

Virulence gene profiles, SCCmec types, integrons, and antimicrobial resistance of clinical *Staphylococcus aureus* isolates from Yasuj, southwest Iran

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Received: May 2026, Accepted: August 2026

ABSTRACT

Background and Objectives: *Staphylococcus aureus* poses clinical challenges through its virulence and antibiotic resistance, including SCCmec-mediated methicillin resistance. Integrated data on virulence profiling, molecular typing, and resistance are limited in Southwest Iran. We characterized virulence genes, SCCmec types, integrons, and antimicrobial resistance in *S. aureus* from diverse clinical sources in Yasuj, Iran.

Materials and Methods: We analyzed 214 *S. aureus* isolates recovered from tonsil, wound, sinus, and blood specimens (2020–2023). Species confirmation was by *nuc* PCR. Antimicrobial susceptibility testing followed CLSI disk diffusion guidelines; MRSA was confirmed by *mecA* PCR. PCR assays detected hemolysin genes (*hla*, *hly*, *hld*), toxin genes (*tst*, *pvl*, *eta*, *etb*, *etd*), MSCRAMM genes (*sdrC*, *sdrD*, *sdrE*), *sak*, integrase genes (*intI*, *intII*), and SCCmec types I, III, and IVa.

Results: Isolates were from tonsils (59.8%), wounds (29.9%), sinusitis (6.1%), and blood (4.2%). MRSA prevalence was 29.0%. Highest resistance was to penicillin (98.6%), erythromycin (59.3%), and tetracycline (54.7%), with MDR in 32.7%. Prevalent virulence genes were *hld* (87.9%), *hla* (68.2%), *sak* (60.3%), *sdrC* (44.4%), *eta* (37.9%), *sdrD* (36.9%), *tst* (32.2%), *sdrE* (29.0%), *etd* (18.2%), and *pvl* (3.7%). Among 104 MDR/MRSA isolates, *intI* and *intII* were found in 14.4% and 10.6%. SCCmec type III dominated (80.5%), followed by I (14.5%) and IVa (5.0%); types I and III were significantly linked to MDR ($P < 0.05$). Four isolates co-harbored *pvl*, *tst*, and *hla*.

Conclusion: Considerable virulence gene carriage and SCCmec type III dominance were observed. Gentamicin, ciprofloxacin, cotrimoxazole, and clindamycin remain effective. Coexistence of life-threatening toxin genes and high resistance rates necessitates enhanced infection control.

Keywords: *Staphylococcus aureus*; Virulence factors; Antibiotic resistance; Public health; Iran

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INTRODUCTION

Staphylococcus aureus (*S. aureus*) is a Gram-positive, facultative anaerobic bacterium, and it is a significant opportunistic pathogen found in healthcare environments. It commonly colonizes the anterior nares, skin, vagina, axillae, umbilical stump of neonates, and oropharynx. This microorganism is associated with a wide range of illnesses, such as abscess formation, pneumonia, sinus infections, skin and soft tissue infections, infections following surgery or wounds, bone infections, toxic shock syndrome, septicemia, bacteremia, and endocarditis (1, 2).

The primary factor contributing to methicillin resistance in *S. aureus* is the expression of the *mecA* gene, which is located on a mobile genetic element called the staphylococcal cassette chromosome (SCC*mec*). This large DNA element integrates into the *orfX* gene on the staphylococcal chromosome; all MRSA strains possess an SCC*mec* element, which enables them to resist methicillin and all β -lactam antibiotics. Community-acquired MRSA (CA-MRSA) strains generally carry SCC*mec* types IV, V, or VII, while hospital-acquired MRSA (HA-MRSA) strains typically contain SCC*mec* types I, II, III, VI, or VIII. Additionally, around 15-20% of the *S. aureus* genome is made up of mobile genetic elements, such as bacteriophage genomes, pathogenicity islands, plasmids, transposons, and chromosomal cassettes (3, 4). SCC*mec* typing has become a key epidemiological tool for tracking the dissemination of MRSA clones, as distinct SCC*mec* types are associated with specific ecological niches, transmission dynamics, and resistance profiles. In Iran and neighboring regions, SCC*mec* types III and IV have been most frequently reported, with type III predominantly linked to hospital-associated isolates and type IV more commonly identified among community-associated strains. Notably, SCC*mec* type III is typically associated with large chromosomal cassettes carrying additional resistance determinants, which contributes to the emergence of multidrug-resistant HA-MRSA lineages and complicates therapeutic management (5, 6).

Integrations are another class of mobile genetic element that contribute substantially to the horizontal dissemination of antibiotic resistance genes; over 70 resistance determinants are carried by integrations. Structurally, integrations possess 5' and 3' conserved segments, an integrase gene, and a variable region. There are six classes of integrations identified based on

the integrase sequences they encode, with class 1 integrations being the most commonly found in bacterial isolates. While the involvement of integrations in the emergence of multidrug resistance in Gram-negative bacteria is well understood, information regarding their frequency in Gram-positive species, especially *S. aureus*, is still sparse (7). The investigation of integration carriage alongside SCC*mec* typing may therefore provide complementary insights into the mechanisms underlying the accumulation and spread of resistance determinants in MRSA populations (8).

