

Antibiotic Resistance Profiles and MLST Typing of *Staphylococcus Aureus* Clone Associated with Skin and Soft Tissue Infections in a Hospital of China

Xiaojuan Ji^{1,*}, Wenjie Zhu^{1,*}, Hongfei Lu², Zhiwei Wu¹, Huaqing Chen¹, Chunli Lin¹, Zhaolin Zeng¹, Cong You¹, Longnian Li¹

¹Department of Dermatology, First Affiliated Hospital of Gannan Medical University, Joint Organization of Jiangxi Clinical Medicine Research Center for Dermatology, Ganzhou, People's Republic of China; ²Clinical Laboratory, First Affiliated Hospital of Gannan Medical University, Ganzhou, People's Republic of China

*These authors contributed equally to this work

Correspondence: Cong You; Longnian Li, Department of Dermatology, First Affiliated Hospital of Gannan Medical University, Ganzhou, People's Republic of China, Email youcong1987@tmu.edu.cn; li_longnian@foxmail.com

Objective: To analyze the antibiotic resistance profile, virulence genes, and molecular typing of *Staphylococcus aureus* (*S. aureus*) strains isolated in skin and soft tissue infections at the First Affiliated Hospital, Gannan Medical University, to better understand the molecular epidemiological characteristics of *S. aureus*.

Methods: In 2023, 65 *S. aureus* strains were isolated from patients with skin and soft tissue infections. Strain identification and susceptibility tests were performed using VITEK 2 and gram-positive bacteria identification cards. DNA was extracted using a DNA extraction kit, and all genes were amplified using polymerase chain reaction. Multilocus sequence typing (MLST) was used for molecular typing.

Results: In this study, of the 65 *S. aureus* strains were tested for their susceptibility to 16 antibiotics, the highest resistance rate to penicillin G was 95.4%. None of the staphylococcal isolates showed resistance to ceftaroline, daptomycin, linezolid, tigecycline, teicoplanin, or vancomycin. *fnbA* was the most prevalent virulence gene (100%) in *S. aureus* strains isolated in skin and soft tissue infections, followed by *arcA* (98.5%). Statistical analyses showed that the resistance rates of methicillin-resistant *S. aureus* isolates to various antibiotics were significantly higher than those of methicillin-susceptible *S. aureus* isolates. Fifty sequence types (STs), including 44 new ones, were identified by MLST.

Conclusion: In this study, the high resistance rate to penicillin G and the high carrying rate of virulence gene *fnbA* and *arcA* of *S. aureus* were determined, and 44 new STs were identified, which may be associated with the geographical location of southern Jiangxi and local trends in antibiotic use. The study of the clonal lineage and evolutionary relationships of *S. aureus* in these regions may help in understanding the molecular epidemiology and provide the experimental basis for pathogenic bacteria prevention and treatment.

Keywords: *Staphylococcus aureus*, skin and soft tissue infections, antibiotic resistance, multilocus sequence typing, virulence gene

Introduction

Staphylococcus aureus (*S. aureus*) is a common pathogen that causes nosocomial and community infections and various infectious diseases. The pan-genome of this bacterium encodes several toxins, including three families of toxins: pore-forming toxins, exfoliating toxins, and superantigens. Most genes encoding toxins are located on mobile genetic elements,¹ including the following representative genes.² Encoding mupirocin-acquired resistance (*mupA*; accession: NG_048008.1), the gene associated with a high-level resistance (minimum inhibitory concentration ≥ 512 $\mu\text{g/mL}$) to mupirocin;³ erythromycin resistance methylase (*ermA*) and *ermC*;⁴ Panton-Valentine leukocidin (*PVL*), the leukocidin toxin gene;^{5,6} fibronectin binding protein A (*fnbA*);^{7,8} arginine catabolism mobile element (*arcA*),^{9,10} which has the advantage of selective skin colonization); toxic shock syndrome toxin (*TSST-1* gene-encoding TSST,¹¹ and *mecA*,

related to β -lactam antibiotic resistance. The distribution of toxin genes in the clonal lineages of *S. aureus* is not random, but phylogenetically characteristic.

It is important to understand the genetic background and pathogenesis of the different clonal lineages of *S. aureus*. Owing to the continuous application of new antibiotics in clinical practice and the widespread abuse of antibiotics in recent years, drug resistance by *S. aureus* has been increasing annually. Particularly, the rise in methicillin-resistant *S. aureus* (MRSA) worldwide has brought greater challenges to the treatment of *S. aureus* infections. Therefore, it is particularly important to further study the resistance of *S. aureus* and its relationship with resistance genes to strengthen the understanding of molecular epidemiology of *S. aureus* in human populations. To date, we have successfully reported primers for the representative genes, *mupA*, *ermA*, *ermC*, *PVL*, *fnbA*, *mecA*, *arcA*, and *TSST-I* in a toxin profile.¹² We also intend to use polymerase chain reaction (PCR) assay to detect gene fragments in pathogenic *S. aureus* toxin profile. In 2023, in this study, 65 *S. aureus* isolates from pus secretions and other samples from the First Affiliated Hospital of Gannan Medical University were included. Drug resistance and virulence gene analyses and molecular typing were performed to analyze the drug resistance and virulence gene-carrying rates of *S. aureus* in patients with skin and soft tissue infections. Differences in the molecular characteristics between MRSA and methicillin-sensitive *S. aureus* (MSSA) isolates were compared.

