hlg: Gamma-hemolysin component; sak: Staphylokinase; scn: Staphylococcal complement inhibitor; lukF-PV, lukS-PV: Leucocidin genes; se: Superantigen enterotoxin genes; lukD, lukE: Interleukin genes; spl: Serine protease genes; tst: Toxic shock syndrome toxin gene.

in 2016. This rise marked CA-MRSA as the predominant cause of MRSA infections in Canada.

In a nationwide epidemiological study spanning 2015 to 2017, conducted by Chen et al.[13] in 22 tertiary hospitals across China, it was observed that CA-MRSA accounted for 24.2% of the 434 cases of community-acquired *S. aureus* infections and 13.8% of the 763 MRSA cases. This study further revealed that among the 18 patients diagnosed with MRSA-related skin and soft tissue infections, 6 cases were attributed to CA-MRSA (33.3%). It highlights the substantial presence of CA-MRSA in MRSA-related skin and soft tissue infections, warranting significant attention. It is important to note that while CA-MRSA refers to MRSA infections occurring without healthcare-associated exposure, the potential for healthcare-associated exposure does not entirely exclude the possibility of patients being infected with CA-MRSA in the community. This factor may lead to a potential underestimation of the incidence of CA-MRSA.

The prevalence of CA-MRSA clones exhibits substantial variation among different countries and regions. In several areas of the United States, many CA-MRSA strains demonstrate resistance to clindamycin. Conversely, in China, CA-MRSA typically remains susceptible to quinolone agents. The SCCmec types carried by CA-MRSA strains predominantly comprise type IV and type V.[14]

A study conducted in a tertiary hospital in China from 2012 to 2017 revealed that the primary SCCmec type among CA-MRSA strains was type IVa, accounting for 70.9% (124/175), followed by type V at 15.4% (27/175). In contrast, type III emerged as the predominant SCCmec type among hospital-associated MRSA (HA-MRSA) strains, representing 58.3% (385/660), followed by type II at 25.5% (168/660).[15]

Based on the genome sequencing results, CA-MRSA strains causing skin and soft tissue infections predominantly exhibited SCCmec types IV and V, with IVg (2B) and V (5C2&5) each representing 16.7%. In the case of HA-MRSA strains, the primary SCCmec type observed was IVa (2B) at 25.0%, followed by II (2A) and V (5C2), both at 16.7%, and V (5C2&5) at 8.3%. Notably, in East Uganda, the spa type t064 emerged as a prevalent spa type among CA-MRSA isolates.[16] In this study, the predominant spa types associated with CA-MRSA causing skin and soft tissue infections included t437, t034, t309, t4549, and t7637, each accounting for 14.3%. Conversely, the principal spa type for HA-MRSA was identified as t311, representing 16.7%.

In a study within a Chinese hospital, ST59 emerged as the dominant MLST type among CA-MRSA isolates, constituting 52.5%.[15] In this investigation, the primary MLST type for CA-MRSA causing skin and soft tissue infections was ST22 (33.3%). It was followed by ST398, ST59, ST88, and ST630, each comprising 16.7% of the cases. Concerning HA-MRSA strains, the leading MLST types included ST398, ST59, ST88, and ST5, each accounting for 16.7%.

A study conducted at a tertiary hospital in China observed that among 175 CA-MRSA strains, ST59-t437-IVa was the predominant clone, comprising 28.8% of the cases. In contrast, among 660 HA-MRSA strains, ST239-t030-III was the most common clone, accounting for 30%.[15-16] Interestingly, ST59-t437-IVa was also identified within the HA-MRSA strains, constituting 6.7%. It suggests that while ST239-t030-III remains the primary clone among HA-MRSA strains, the community clone ST59-t437-IVa may be emerging as a significant component of HA-MRSA in this hospital.[16]

Wang et al.[17] conducted whole-genome sequencing on 565 MRSA strains collected from seven provinces and cities in China from 2014 to 2020. Their findings indicated that clones predominantly characterized by ST59-t437-IV (14.9%), ST239-t030-III (6.4%), and ST5-t2460-II (6.0%) were the most prevalent. These results suggest that the community-acquired clone ST59-t437-IV holds dominance in China.

Furthermore, Liao et al.[18] examined cytokine storm patterns during infection and discovered that the CA-MRSA strain ST59-t439-IVa had the most severe lethality in BALB/c mice. It was followed by the CA-MRSA strain ST59-t437-Vb. No BALB/c mice succumbed to infection with the typical HA-MRSA strain ST239-t030-III. Mice infected with CA-MRSA strains exhibited severe inflammatory reactions, tissue damage, and pronounced infiltration of inflammatory mediators and cells.

This study identified ST59-t437-IVg(2B) and ST630-t4549-V(5C2&5) as the predominant clones among CA-MRSA strains causing skin and soft tissue infections, each accounting for 16.7% of cases. In contrast, the primary clones within the HA-MRSA strains included ST59-t437-

IVa(2B), ST630-t4549-V(5C2&5), ST6-t304-IVa(2B), ST5-t311-II(2A), ST59-t172-IVa(2B), ST398-t571-V(5C2), ST398-t034-V(5C2), and ST5-t311-II(2A), each constituting 8.3% of cases. The presence of the ST59-t437-IVa(2B) clone of HA-MRSA in this study suggests that community clones might have infiltrated healthcare facilities.

