



Antibiotic Resistance Patterns of *Staphylococcus aureus* Isolates from Two Healthcare Facilities in Qazvin, Iran: A Retrospective Study

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Received: 29 December, 2025; Revised: 1 February, 2026; Accepted: 5 March, 2026

Abstract

Background: *Staphylococcus aureus* is a common cause of healthcare-associated infections. The increasing prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA) has reduced treatment options and remains a major challenge for infection control. Local surveillance of antimicrobial resistance is necessary to guide empiric therapy and support antibiotic stewardship.

Objectives: This study evaluated the antimicrobial resistance patterns of *S. aureus* clinical isolates collected from two tertiary healthcare facilities in Qazvin, Iran, and determined the prevalence of MRSA.

Methods: This retrospective, descriptive-analytical, cross-sectional laboratory surveillance study included 565 *S. aureus* isolates collected from hospitalized patients at Bou-Ali Hospital and Velayat Center between 2021 and 2024. Isolates were identified using standard microbiological methods. Antimicrobial susceptibility testing was performed using the Kirby-Bauer disk diffusion method in accordance with the Clinical and Laboratory Standards Institute (CLSI) 2020 guidelines. Cefoxitin resistance was used as a phenotypic marker for MRSA. Molecular confirmation by *mecA* or *mecC* detection was not performed. The antimicrobial panel included cefoxitin, gentamicin, clindamycin, ciprofloxacin, erythromycin, trimethoprim-sulfamethoxazole, penicillin, and doxycycline. Inducible clindamycin resistance was not evaluated because D-testing was unavailable. Statistical analyses were performed using SPSS version 27. Associations were assessed using the chi-square test, and temporal trends were assessed using the Cochran-Armitage trend test.

Results: MRSA accounted for 24.4% of all isolates (138/565, 95% CI: 20.9%–28.0%). Blood cultures were the most common specimen source (30.6%), followed by wound swabs (23.5%), urine (13.0%), sputum (10.1%), respiratory secretions (9.7%), and other clinical specimens (12.9%). Resistance was highest to penicillin (96.1%), erythromycin (61.1%), clindamycin (57.4%), and ciprofloxacin (55.1%), whereas gentamicin showed the lowest resistance rate (8.0%). Wound isolates exhibited higher resistance to ciprofloxacin (66.1%), erythromycin (69.0%), and trimethoprim-sulfamethoxazole (45.2%) than isolates from other specimen types. Significant differences between hospitals were observed for erythromycin ($P = 0.004$) and trimethoprim-sulfamethoxazole ($P < 0.001$). Compared with methicillin-sensitive *S. aureus* (MSSA), MRSA isolates showed significantly higher resistance to ciprofloxacin, erythromycin, gentamicin, and trimethoprim-sulfamethoxazole (all $P < 0.05$). Resistance to erythromycin and trimethoprim-sulfamethoxazole also differed significantly by specimen source. No significant temporal changes in resistance were detected over the study period.

Conclusions: MRSA remains common among hospitalized patients in the participating healthcare facilities. High resistance to several commonly prescribed antibiotics underscores the need for continued surveillance, evidence-based antimicrobial stewardship, and regular review of empiric treatment protocols.

Keywords: *Staphylococcus aureus*, Methicillin-Resistant *Staphylococcus aureus*, Drug Resistance, Antimicrobial Susceptibility Testing, Iran

1. Background

Staphylococcus aureus is a major Gram-positive pathogen responsible for both community-acquired and healthcare-associated infections. Clinical manifestations range from superficial skin and soft tissue infections to severe diseases,

including pneumonia, osteomyelitis, infective endocarditis, and bloodstream infection (1). Although *S. aureus* commonly colonizes the skin and mucosal surfaces of healthy individuals, it can become pathogenic when host defenses are impaired by conditions such as immunosuppression, surgery, burns, or prolonged hospitalization (2). Infection results from complex

interactions between bacterial virulence factors and the host immune response, leading to inflammatory activation and tissue injury.