Materials and Methods

Source, Identification, and Drug Sensitivity Profile of *S. aureus* Strains

In 2023, 65 strains of *S. aureus* were isolated from pus and secretion samples of 65 patients with skin and soft tissue infections in our hospital. The distribution of departments were as follows: dermatology (23.15%), orthopedic (21.5%), endocrinology (12.3%), burn (10.8%) and so on. (Figure 1). Automated matrix-assisted laser desorption ionization–time-of-flight mass spectrometry was used to identify the strains, AST-P639 Chinese customized card in VITEK 2 compact (French bioMérieux Ltd.) was used for drug susceptibility testing and drug susceptibility results were determined according to the Clinical and Laboratory Standards Institute (CLSI) M100 31st edition.¹³ *S. aureus* American Type Culture Collection (ATCC) 27,696 and 27,697 were used as quality control strains. This study was approved by the Ethics Committee of the First Affiliated Hospital of Gannan Medical University (process number: LLSC-2023175). All patients provided written informed consent for their data to be published in the article.

DNA Extraction and Detection and MRSA Identification

Bacterial DNA was extracted by using a centrifugal column bacterial genomic DNA extraction kit (Tianlong Technology Co., Ltd. Xi'an, China), according to the manufacturer's manual. After preliminary screening based on drug sensitivity results and *mecA* amplification by PCR, the drug sensitivity results for *S. aureus* indicated resistance to oxacillin and the

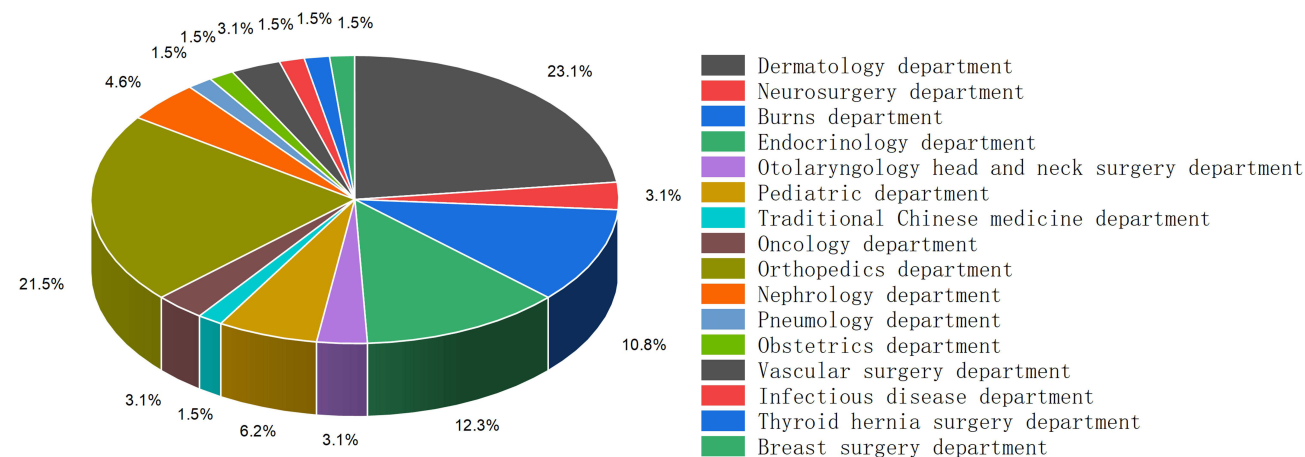


Figure 1 Distribution constituent ratio of *Staphylococcus aureus* infection departments in 2023.

virulence gene *mecA* test was positive. On the basis of these results, the strain was judged to be MRSA; otherwise, it was judged to be MSSA. Representative samples with successful amplification were selected for gene sequencing by General Biology (Anhui) Co., LTD, to verify the success of eight-primer amplification of target genes. After the results were returned, the peak map was observed by SeqMan software to confirm the sequence quality. The sequencing results were compared and analyzed using the GenBank database.¹²

Virulence Genes and Resistance Genes Detection

Eight types of toxin genes were detected by PCR, including *TSST*, *PVL*, and *mupA*. These promote the invasion, colonization, and growth of *S. aureus* in the host by enhancing the bacterial growth microenvironment and inhibiting immune response. Others included genes associated with resistance to oxacillin, erythromycin, levofloxacin, and gentamicin (*arcA*); promoting the adhesion of *S. aureus* to host tissues (*fnbA*); associated with resistance to macrolides, lincosamide, and streptogramin B (MLSB) (*ermA* and *ermC*); and associated with resistance to erythromycin, levofloxacin, and gentamicin (*arcA*); genes for β -lactam resistance (*mecA*). The primer sequences and product sizes of the eight toxin genes are detailed in Table 1, and the PCR electrophoresis patterns in Figure 2.

Multilocus Sequence Typing (MLST) of *S. Aureus*

According to the *S. aureus* MLST database (<https://pubmlst.org/saureus/>), there are seven housekeeping genes (*arcC*, *aroE*, *glpF*, *GMK*, *pta*, *tpi*, and *yqiL*) for the 65 strains of *S. aureus* causing skin and soft tissue infections. All seven primer pairs were sent to General Biology Co., Ltd for primer synthesis. The primer sequences and product sizes are detailed in Table 2. The returned sequencing results were assembled using DNASTAR software (<https://www.dnastar.com/>) and uploaded to the *S. aureus* multilocus typing database to obtain the corresponding genotype and sequence type (STs). When the uploaded data did not match the data in the database, the website administrator was contacted to obtain new genotypes and STs after confirming the sequencing results.

Statistical Analysis

IBM SPSS Statistics for Windows, version 27 (IBM Corp., Armonk, NY, USA) was used for statistical analysis in this study. The χ^2 test or Fisher's exact probability method was used for count data as applicable. Results were considered statistically significant at $P < 0.05$.