The clinical consequences of *S. aureus* not only stem from its quick development of antimicrobial resistance but also from a wide range of virulence factors, such as surface proteins, toxins, and enzymes. Among the primary toxins are the leukocidins, including Panton-Valentine leukocidin (PVL) and Luke/D, which are powerful cytotoxins that create pores in the membranes of neutrophils, resulting in dermonecrosis, recurrent mucocutaneous infections, and necrotizing pneumonia. Exfoliative toxins (ETA, ETB, ETD) degrade desmoglein in the upper layers of the skin, resulting in staphylococcal scalded skin syndrome (SSSS). Toxic shock syndrome toxin-1 (TSST-1) functions as a superantigen, which can trigger fever, low blood pressure, rash, multi-organ dysfunction, and potentially fatal shock (9). *S. aureus* also produces hemolysins (α , β , and δ) that lyse erythrocytes and leukocytes. The α -toxin, encoded by *hla*, contributes to pneumonia, sepsis, and brain abscess; β -toxin (*hly*) plays a role in lung and corneal infections; and δ -toxin (*hld*) is secreted by 97% of strains (10). In the realm of surface proteins, the serine-aspartate repeat (Sdr) proteins are categorized within the microbial surface components that bind to adhesive matrix molecules (MSCRAMM) family. The *sdr* locus encompasses *sdrC*, *sdrD*, and *sdrE*, with every strain carrying at least two *sdr* genes. A close association has been demonstrated between the presence of these genes and the invasive capacity and pathogenicity of *S. aureus* (11). Enzymes that are secreted, including coagulase, proteases, and staphylokinase, aid in avoiding the immune response and invading tissues by primarily breaking down host molecules or disrupting signaling pathways and metabolic processes within the host (12). Importantly, the co-carriage of virulence determinants such as *hla*, *hld*, *tst*, *pvl*, and exfoliative toxin genes with antimicrobial resistance traits may enhance both the pathogenic potential and clinical severity of MRSA

infections, leading to poorer outcomes and limiting effective treatment options. Understanding the distribution of these virulence factors in relation to resistance profiles is therefore essential for assessing the clinical risk associated with circulating strains (13).

Despite the global burden of *S. aureus* infections, comprehensive data integrating virulence factor profiling, molecular typing, and antimicrobial resistance patterns are scarce for many regions, including Southwestern Iran. In Yasuj, the epidemiological landscape of *S. aureus*, particularly the distribution of SCCmec types, integron classes, and key toxin genes across diverse clinical sources, has not been characterized. Furthermore, the interplay between these genetic determinants and resistance phenotypes in local isolates remains poorly understood. This gap is of particular concern suggesting that the local molecular epidemiology of *S. aureus* in Yasuj may differ meaningfully from patterns described elsewhere in Iran and cannot be reliably extrapolated from existing regional data. An integrated approach that simultaneously characterizes SCCmec type, integron carriage, resistance phenotype, and virulence gene content is therefore needed, as it allows these determinants to be examined not in isolation but as interconnected features of circulating clones, thereby providing a more clinically meaningful picture than any single typing method alone. Addressing this knowledge gap is essential for informing region-specific infection control strategies, guiding empirical antimicrobial therapy, and limiting the dissemination of multidrug-resistant and virulent clones. Accordingly, the present study was designed to evaluate the virulence factor profiles, molecular typing characteristics, and antimicrobial resistance patterns of *S. aureus* strains isolated from different clinical specimens in Yasuj, Southwest Iran.

MATERIALS AND METHODS

Study design and bacterial isolates. This cross-sectional study was conducted on 214 *S. aureus* stock isolates that had been stored at -21°C in the microbiology laboratory of the School of Medicine, Yasuj University of Medical Sciences. The isolates had been recovered between 2020 and 2023 from different clinical specimens, including tonsil swabs, wound exudates, sinus aspirates and blood cultures. The study was approved by the Ethics Committee of

Yasuj University of Medical Sciences (approval code: IR.YUMS.REC.1400.123). Isolates were selected by convenience sampling from the available archived collection. When more than one isolate had been obtained from the same patient, only the first non-duplicate isolate was included. Isolates with incomplete laboratory records or doubtful species identification were excluded.

Phenotypic confirmation of *S. aureus*. All stored isolates were initially sub-cultured on nutrient agar to verify purity. A single colony from each pure culture was subjected to Gram staining, catalase testing, slide and tube coagulase tests, DNase test, and mannitol fermentation on Mannitol Salt Agar (MSA). Gram-positive cocci in clusters that were catalase-positive, produced coagulase (clot formation in rabbit plasma with EDTA after 1-4 h at 37°C), displayed a clear halo on DNase agar after flooding with 1 % HCl, and changed the color of MSA from pink to yellow were identified as *S. aureus*. A single yellow colony from MSA was re-streaked on Mueller-Hinton agar to obtain a pure lawn culture, which was then used for DNA extraction and for the preparation of glycerol stocks (TSB plus 15 % glycerol) stored at -21°C. Clinical specimens had been processed using standard bacteriological procedures before storage, and the stored isolates represented the confirmed *S. aureus* strains recovered from those specimens.