MRSA strains inherently possess a substantial repertoire of virulence genes.[17] The heightened pathogenicity of MRSA is intricately linked to its virulence factors. Distinct disparities in the virulence gene profiles exist between CA-MRSA and HA-MRSA strains.[15] Notably, PVL, a cytotoxin encoded by the lukS-PV and lukF-PV genes collectively known as lukSF-PV, are critically important. This virulence factor can potentially induce leukocyte destruction and tissue necrosis.[19] PVL is regarded as a critical virulence factor for CA-MRSA, while it is infrequently found in most HA-MRSA strains.

Findings from El-Baghdady et al.[20] revealed that a substantial 92.2% of CA-MRSA strains exhibited positivity for the PVL gene, in stark contrast to HA-MRSA strains, of which only 28.6% tested positive for the PVL gene. However, Nakaminami et al.[11] reported a different scenario based on their study of 362 MRSA strains isolated from skin and soft tissue infections in Japan. In their study, a mere 56 strains (15.5%) were identified as PVL-positive, with a notable association between PVL-positive strains and deep skin infections. Our study revealed a significant disparity in the detection rate of lukSF-PV virulence genes between CA-MRSA strains causing skin and soft tissue infections (50.0%) and HA-MRSA strains (16.7%) ($P = .268$).

A noteworthy trend emerged in a study by McManus et al.,[8] which investigated isolates suspected of being related to MRSA outbreaks across multiple hospitals in Ireland using whole genome multilocus sequence typing. PVL-positive CA-MRSA strains exhibited an increasing association with infection outbreaks, and these PVL-positive CA-MRSA isolates were inevitably disseminated to hospitalized patients.

In the Klein et al.[21] study, 46 PVL-positive MRSA strains were identified through whole-genome sequencing. Remarkably, it was observed that 32.6% of these PVL-positive MRSA strains fulfilled the criteria for hospital-associated infections. The occurrence of hospital infections attributed to PVL-positive CA-MRSA clones entering healthcare facilities underscores the imperative for ongoing surveillance and implementing preventative measures to prevent transmission and clone-related outbreaks.

The investigation into MRSA strains responsible for skin and soft tissue infections in our hospital unveiled a noteworthy prevalence of CA-MRSA isolates, warranting profound concern. Through whole-genome sequencing, we perceived that the predominant CA-MRSA strains responsible for skin and soft tissue infections were ST59-t437-IVg(2B) and ST630-t4549-V(5C2&5). Conversely, the primary HA-MRSA strains comprised ST59-t437-IVa(2B), ST630-t4549-V(5C2&5), ST6-t304-IVa(2B), ST5-t311-II(2A), ST59-t172-IVa(2B), ST398-t571-V(5C2), ST398-t034-V(5C2), and ST5-t311-II(2A).

Our findings suggest that the MRSA strains carried numerous virulence genes, with the lukSF-PV gene emerging as a pivotal virulence factor in CA-MRSA, exhibiting a notably high detection rate. These findings emphasize the imperative for increased vigilance and ongoing surveillance of MRSA infections to prevent the spread of these highly virulent strains.

### Study Limitations

While contributing valuable insights into MRSA epidemiology, our study presents certain limitations. Firstly, our research was conducted within the confines of a single hospital in a specific geographical region, which may limit the generalizability of our findings to broader populations. Additionally, the retrospective nature of the study design imposes inherent constraints, including the reliance on medical records and sample availability, which might introduce selection bias. Furthermore, our study's sample size may warrant caution when extrapolating these results to larger settings. Moreover, despite utilizing advanced molecular techniques, our study's focus on a particular time frame and location may not fully capture the dynamic nature of MRSA epidemiology, which can evolve over time and exhibit geographical variations. Thus, further research incorporating diverse settings and methodologies is needed to understand MRSA dynamics and its impact comprehensively.

## CONCLUSION

In conclusion, this study sheds light on the epidemiology of MRSA strains causing skin and soft tissue infections within our hospital setting. Our findings reveal a noteworthy prevalence of CA-MRSA isolates, particularly the ST59-t437-IVg(2B) and ST630-t4549-V(5C2&5) clones, highlighting the significance of community-acquired MRSA in our region. We have also identified a substantial array of virulence genes, with the lukSF-PV gene emerging as a pivotal virulence factor in CA-MRSA. These insights emphasize the need for heightened vigilance and continued monitoring of MRSA infections, particularly PVL-positive strains, to mitigate transmission and outbreaks. While our study contributes valuable local data, further research encompassing diverse populations and settings is warranted to garner a comprehensive understanding of MRSA epidemiology and inform effective prevention and control strategies.

### CONFLICT OF INTEREST

The authors have no potential conflicts of interest to report relevant to this article.

### AUTHORS' CONTRIBUTIONS

MS and HZ designed the study and performed the experiments, YZ and DW collected the data, YR and ML analyzed the data, and MS and HZ prepared the manuscript. All authors read and approved the final manuscript.

### FUNDING

This study did not receive any funding in any form.

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## **Sup Table 1.** The infection site of CA-MRSA and HA-MRSA Strains

| Site | CA-MRSA | HA-MRSA |
|---|---|---|
| The adenoid tissue | 1 | 0 |
| Perianal | 1 | 0 |
| Penis | 1 | 0 |
| Upper Limb | 1 | 0 |
| Nose | 1 | 1 |
| Lower Limb | 1 | 4 |
| Breast | 0 | 2 |
| Hip | 0 | 1 |
| Abdominal Wall | 0 | 1 |
| Finger | 0 | 3 |

Note: Supplementary Table 1 provides information on the infection sites of CA-MRSA and HA-MRSA strains. Site: The specific anatomical site of infection; CA-MRSA: Community-Acquired Methicillin-Resistant *Staphylococcus aureus;* HA-MRSA: Hospital-Acquired Methicillin-Resistant *Staphylococcus aureus.*