Table 1 Pre-Amplified Nucleotide Sequences of Primers

Genes	Primer Sequence (5'-3')	Product Size	Reference
mupA	F: TATATTATGCGATGGAAGGTTGG R: AATAAAATCAGCTGGAAAGTGTG	458bp	McClure JA et al 2017 ¹
fnbA	F: GATACAAACCCAGGTGGTGG R: TGTGCTTGACCATGCTCTTC	191bp	Arciola CR et al 2005 ³
arcA	F: GATATCATCTATACCTAGTACG R: GAAAATCCTCAAGTAAGAAGTG	762bp	Ellington MJ et al 2008 ¹⁴
PVL	F: GTAAAATGTCTGGACATGATCCA R: CAACTGTATTGGATAGCAAAAAGC	421bp	Johnsson D et al 2004 ⁴
TSST	F: ACCCCTGTTCCCTTATCATC R: TTTTCAGTATTTGTAACACC	326bp	Mehrotra M et al 2000 ⁷
mecA	F: GGCAATATTAMCGCACCTCA R: GTCTGCCASTTTCTCCTTGT	214bp	Pichon B et al 2012 ⁸
ermC	F: GCTAATATTGTTAAATCGTCAATTCC R: GGATCAGGAAAAGGAAAAGGACATTTTAC	520bp	Sabet NS et al 2007 ¹⁰
ermA	F: GTTCAAGAACAATCAATACAGAG R: GGATCAGGAAAAGGACATTTTAC	421bp	Lina G et al 1999 ¹¹

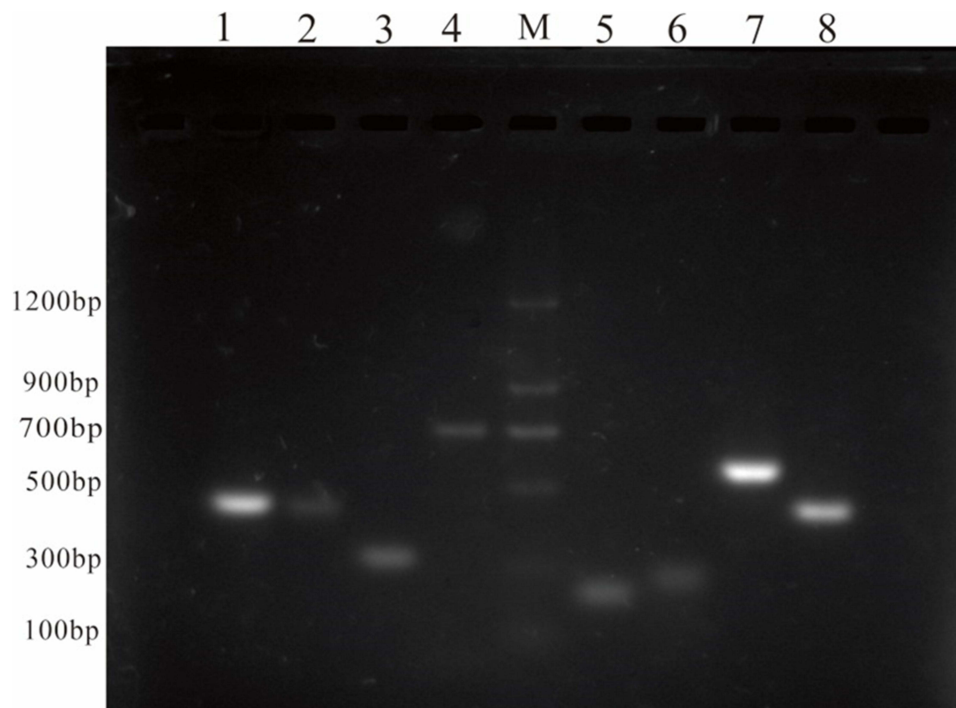


Figure 2 PCR electrophoresis of eight genes. M bands (marker): 100, 300, 500, 700, 900, and 1200 bp markers from bottom to top, 1–8: *Staphylococcus aureus* clinical samples: (1: *mupA*, 2: *PVL*, 3: *TSST*, 4: *arcA*, 5: *fnbA*, 6: *mecA*, 7: *ermC*, 8: *ermA*).

Results

Distribution of MRSA and MSSA Strains

In this study, oxacillin was used to replace methicillin, and oxacillin-resistant *S. aureus* with a positive *mecA* gene were defined as MRSA. In total, 21 MRSA and 44 MSSA strains were detected, with an MRSA detection rate of 32.3%.

Drug Resistance Rate of Strains

In this study, 65 *S. aureus* strains were tested for their susceptibility to 16 antibiotics. All MRSA isolates were resistant to oxacillin and penicillin, but none were resistant to daptomycin, ceftaroline, linezolid, tigecycline, teicoplanin, or

Table 2 Primer Sequences and Product Sizes of Seven Housekeeping Genes for MLST Molecular Typing

Genes	Primer Sequence (5'-3')	Product Size
<i>arcC</i>	F: TTGATTCACCAGCGGTATTGTC R: AGGTATCTGCTTCAATCAGCG	570 bp
<i>aroE</i>	F: ATCGGAAATCCTATTTACATTC R: GGTGTTGTATTAATA ACGATATC	536 bp
<i>glpF</i>	F: CTAGGAACTGCAATCTTA ATCC R: TGGTAAAATCGCATGTCCAATTC	576 bp
<i>gmk</i>	F: ATCGTTTTATCGGGACCATC R: TCATTA ACTACA ACGTAATCGTA	488 bp
<i>pta</i>	F: GTTAAAATCGTATTACCTGAAGG R: GACCCTTTTGTTGAAAAGCTTAA	575 bp
<i>tpi</i>	F: TCGTTCATTCTGAACGTCGTGAA R: TTTGCACCTTCTAACAATTGTAC	475 bp
<i>yqiL</i>	F: CAGCATA CAGGACACCTATTGGC R: CGTTGAGGAATCGATACTGGAAC	598 bp