Antimicrobial susceptibility testing. Antimicrobial susceptibility was assessed using the Kirby-Bauer disk diffusion technique following the guidelines set by the Clinical and Laboratory Standards Institute (CLSI M100, 2018 edition) (14). A bacterial suspension with a turbidity of 0.5 McFarland was created by combining 1.175 g of BaCl₂ in 100 mL of distilled water and 1 mL of H₂SO₄ in 99 mL of distilled water; the absorbance measured between 0.08 and 0.13 at 625 nm. This suspension was then swabbed onto Mueller-Hinton agar plates. The following antibiotic discs (Mast, UK) were evaluated at the specified concentrations: erythromycin (15 µg), cefoxitin (30 µg), gentamicin (10 µg), tetracycline (30 µg), ciprofloxacin (5 µg), clindamycin (2 µg), penicillin (10 µg), and trimethoprim/sulfamethoxazole (25 µg). The discs were positioned at least 12 mm apart. After incubating for 24 hours at 37°C, the diameters of the inhibition zones were measured and classified as susceptible, intermediate, or resistant based on the CLSI breakpoints. *S.*

aureus ATCC 25923 was used as the quality control strain for disk diffusion testing.

Determination of MRSA and multi-drug resistance (MDR). MRSA isolates were first recognized by their resistance to the cefoxitin disk (30 µg) according to CLSI guidelines (14), and confirmation was achieved by PCR identification of the *mecA* gene. An isolate was classified as multi-drug resistant (MDR) if it exhibited resistance to at least one antimicrobial agent from three or more different classes of antibiotics (such as penicillins, cepheems, aminoglycosides, tetracyclines, macrolides, lincosamides, fluoroquinolones, and folate-pathway inhibitors).

DNA extraction. Genomic DNA extraction was performed using the boiling technique. A culture grown for 24 hours on Mueller-Hinton agar was diluted in sterile distilled water to achieve a turbidity corresponding to the 0.5 McFarland standard. Two hundred microliters of the diluted culture were placed into a sterile 1.5 mL microcentrifuge tube and boiled for 15 to 20 minutes. The tube was subsequently centrifuged at 12,000 rpm for 10 minutes at 4°C. The supernatant containing the DNA was carefully retrieved, transferred to a sterile 0.5 mL tube, and stored at -21°C for future use.

PCR amplification of virulence and resistance genes. Oligonucleotide primers were selected from published studies, verified by BLAST analysis and synthesised by Pishgam Company (Tehran, Iran). Lyophilised primers were reconstituted with sterile double-distilled water to a stock concentration of 100 pmol/µL, and working solutions were prepared at 10 pmol/µL. The targeted genes, primer sequences, expected amplicon sizes and references are listed in Table 1. Also, PCR specificity was verified by the expected product size on agarose gel electrophoresis and by inclusion of appropriate controls.

PCR amplification was conducted in a total volume of 12.5 µL, which included 6.25 µL of 2× Master Mix (Amplicon, Denmark), 1 µL of each forward and reverse primer (10 pmol/µL), 1.25 µL of sterile double-distilled water, and 3 µL of template DNA. All reaction mixtures were prepared on ice under sterile conditions. The PCR was executed using a Bio-Rad thermal cycler (T100, USA). The cycling conditions were specific to each gene and are outlined in

Table 2. For each PCR assay, a positive control strain carrying the target gene and a no-template negative control were included in every run.

Gel electrophoresis. PCR amplicons were analyzed through electrophoresis on 1 % (w/v) agarose gels that were created using 0.5× TBE buffer (130 mL) and were stained with 4 µL of Gel Stain. A 5 µL sample of a DNA molecular weight marker (ladder) was loaded into either the first or the last well, while 7 µL of each PCR product was placed into the other wells. Electrophoresis was performed at a voltage of 95 V for a duration of 50 minutes. The gels were examined under UV light with a Gel Documentation system. Band sizes were assessed by comparing them to the molecular weight marker and were verified against both positive and negative controls.

Statistical analysis. The data analysis was conducted using SPSS software version 27 (IBM Corp., Armonk, NY, USA). Descriptive statistics, such as frequencies and percentages, were utilized to summarize the prevalence of antimicrobial resistance, virulence genes, and SCC*mec* types. The chi-square test was used to evaluate the associations between categorical variables. A p-value of less than 0.05 was regarded as statistically significant. For statistically significant findings, and odds ratios (ORs) with 95% confidence intervals (CIs) were calculated for the main significant associations to provide an estimate of effect size. Missing data were handled by case-wise exclusion in the relevant analysis.

Ethics approval. This project was approved by the Ethical Committee of Yasuj University of Medical Sciences (IR.YUMS.REC.1400.123).