Table 3 Comparison of the Resistance Rates of MRSA and MSSA Strains Among Staphylococcus Aureus in Skin Infections

Antibiotics	CLSI Breakpoint/(mg/L)		MRSA (n=21) n (%)	MSSA (n=44) n (%)	χ^2	P
	S	R				
Oxacillin	≤2	≥4	21(100.0)	0(0.0)	65	<0.001
Rifampicin	≤1	≥4	5(23.8)	6(13.6)	0.45	0.503
Sulfamethoxazole	≤40	≥80	3(14.3)	5(11.4)	0	1
Levofloxacin	≤1	≥8	5(23.8)	4(9.1)	1.49	0.221
Cefoxitin	≤1	≥4	20(95.2)	1(2.3)	56.18	<0.001
Clindamycin	NA	NA	16(76.2)	15(34.1)	10.09	0.001
Erythromycin	≤6	≥9	16(76.2)	17(38.6)	8.02	0.005
Gentamicin	≤0.5	≥4	3(14.3)	0(0.0)	3.74	0.053
Moxifloxacin	≤0.5	≥8	4(19.0)	5(11.4)	0.21	0.649
Penicillin G	≤4	≥16	21(100)	41(93.2)	0.35	0.553
Ceftaroline	≤4	≥8	0(0.0)	0(0.0)	NA	NA
Daptomycin	≤0.5	≥2	0(0.0)	0(0.0)	NA	NA
Linezolid	≤0.12	≥0.25	0(0.0)	0(0.0)	NA	NA
Tigecycline	≤0.5	NA	0(0.0)	0(0.0)	NA	NA
Teicoplanin	≤8	≥32	0(0.0)	0(0.0)	NA	NA
Vancomycin	≤2	≥16	0(0.0)	0(0.0)	NA	NA

Abbreviations: MRSA, methicillin-resistant *S. aureus*; MSSA, methicillin-sensitive *S. aureus*; CLSI, Clinical and Laboratory Standards Institute.

vancomycin. In general, the resistance rate of the MRSA strains to the tested antibiotics was much higher than that of the MSSA strains. In this study, the resistance rates to rifampicin, levofloxacin, gentamicin, moxifloxacin, and penicillin G were not statistically significant, whereas those to other drugs were significant ($P<0.05$) (Table 3 and Figure 3).

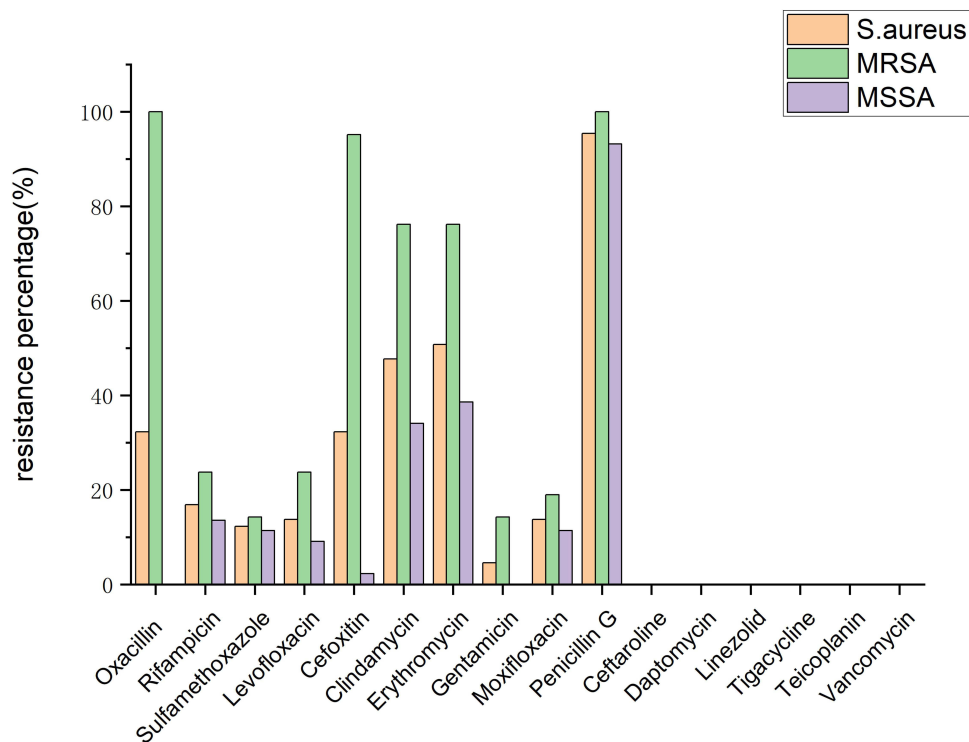


Figure 3 Antibiotic resistance analysis of *S. aureus*, MRSA and MSSA.