RESULTS

A total of 214 confirmed *S. aureus* isolates were included in the present study, of which 62 (29.0%) were MRSA and 70 (32.7%) were MDR. Penicillin resistance was the most frequent finding (98.6%), followed by erythromycin (59.3%) and tetracycline (54.7%), whereas gentamicin resistance was the lowest among the tested agents (13.1%) (Table 3). These resistance patterns indicate that a substantial proportion of the isolates retained resistance to sever-

Table 1. Oligonucleotide primers used for PCR detection of resistance and virulence genes

Gene	Sequence (5'→3')	Amplicon (bp)	Ref.
<i>nuc</i>	F: CTGGCATATGTATGGCAATTGTT R: TATTGACCTGAATCAGCGTTGTCT	664	(15)
<i>mecA</i>	F: GTGAAGATATAACCAAGTGATT R: ATGCGCTATAGATTGAAAGGAT	147	(15)
<i>hla</i>	F: CTGATTACTATCCAAGAAATTCGATTG R: CTTTCCAGCCTACTTTTTTATCAGT	209	(15)
<i>hlb</i>	F: GTGCACTTACTGACAATAGTGC R: GTTGATGAGTAGCTACCTTCAGT	309	(15)
<i>hld</i>	F: AAGAATTTTATCTTAATTAAGGAAGGAGTG R: TTAGTGAATTTGTTCCTACTGTGTCGA	111	(15)
<i>pvl</i>	F: ATCATTAGGTAAAATGTCTGGACATGATCCA R: GCATCAASTGTATTGGATAGCAAAAGC	433	(15)
<i>tst</i>	F: ACCCCTGTTCCCTTATCATC R: TTTTCAGTATTTGTAACGCC	398	(16)
<i>eta</i>	F: TTTGCTTTCTTGATTGGATTG R: GATGTGTTCCGTTTGATTGAC	464	(16)
<i>etb</i>	F: ACGGCTATATACATTCAATT R: TCCATCGATAATATACCTAA	226	(16)
<i>etd</i>	F: GGGGAGACTATAGCTTCTGGTGTATTA R: TCCAACATGAATACCAACTAACTCT	477	(16)
<i>sak</i>	F: ATCCCGTTTCATAAGGCGAGT R: CACCTTACCGCCCAAAGCTG	260	(17)
<i>sdrC</i>	F: AAAAGGCATGATACCAAATCGA R: AATTCTCCATTTCGTATGTTCTG	144	(11)
<i>sdrD</i>	F: AGTGGAACAGCATCAATTTTA R: GTGGTAGATTGTACACTTTCTT	272	(11)
<i>sdrE</i>	F: AGAAAGTATACTGTAGGAAGCTG R: GATGGTTTTGTAGTTACATCGT	433	(11)
SCCmec I	F: GCTTTAAAGAGTGTCGTTACAGG R: GTTCTCTCATAGTATGACGTCC	613	(18)
SCCmec II	F: CGTTGAAGATGATGAAGCG R: CGAAATCAATGGTTAATGGACC	398	(18)
SCCmec III	F: CCATATTGTGTACGATGCG R: CCTTAGTTGTCGTAACAGATCG	280	(18)
SCCmec IVa	F: GCCTTATTTCGAAGAAACCG R: CTACTCTTCTGAAAAGCGTCG	776	(18)
SCCmec V	F: GAACATTGTTACTTAAATGAGCG R: TGAAAGTTGTACCCTTGACACC	325	(18)
<i>intI1</i>	F: CCTCCCGCACGATGATC R: TCCACGCATCGTCAGGC	280	(19)
<i>intI2</i>	F: GTAGCAAACGAGTGACGAAATG R: CACGGATATGCGACAAAAGGT	788	(19)
<i>intI3</i>	F: GCCTCCGGCAGCGACTTTTCAG R: ACGGATCTGCCAAACCTGACT	979	(19)
ACME	F: CTAACACTGAACCCCAATG R: GAGCCAGAAGTACGCGAG	1941	(20)

Table 2. PCR thermal cycling conditions

Target gene(s)	Primary denaturation	Cycle conditions (denaturation, annealing, extension)	No. of cycles	Final extension	Ref.
<i>nuc, mecA, hla, hlb, hld</i>	94°C, 5 min	94°C 45 s, 57°C 45 s, 72°C 1 min	30	72°C, 5 min	(15)
<i>pvl</i>	95°C, 5 min	95°C 40 s, 54°C 40 s, 72°C 45 s	30	72°C, 5 min	(15)
<i>tst</i>	94°C, 5 min	94°C 2 min, 57°C 2 min, 72°C 1 min	35	72°C, 7 min	(16)
<i>eta</i>	95°C, 5 min	95°C 1 min, 54°C 1 min, 72°C 1 min	35	72°C, 5 min	(16)
<i>etb</i>	95°C, 5 min	95°C 1 min, 50°C 1 min, 72°C 1 min	35	72°C, 5 min	(16)
<i>etd</i>	95°C, 5 min	95°C 1 min, 47°C 1 min, 72°C 1 min	35	72°C, 5 min	(16)
<i>sdrC, sdrD, sdrE</i>	94°C, 3 min	94°C 30 s, 53°C 30 s, 72°C 15 s	34	72°C, 5 min	(11)
<i>sak</i>	95°C, 5 min	94°C 30 s, 52°C 45 s, 72°C 45 s	30	72°C, 5 min	(17)
SCCmec types I–V	94°C, 4 min	94°C 45 s, 60°C 45 s, 72°C 40 s	35	72°C, 5 min	(18)
<i>intI1, intI2, intI3</i>	94°C, 4 min	94°C 45 s, 55°C 45 s, 72°C 55 s	30	72°C, 8 min	(19)
ACME	95°C, 5 min	95°C 1 min, 50°C 1 min, 72°C 2 min	30	72°C, 5 min	(20)

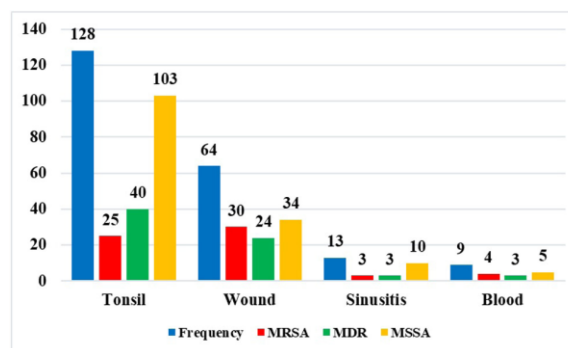
Table 3. Antimicrobial susceptibility of *S. aureus* isolates

Antibiotic	Resistant n (%)	Intermediate n (%)	Susceptible n (%)
Penicillin	211 (98.6)	-	3 (1.4)
Erythromycin	127 (59.3)	8 (3.7)	79 (36.9)
Tetracycline	117 (54.7)	10 (4.7)	87 (40.7)
Clindamycin	70 (32.7)	10 (4.7)	134 (62.6)
Cefoxitin	62 (29.0)	-	152 (71.0)
Ciprofloxacin	55 (25.7)	13 (6.1)	146 (68.2)
Trimethoprim-sulfamethoxazole	45 (21.0)	32 (15.0)	137 (64.0)
Gentamicin	28 (13.1)	1 (0.5)	185 (86.4)

al commonly used therapeutic agents, particularly β -lactams and macrolides.

The highest proportions of MRSA and MDR isolates were observed in wound and blood specimens, while tonsil and sinus isolates showed comparatively lower rates. This distribution suggests that isolates from more invasive clinical sources were more likely to exhibit resistance phenotypes (Fig. 1).

Among virulence genes, *hld* was detected in 188 isolates (87.9%) and *hla* in 146 (68.2%), whereas *hlb* was not detected in any isolate. The *tst* gene was present in 69 isolates (32.2%), *pvl* in 8 (3.7%), *eta* in 81 (37.9%), *etb* in 7 (3.3%), *etd* in 39 (18.2%), and *sak* in 129 (60.3%). The predominance of *hld*, *hla*, and *sak* indicates a broad virulence potential among the studied isolates. Significant associations were observed between several virulence genes and resistance phenotypes. The *sdrD* gene was significantly more common in MRSA than in MSSA isolates (48.4% vs. 32.2%, $p = 0.030$; OR = 1.98, 95% CI:

**Fig 1.** MRSA, MDR, and MSSA distribution among different clinical specimens

1.05–3.71). The *sdrE* gene showed a similar association with MRSA (38.7% vs. 25.0%, $p = 0.048$; OR = 1.89, 95% CI: 1.01–3.56). The *etb* gene was also more frequent among MRSA than MSSA isolates (8.1% vs. 1.3%, $p = 0.023$; OR = 6.74, 95% CI: 1.23–37.10). In contrast, *hla*, *hld*, *tst*, *pvl*, *eta*, and *sak* did not differ significantly between MRSA and MSSA isolates.

Among MDR and non-MDR isolates, *etd* was significantly more common in MDR strains (27.1% vs. 13.9%, $p = 0.024$; OR = 2.24, 95% CI: 1.04–4.84). The *intI* gene was significantly associated with MRSA (22.6% vs. 2.4%, $p = 0.004$; OR = 11.76, 95% CI: 1.53–90.20). The *intII* gene was detected only in MRSA isolates (17.7%, $p = 0.003$) and only in MDR isolates (15.7%, $p = 0.015$). In addition, no isolate carried *intIII*. Among the 62 MRSA isolates, SCCmec type III was predominant, accounting for 50 isolates (80.5%), followed by type I (9 isolates, 14.5%) and type IVa (3 isolates, 5.0%). SCCmec type I was found only among MDR isolates, whereas SCCmec type III was significantly associated with MDR status ($p = 0.004$; OR = 0.41, 95% CI: 0.18–0.92). The distribution of SCCmec types did not differ significantly by clinical specimen source. Overall, SCCmec type III represented the dominant molecular background among MRSA isolates in this collection and was closely linked to multidrug resistance (Table 4).