Table 4 Comparison of the Detection Rates of MRSA and MSSA Toxin Genes in Skin- Infected Staphylococcus Aureus

Genes	<i>S. aureus</i> (n =65) n (%)	MRSA (n=21) n (%)	MSSA (n=44) n (%)	χ^2	P
mupA	6(9.2)	2(9.5)	4(9.1)	0	1
fnbA	65(100.0)	21(100.0)	44(100.0)	–	–
arcA	64(98.5)	20(95.2)	44(100.0)	0.15	0.7
PVL	8(12.3)	3(14.3)	5(11.4)	0	1
TSST	13(20.0)	5(23.8)	8(18.2)	0.04	0.84
mecA	37(56.9)	21(100.0)	16(36.4)	23.48	<0.01
ermC	12(18.5)	4(19.0)	8(18.2)	0	1
ermA	14(21.5)	7(33.3)	7(15.9)	1.63	0.2

Abbreviations: *S. aureus*, *Staphylococcus aureus*; MRSA, methicillin-resistant *S. aureus*; MSSA, methicillin-sensitive *S. aureus*.

As shown in Table 4, among the eight *S. aureus* toxin genes, *fnbA*, which promotes the adhesion of *S. aureus* to host tissues and *arcA*, which promotes the invasion, colonization, and growth of *S. aureus* in the host had the highest detection rates (100% vs 98.5%). The detection rates of *PVL*, *TSST*, *mupA* (related to mupirocin resistance), *mecA* (oxacillin resistance), and *ermA* and *ermC* (macrolide resistance) were 12.3%; 20%; 9.2%; 56.9%; and 21.5% and 18.5%, respectively. The gene *mecA*, detected in both the MSSA and MRSA groups, had a higher detection rate in the MRSA group than that in the MSSA group.

MLST Typing of *S. Aureus*

Fifty STs were identified in the 65 *S. aureus* isolates, including 44 new STs. The information on the new STs was uploaded to the database, and the new STs are numbered as ST8815-8831, ST8833-8842, ST8844-8855, ST8858-8861, and ST8864. The distribution of the major STs is shown in Figure 4. All ST data were entered into the PHYLOVIZ

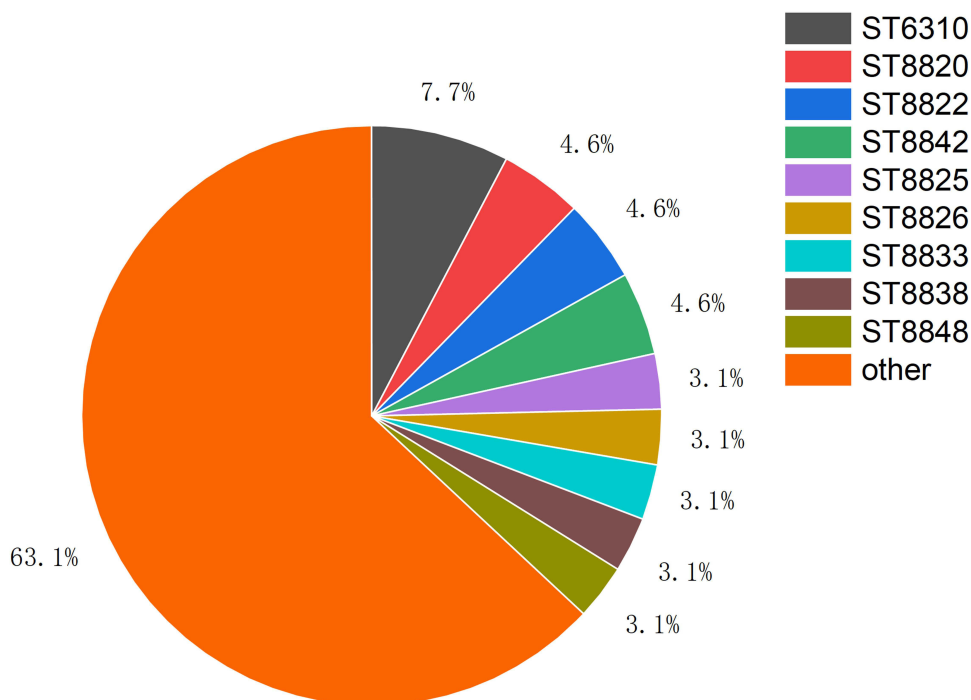


Figure 4 Distribution of major ST types. All 50 STs are represented by elliptical spheres, each of which represents a ST in the figure. The yellow-green oval ball in the minimum spanning tree is the representative ST of this lineage, which we set as the origin of this clonal complex. Values between lines indicate the number of distinct alleles between two adjacent STs, and other STs connected to represent the central oval sphere of the ST are single-site mutants or multisite mutants.