DISCUSSION

This study elucidates the antimicrobial resistance profiles, molecular epidemiology, and virulence gene carriage of *S. aureus* isolated from diverse clinical sources in Yasuj, southwest Iran. We found that 29.0% of isolates were MRSA and 32.7% were multidrug-resistant (MDR), with SCCmec type III dominating (80.5%), indicating a predominance of hospital-associated clones. A diverse array of virulence genes was detected, though prevalences varied markedly across specimen types and resistance phenotypes. A comparative summary of the main findings of the present study with selected national and international studies is presented in Table 5.

Our MRSA rate (29.0%) aligns with several Iranian reports, such as 31.4% and 39.4% (5, 21), and with global data from Brazil (33.3%), Italy (38.3%), and India (35.3%) (22). However, markedly higher rates (up to 88.6% in some Iranian studies (21, 23, 24)) reflect differences in patient populations, infec-

Table 4. Prevalence of virulence and resistance genes in *S. aureus* isolates and their associations with methicillin resistance, multidrug resistance, and clinical source

Gene	Total n (%)	MRSA n (%)	MSSA n (%)	P	MDR n (%)	Non MDR n (%)	P	Tonsil n (%)	Wound n (%)	Sinusitis n (%)	Blood n (%)	P
<i>nuc</i>	214 (100)	62 (100)	152 (100)	-	70 (100)	144 (100)	-	128 (100)	64 (100)	13 (100)	9 (100)	-
<i>mecA</i>	62 (29.0)	62 (100)	0 (0)	-	24 (34.3)	38 (26.4)	-	25 (19.5)	30 (46.9)	3 (23.1)	4 (44.4)	-
<i>hla</i>	146 (68.2)	48 (77.4)	98 (64.5)	0.076	48 (68.6)	98 (68.1)	1.000	85 (66.4)	43 (67.2)	10 (76.9)	8 (88.9)	0.484
<i>hld</i>	188 (87.9)	55 (88.7)	133 (87.5)	1.000	59 (84.3)	129 (89.6)	0.273	115 (89.8)	53 (82.8)	12 (92.3)	8 (88.9)	0.522
<i>hlb</i>	0 (0)	0 (0)	0 (0)	-	0 (0)	0 (0)	-	0 (0)	0 (0)	0 (0)	0 (0)	-
<i>tst</i>	69 (32.2)	21 (33.9)	48 (31.6)	0.750	24 (34.3)	45 (31.3)	0.755	29 (22.7)	23 (35.9)	8 (61.5)	9 (100)	<0.001
<i>pvl</i>	8 (3.7)	1 (1.6)	7 (4.6)	0.443	0 (0)	8 (5.6)	0.055	4 (3.1)	1 (1.6)	0 (0)	3 (37.5)	<0.001
<i>sdrC</i>	95 (44.4)	32 (51.6)	63 (41.4)	0.225	27 (38.6)	68 (47.2)	0.245	35 (27.3)	48 (75.0)	8 (61.5)	4 (44.4)	<0.001
<i>sdrD</i>	79 (36.9)	30 (48.4)	49 (32.2)	0.030	24 (34.3)	55 (38.2)	0.651	33 (25.8)	30 (46.9)	9 (69.2)	7 (77.8)	<0.001
<i>sdrE</i>	62 (29.0)	24 (38.7)	38 (25.0)	0.048	22 (31.4)	40 (27.8)	0.631	23 (18.0)	32 (50.0)	5 (38.5)	2 (22.2)	<0.001
<i>eta</i>	81 (37.9)	26 (41.9)	55 (36.2)	0.441	27 (38.6)	54 (37.5)	0.882	42 (52.0)	36 (44.5)	0 (0)	3 (3.7)	<0.001
<i>etb</i>	7 (3.3)	5 (8.1)	2 (1.3)	0.023	2 (2.9)	5 (3.5)	1.000	2 (28.6)	3 (42.9)	0 (0)	2 (28.6)	0.007
<i>etd</i>	39 (18.2)	14 (22.6)	25 (16.4)	0.330	19 (27.1)	20 (13.9)	0.024	25 (64.1)	9 (23.1)	1 (2.6)	4 (10.3)	0.111
<i>sak</i>	129 (60.3)	38 (61.3)	91 (59.9)	0.879	37 (52.9)	92 (63.9)	0.138	71 (55.5)	45 (35.2)	6 (4.7)	7 (5.5)	0.104
Integrans												
<i>intI</i>	15 (14.4)	14 (22.6)	1 (2.4)	0.004	13 (18.6)	2 (5.9)	0.135	5 (33.3)	9 (60.0)	0 (0)	1 (6.7)	0.171
<i>intII</i>	11 (10.6)	11 (17.7)	0 (0)	0.003	11 (15.7)	0 (0)	0.015	4 (36.4)	7 (63.6)	0 (0)	0 (0)	0.255
<i>intIII</i>	0 (0)	0 (0)	0 (0)	-	0 (0)	0 (0)	-	0 (0)	0 (0)	0 (0)	0 (0)	-
SCCmec in MRSA												
Type I	9 (14.5)	-	-	-	9 (100)	0 (0)	<0.001	4 (44.4)	5 (55.6)	0 (0)	0 (0)	0.719
Type III	50 (80.5)	-	-	-	18 (36.0)	32 (64.0)	0.004	18 (36.0)	25 (50.0)	3 (6.0)	4 (8.0)	0.389
Type IVa	3 (5.0)	-	-	-	1 (33.3)	2 (66.7)	1.000	3 (100)	0 (0)	0 (0)	0 (0)	0.198