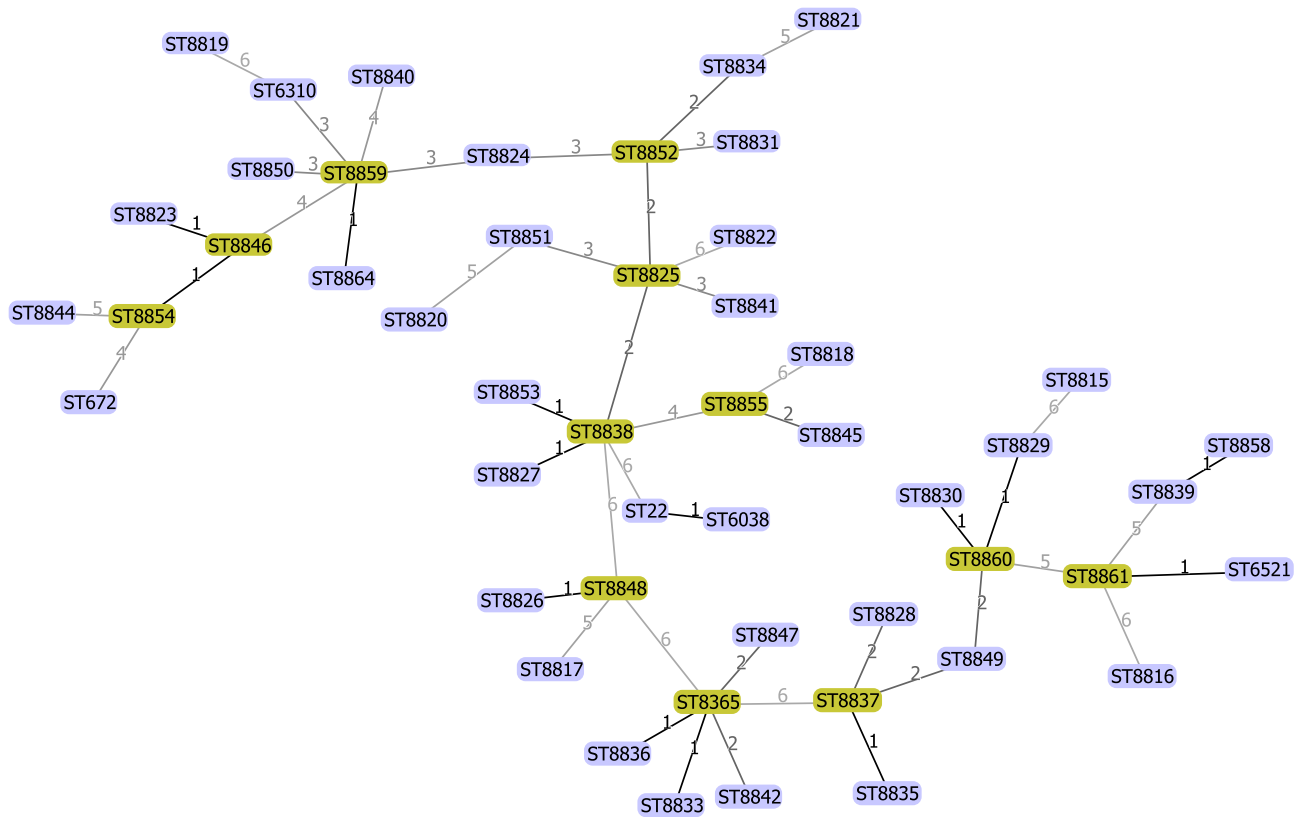


Figure 5 Details of the 12 clonal complexes detected in this study. Putative founder genotypes (green) are positioned centrally in each cluster, and subgroup founders are shown in purple. The lengths of lines reflect the distant of isolates in the whole dataset employed for the analysis.

software (<http://www.phyloviz.net>) for cluster analysis, and the minimum number of identical alleles required to clone the complex (CC) was set at five; the Results are shown in Figure 5. The 17 STs were grouped into the following 12 clusters: ST8854, ST8846, ST8859, ST8852, ST8825, ST8838, ST8855, ST8848, ST8365, ST8837, ST8860, and ST8861 as nodes of CC8854, CC8846, CC8859, CC8852, CC8825, CC8838, CC8855, CC8848, CC8365, CC8837, CC8860, and CC8861, respectively. Multilocus sequence typing is detailed in Table 5. The genetic distance between

Table 5 Multilocus Sequence Typing and Cloning Complexes of *Staphylococcus Aureus*

CC	ST
CC8854	ST8854
CC8846	ST8846, ST8823
CC8859	ST8859, ST8864
CC8852	ST8852, ST8834
CC8825	ST8825
CC8838	ST8838, ST8827, ST8853
CC8855	ST8855, ST8845
CC8848	ST8848, ST8826
CC8365	ST8365, ST8847, ST8842, ST8836, ST8833
CC8837	ST8837, ST8828, ST8835, ST8849
CC8860	ST8860, ST8829, ST8830
CC8861	ST8861, ST6521

Abbreviations: CC, Clonal Complex; ST, multilocus sequence typing.

ST8854 and ST8846 was 1, indicating that the evolutionary difference was small and that the two types were genetically close. The evolutionary divergence between STs that are genetically distant from each other is also greater and the genetic relationships are distant.

Discussion

In this study, 16 antibiotics, penicillin, clindamycin, erythromycin, oxacillin, cefoxitin, moxifloxacin, levofloxacin, rifampicin, sulfamethoxazole, gentamicin, daptomycin, linezolid, tigecycline, teicoplanin, cephalosporin, and vancomycin, were tested against *S. aureus* isolates from infected patients. Genes associated with *S. aureus* pathogenicity and resistance (*mupA*, *fnbA*, *arcA*, *PVL*, *TSST*, *mecA*, *ermC*, and *ermA*) were targeted because of their prevalence in the invasive isolates. After PCR amplification, Sanger sequencing was used. Consistent amplified bands with the normal sequences of the eight genes was obtained. It indicates that the primer design was reasonable and amplification was successful. The results showed the detection rate of *fnbA* (100%) as the highest, followed by that of *arcA* (98.5%).

The significant susceptibility of *S. aureus* to vancomycin, linezolid, and chloramphenicol may be related to the limited use of these antibiotics due to market shortages, high costs, and high toxicity.¹⁵ The 100% susceptibility of *S. aureus* isolated from patient secretions to vancomycin confirms this observation,^{16,17} thereby strengthening the finding of vancomycin efficacy against this pathogen. However, large doses of vancomycin can increase the risk of nephrotoxicity. Therefore, when using vancomycin, the test for vancomycin therapeutic drug concentration monitoring, renal function and the MIC value of the causative organism to vancomycin should be conducted.¹⁸ In addition, this study revealed significant resistance to penicillin and oxacillin (84.6% vs 76.9%).¹⁶ In our study, the resistance rates of penicillin and oxacillin were 95.4% and 32.3%, respectively. The resistance rate of penicillin was higher than that of oxacillin, and the resistance rates of penicillin and oxacillin were different from the literature, which may be related to the different tendency of using antibiotics in different regions. Studies have shown that MRSA prevalence in infectious diseases is high (89.9%).¹⁹ Although our study reported a lower MRSA prevalence, the rising incidence of MRSA infection has resulted in increased treatment costs and longer hospital stays.²⁰ Therefore, detailed molecular epidemiological studies of *S. aureus* are essential.

Multidrug resistance (MDR) is defined as nonsusceptibility to at least one agent in three or more antimicrobial classes. In our study, the MDR of *S. aureus* isolates was 63.1%, which was higher than the 52.4% rate reported in previous studies,¹⁹ indicating a high incidence in this study area. Another study reported an MDR rate as high as 94.8%,¹⁶ higher than that reported in this study; indicating a lower rate in this area than that in other areas. This MDR of *S. aureus* may be related to the irrational use of antibacterial drugs. The pattern of high resistance to commonly used antibiotics, such as penicillin G, clindamycin, erythromycin, and oxacillin, may be attributed to increased exposure to specific classes of antibiotics. This results in drug target mutations that cause resistance or cell wall rearrangements, leading to the disruption of drug accumulation in the cytoplasm.²

Owing to the diversity of *S. aureus* strains and the influence of clinical treatment, the number of STs in the MLST database continues to increase. To date, 8914 STs have been identified. Minimum spanning tree plot of the 65 MLST clinical isolate data of *S. aureus* in skin infections were clustered (Figure 5). All STs are represented by elliptical spheres, and each ellipsoid represents an ST. We set the elliptical sphere at the center of each branch in the evolutionary tree, the representative ST of the lineage, as the origin of the clonal complex. Other STs connected to the oval sphere, representing the ST center, were single-site or multisite mutants.

Many studies have used MLST to determine the population structure of highly clonal *S. aureus*.²¹ The MLST database contains sequence data for thousands of *S. aureus* strains and is an important data source for large-scale epidemiological and genetic association studies on *S. aureus*.²² A previous study reported that alleles with a single-nucleotide mutation should be marked as a novel ST.²³ The 65 strains of *S. aureus* typed by MLST clearly reflected the molecular characteristics of *S. aureus* isolated from Jiangxi Province. In this study, 50 STs of *S. aureus* were identified, of which 44 were newly discovered, indicating a rich diversity of *S. aureus* from southern Jiangxi. Ganzhou area, located in the south of Jiangxi Province in eastern China, upstream of the Ganjiang River, in the transitional zone extending from the southeast coastal area to the central inland area, is an important channel from the mainland to the southeast coastal area. This prefecture-level city has the largest population and subordinate counties and cities in Jiangxi Province, and the

resident population is approximately 20%. It is possible that this densely populated host environment led to the rich diversity of *S. aureus* isolates from southern Jiangxi.

The emergence of these new STs is not accidental; the associated mutants may have emerged a long time ago and spread throughout the population. However, these new STs were only recently identified, probably because of the lack of studies on *S. aureus* molecular typing in Jiangxi Province. These new STs may become important molecular types of MRSA in Jiangxi Province. Surveillance of new STs using isolates obtained during epidemics should be enhanced. We speculate that isolates from different countries and regions often have different molecular subtypes. Isolates of the same molecular type may have the same or similar antibiotic-resistance profiles. Isolates obtained from different regions or sources may have different molecular types, and isolates with different molecular types may have different antibiotic resistance, which is presumed to be the result of different molecular types competing under antibiotic screening pressure in different regions.²⁴ The prevalence of dominant molecular types promotes the spread of antibiotic-resistant bacteria.

In this study, cluster analysis of the 50 STs showed that they were co-clustered into 12 clonal complexes. These unique clonal complexes all originate from southern Jiangxi, according to the MLST analysis. Thus, MLST analysis of strains in different regions may reveal the clonal lineage and evolutionary relationships of *S. aureus* in those regions and help in understanding the molecular epidemiology and provide the experimental basis for pathogenic bacteria prevention and treatment.

fnbA, a cell wall-anchoring protein involved in host cell adhesion and invasion, is the main protein involved in *S. aureus* infection.²⁵ This protein interacts with host-cell integrins via a fibrin bridge to induce actin rearrangement, leading to bacterial internalization.²⁶ Among 65 strains of *S. aureus* isolated from skin infection secretion samples, the PCR detection rate of *fnbA* (100%) exceeded the 45.8% reported in another study.¹⁴ However, the prevalence of *fnbA* in other hospitals' burn wards was significantly lower than 2.9%.²⁷ This difference suggests that *S. aureus* may adjust its virulence gene expression in response to environmental conditions in patients with burns who lack intact skin barrier. The 100% detection rate of *fnbA* may underscores its critical role in promoting *S. aureus* adherence to host tissues in infections. The *S. aureus* isolated in this study from secretion samples of patients with skin infections was highly invasive.

In this study, the detection rate of *arcA* (98.5%) was the highest, followed by that of *mecA* (56.9%), *ermC* (18.5%), *TSST* (20.0%), *ermA* (21.5%), *mupA* (9.2%), and *PVL* (12.3%). *arcA* is known to promote the invasion, colonization, and growth of *S. aureus*; enhance the bacterial growth microenvironment; and suppress immune responses. It is also associated with resistance to oxacillin, erythromycin, levofloxacin, and gentamicin.²⁸ The high detection rate of *arcA* in *S. aureus* samples may indicate a strong invasive capacity and substantial resistance to antibiotics. These findings are consistent with our drug susceptibility test results, and further confirm the strong invasive potential and antibiotic resistance of *S. aureus* in hospitalized patients with skin infections at our hospital.