Table 5. Comparison of the main findings of the present study with selected national and international studies

Study Category	Location	Main focus	Key findings	Ref.
National	Yasuj, Iran	SCCmec types, integrons, virulence genes, and antimicrobial resistance	MRSA prevalence was 29.0%, MDR was 32.7%, SCCmec type III was predominant (80.5%), <i>hld</i> , <i>hla</i> , and <i>sak</i> were common, <i>intI</i> and <i>intII</i> were detected in resistant isolates, PVL prevalence was low.	Present study
	Birjand, Iran	SCCmec types and antibiotic resistance in CA- and HA-MRSA	MRSA prevalence was 39.4%, SCCmec types I, III, and IV were detected, with type IV common in HA-MRSA and type III present in both HA- and CA-MRSA, MDR was significantly higher in MRSA isolates.	(5)
	Shiraz, Iran	SCCmec and <i>spa</i> typing of MRSA isolates	MRSA prevalence was 31.4%, SCCmec type III was the dominant type, <i>spa</i> type t030 was the most common among MRSA isolates, SCCmec II, III, and IV appeared to circulate between hospital and community settings.	(21)
	Tehran, Iran	SCCmec IIIA, virulence genes, antimicrobial resistance, and <i>dru</i> typing	MRSA prevalence was 69%, most MRSA isolates carried SCCmec IIIA, more than 68% of SCCmec IIIA isolates were mupirocin resistant, <i>dru</i> typing showed distinct clonal clusters linked to resistance and virulence patterns.	(24)
International	China	Class 1 integrons and resistance gene cassettes in <i>S. aureus</i>	All isolates carried <i>intI1</i> , <i>intI11</i> and <i>intI111</i> were absent; most integron-positive isolates carried resistance genes and were resistant to aminoglycosides.	(31)
	China	Virulence genes, resistance, and molecular characteristics of SSTI isolates	All isolates carried multiple virulence genes, MRSA isolates had significantly higher carriage of several virulence genes, including <i>pvl</i> and <i>sdrE</i> , MRSA-ST59-SCCmec IV was the most common clone.	(25)
	India	SCCmec types, PVL, and clonal spread in HA- and CA-MRSA	SCCmec IV/V clones were common in both hospital and community isolates, HA-MRSA SCCmec IV/V strains were associated with PVL carriage, highlighting movement between community and hospital settings.	(33)
	Egypt	MDR-MRSA prevalence and genetic diversity	MRSA prevalence was 81.2%, 79% of MRSA isolates were MDR, isolates showed resistance to multiple antibiotic classes and marked genetic diversity, supporting the need for local surveillance.	(26)

tion control policies, and diagnostic techniques. The present MRSA rate therefore appears intermediate in relation to both national and international reports, suggesting a substantial but not exceptional burden of methicillin resistance in Yasuj. Penicillin resistance was virtually universal (98.6%), and erythromycin and tetracycline resistance exceeded 50%, whereas gentamicin (13.1%), ciprofloxacin (25.7%), and cotrimoxazole (21.0%) resistance remained moderate, suggesting these agents may retain therapeutic utility. Consistent with previous studies, MRSA isolates showed significantly higher resistance to most tested antibiotics and a higher frequency of MDR

than MSSA isolates (25, 26). Gentamicin resistance was lower than that observed in several studies (21.9–32.9%) (25, 27), possibly reflecting more restricted aminoglycoside usage in our setting. The resistance profile observed here may therefore reflect local prescribing pressure and the cumulative effect of antibiotic exposure in hospital-associated isolates.

Among the 104 MDR and MRSA isolates examined, class 1 and class 2 integrons were detected in 14.4% and 10.6%, respectively, without any class 3 integrons. These frequencies are lower than those reported from other parts of Iran (class 1: 34.1–59.4%) (28–30) and China (53%) (31), yet they confirm the

presence of these mobile elements in Gram-positive clinical isolates. Importantly, both *intI* and *intII* were significantly associated with MRSA, and *intII* was associated with MDR. Moreover, integron carriage correlated with resistance to gentamicin, cefoxitin, clindamycin, and cotrimoxazole, and *intI* additionally with ciprofloxacin resistance. These findings support the role of integrons in multidrug resistance dissemination in *S. aureus* (8, 31). Although these associations are biologically plausible, they should be interpreted as correlational rather than causal because the study design does not allow inference about the direction of resistance acquisition.