PVL is mainly associated with community-acquired MRSA infections, especially skin or soft tissue infections. One study reported a *PVL* positivity rate of 11.6%.²⁹ This finding is consistent with the prevalence of *PVL* in our study. However, another study on *S. aureus* in skin and soft tissue infections found a significantly higher *PVL*-positive rate of 63.5%.³⁰ In the same study,³⁰ 48 strains (50%) were *mecA*-positive, similar to those in our study, indicating that *S. aureus* isolates from these two studies had similar resistance patterns.

Previous studies have shown that among 197 strains,³¹ 134 (68%) included *TSST* and 172 (87.3%) *mecA*; these values are much higher than our data. Because we included secretion samples of patients with skin infections, this may indicate that *S. aureus* in skin infections is less likely to express *TSST*. The findings may be related to the lesser role played by *TSST* in the invasion of the skin by *S. aureus* in skin infections. *TSST-1*, encoded by the *TSST* gene, is an important member of the *S. aureus* superantigen (sags) and may cause staphylococcal toxic shock syndrome (TSS) in susceptible hosts.³² The relatively high rate of *TSST*-positive *S. aureus* isolation coupled with the low incidence of TSS strongly suggests that adequate expression of *TSST* leads to disease only under appropriate environmental and/or genetic regulation.³³ *mecA* confers resistance to β -lactam antibiotics in *S. aureus*. The positivity rate of *mecA* in our *S. aureus* isolates was lower than that reported in the literature, indicating that our isolates were less resistant to β -lactam antibiotics, which may facilitate the clinical use of antibiotics.

According to previous studies, 18.7% of isolates carry *ermC*, followed by 15.6% for *ermA*.³⁴ These are similar to the results of the present study, indicating that the prevalence of macrolide-resistant *S. aureus* is similar in different regions. In contrast to our results, *mupA* was not detected in isolates in one study.³⁵ In addition, a systematic review and meta-analysis

reported a low proportion of *mupA*-positive *S. aureus* in Africa (0.5% and 8%), while the expression rate of *mupA* in our study of 9.2% differs from the data reported in the literature.³⁶ Given that *mupA* is associated with acquired resistance to mupirocin,³⁷ the higher use of mupirocin in our study area compared to other regions may account for this difference. Thus, this highlights the need to consider mupirocin dosing to reduce resistance in the future, or use mupirocin in combination with other antibiotics to reduce treatment cycles.³⁸

S. aureus in southern Jiangxi has abundant molecular types and varying degrees of antibiotic resistance to various antibiotics. The emergence and rapid spread of antibiotic resistance genes has brought serious challenges to global public health, and also complicates the clinical treatment of infection. The results of this study will be helpful for promoting drug resistance monitoring of MRSA isolates in southern Jiangxi, China. The results of this study suggest that the use of β -lactam, macrolide, and lincosamide antimicrobial agents should be reduced. Therefore, in the medical environment, we need to use antibiotics carefully,³⁹ strengthen the monitoring of drug resistance, and choose antibiotics rationally according to the results of drug sensitivity. The dosage of antibiotics should be strictly controlled, and the rotation of drugs and withdrawal period should be strictly implemented. In addition, it is necessary to actively research, develop, and promote use of Chinese herbal medicines, microecological agents, and other new non-antibiotic drugs.⁴⁰

A limitation of this study is the inability to detect more virulence genes. The inclusion of a larger number of isolated bacterial specimens could enhance the referential values of the conclusions.

Conclusion

The increasing prevalence of bacterial resistance poses a serious challenge to the effectiveness of antibiotics, especially with the increase in MRSA. The results showed that MRSA strains were significantly associated with *mecA*. Resistance rates of MRSA to oxacillin, cefoxitin, clindamycin, and erythromycin were higher than those of MSSA. The high carrying rate of virulence gene *fnbA* and *arcA* of *S. aureus* were determined, and 44 new STs were identified. These may be associated with the geographical location of southern Jiangxi and local trends in antibiotic use. The study of the clonal lineage and evolutionary relationships of *S. aureus* in these regions may help in understanding the molecular epidemiology and provide the experimental basis for pathogenic bacteria prevention and treatment. Future research should explore a wider range of virulence genes and employ a wider range of genetic characterization approaches to enhance the overall understanding of *S. aureus* isolates, contributing to ongoing efforts to combat antibiotic resistance.

Abbreviations

MLST, multilocus sequence typing; MRSA, methicillin-resistant *S. aureus*; PCR, polymerase chain reaction; MSSA, methicillin-sensitive *S. aureus*; CLSI, Clinical and Laboratory Standards Institute; ATCC, American Type Culture Collection; STs, sequence types; CC, clone the complex.

Data Sharing Statement

This paper reports the data is stored in national genomics GenBase Beijing genomics institute, Chinese Academy of Sciences, China data center¹² biological information center, Chinese Academy of Sciences, the entry numbers are C_AA042252.1, C_AA042259.1, C_AA042258.1, C_AA042257.1, C_AA042256.1, C_AA042255.1, C_AA042254.1, C_AA042253.1, publicly to <https://ngdc.cncb.ac.cn/genbase>.

Ethics Approval and Informed Consent

This study was approved by the Ethics Committee of the First Affiliated Hospital of Gannan Medical University (process number: LLSC-2023175). All patients provided written informed consent for their data to be published in the article.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically

reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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