The overwhelming predominance of SCCmec type III (80.5%) among MRSA isolates, with type I (14.5%) and type IVa (5.0%) being infrequent, is consistent with the HA-MRSA epidemiology reported in Iran, where type III has been documented as the most prevalent type in Tehran (98%), Tabriz (69.8%), and Shiraz (74.3%) (22, 23, 32). This strong predominance of SCCmec type III likely reflects sustained hospital transmission and selective antibiotic pressure favoring successful hospital-associated lineages. Type I and III isolates exhibited significantly higher MDR rates and resistance to multiple antibiotics compared with type IVa, corroborating that these HA-MRSA clones typically carry broader resistance determinants (5, 33). By contrast, the rarity of SCCmec IVa suggests limited circulation of community-associated lineages in the present collection.

The hemolysin genes *hla* and *hld* were highly prevalent (68.2% and 87.9%, respectively), with no *hly* detected, a pattern similar to that reported by Maleki et al. (16) and Tajik et al. (23). No significant associations with MRSA or MDR were found, indicating that these toxins are widely distributed regardless of resistance phenotype. The *tst* gene, encoding TSST-1, was present in 32.2% of isolates, comparable to rates of 27.7–50.79% documented in other studies (34, 35) but higher than the 9.7% reported from Zabol (36). Its prevalence varied significantly by specimen type, being highest in blood and sinusitis samples, which may reflect the severe invasive diseases associated with TSST-1-producing strains (37). Nevertheless, because clinical severity and patient outcomes were not available, this pattern should be viewed only as a specimen-level association rather than proof of disease severity. PVL (*pvl*) was uncommon (3.7%), mostly detected in MSSA isolates (4.6%), with only a single MRSA (SCCmec III) carrying the gene. This

low frequency, consistent with some national data (2.8–5.7%) (38, 39), likely supports the broader impression that the isolate population was dominated by hospital-associated rather than community-associated strains.

The exfoliative toxin genes *eta*, *etb*, and *etd* were detected in 37.9%, 3.3%, and 18.2% of strains, respectively. *eta* predominance agrees with global trends (40), while *etb* was significantly associated with MRSA. The *etd* gene was significantly linked to MDR and was more frequent among SCCmec I isolates, whereas *eta* and *etb* clustered in type III. Significant inter-specimen variations were observed for *eta* and *etb*, with higher rates in wound and tonsil isolates. The serine-aspartate repeat proteins *sdrC*, *sdrD*, and *sdrE* were carried by 44.4%, 36.9%, and 29.0% of isolates, respectively. These rates are lower than those reported among skin and soft tissue infection isolates from China (25). However, the significant association of *sdrD* and *sdrE* with MRSA, and the marked specimen-dependent distribution, highlight their potential role in host tissue invasion and persistence under antibiotic pressure.

Staphylokinase (*sak*) was present in 60.3% of isolates, with no significant difference between MRSA and MSSA, in agreement with Gomez et al. (17). The significant association with SCCmec type I may reflect clonal lineage-specific carriage. Finally, ACME, a marker of the USA300 clone, was not detected in any isolate, consistent with previous reports from Kuwait and other Asian countries (3, 23), indicating the absence of this epidemic CA-MRSA lineage in our region. This finding is also consistent with the overall molecular profile observed in the present study, which was dominated by SCCmec type III rather than community-associated elements.

This study has some limitations that should be acknowledged explicitly. First, it was a single-center investigation, and the findings may not be generalizable beyond its surrounding referral area. Second, no patient-level epidemiological information or clinical outcome data were available; therefore, associations between molecular markers and disease severity, treatment response, or prognosis could not be evaluated. Third, clonal typing methods such as spa typing, MLST, or whole-genome sequencing (WGS) were not performed, so the relatedness of the isolates and the transmission dynamics of the detected SCCmec types could not be determined. Finally, the study relied on phenotypic resistance testing and gene de-

tection, so molecular findings could not be directly linked to patient-level clinical outcomes. Given the emergence of integrons and their role in spreading antibiotic resistance in bacteria, the prevalence of integrons in Gram-positive bacteria should be investigated at different time intervals. Also, other molecular typing methods should be used to assess the diversity of MRSA strains.

CONCLUSION

In the present study, the highest antimicrobial susceptibility among isolates was observed for gentamicin, ciprofloxacin, cotrimoxazole, and clindamycin, suggesting that these agents may be considered effective therapeutic options against these strains. Our findings reveal genetic diversity among *S. aureus* strains circulating in hospitals in Yasuj, with a relatively high prevalence of toxins and MSCRAMMs, underscoring the considerable colonization and pathogenic capacity of this bacterium. Notably, the simultaneous presence of three important toxins, Pantone-Valentine leukocidin (PVL), toxic shock syndrome toxin-1 (TSST-1), and alpha-hemolysin, can render a strain potentially life-threatening; four isolates in our collection harbored all three toxins concurrently. Furthermore, SCCmec type III, characteristic of hospital-associated clones, was predominant. Enhanced education concerning the transmission dynamics of this pathogen and its stringent control in both community and hospital environments is therefore warranted.

ACKNOWLEDGEMENTS

This work was a part of the MD-Ph.D. thesis of Sahar Milani and supported by Yasuj University of Medical Sciences (Grant no: 990347).

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