The increasing prevalence of antimicrobial resistance has made the management of *S. aureus* infections more challenging. Methicillin-resistant *S. aureus* (MRSA) is of particular concern because resistance mediated by the *mecA* gene produces penicillin-binding protein 2a (PBP2a), reducing susceptibility to β -lactam antibiotics (3). Since its first description shortly after the introduction of methicillin, MRSA has spread worldwide and has been associated with increased morbidity, mortality, and healthcare costs (4). The prevalence of MRSA varies across regions and healthcare systems. Differences in antimicrobial prescribing practices, infection prevention measures, and patient movement between healthcare facilities contribute to this variation (5, 6). Similar patterns have been reported in Iran, where regional studies have demonstrated substantial differences in MRSA prevalence and resistance profiles (7-9). Investigations among healthcare workers have also identified asymptomatic nasal carriage as a potential source of hospital transmission (10, 11, 12). Recent studies have further described emerging resistance to agents such as vancomycin and linezolid, underscoring the need for continued surveillance (13). Environmental studies have detected resistant *S. aureus* isolates in hospital wastewater, suggesting that environmental reservoirs may contribute to the persistence and spread of resistant strains (14).

Hospital-acquired infections caused by *S. aureus*, particularly MRSA, continue to impose a considerable burden on healthcare systems. These infections are common in intensive care units and surgical wards, where opportunities for transmission are increased by direct contact and contaminated surfaces (15). The emergence of multidrug-resistant strains has further complicated treatment by prolonging hospitalization, increasing healthcare costs, and limiting therapeutic options (16, 17). Local surveillance is essential because resistance patterns differ across geographic regions and healthcare institutions. Understanding these differences supports empirical antibiotic selection, antimicrobial stewardship, and infection prevention programs. This study evaluated antimicrobial resistance patterns among *S. aureus* isolates recovered from two referral hospitals in Qazvin, Iran, to provide updated regional surveillance data and inform local clinical practice.

2. Objectives

The primary objective of this study was to characterize antimicrobial susceptibility patterns among clinical *Staphylococcus aureus* isolates collected from Bou-Ali

Hospital and Velayat Center in Qazvin, Iran, from 2021 to 2024.

The specific objectives were to:

- 1) determine the prevalence of MRSA using cefoxitin susceptibility testing;
- 2) evaluate resistance to commonly prescribed antimicrobial agents;
- 3) compare resistance patterns between the participating hospitals;
- 4) examine differences in resistance by specimen source; and
- 5) assess temporal changes in antimicrobial resistance during the study period.

These findings are intended to inform empiric antibiotic selection, strengthen antimicrobial stewardship initiatives, and provide regional surveillance data for future monitoring.

3. Methods

3.1. Study Design and Bacterial Isolation

This retrospective, descriptive-analytical, cross-sectional laboratory surveillance study was conducted using *Staphylococcus aureus* isolates recovered from hospitalized patients at Bou-Ali Hospital and Velayat Center in Qazvin, Iran, between January 2021 and December 2024.

Eligible participants included all inpatients with culture-confirmed *S. aureus* isolated from clinical specimens during the study period. Isolates were obtained from multiple hospital departments, including internal medicine, surgery, intensive care units (ICUs), and emergency services. Clinical specimens included blood, wound swabs, urine, sputum, respiratory secretions, and other routinely collected samples, providing broad representation of infections encountered in the participating hospitals.

The required sample size was initially estimated using a previously reported MRSA prevalence of 43%, a precision of 5%, and a 95% confidence level, resulting in a minimum of 377 isolates (7). Owing to the retrospective design, all eligible isolates available during the study period were included using a census sampling approach. A total of 565 isolates met the eligibility criteria, exceeding the calculated minimum sample size. The annual distribution was 51 isolates in 2021, 104 in 2022, 221 in 2023, and 245 in 2024.

Inclusion criteria comprised laboratory-confirmed identification of *S. aureus* and the availability of essential clinical information, including patient sex, hospital

department, specimen source, and inpatient status. Samples showing mixed bacterial growth, contaminated cultures, or incomplete laboratory records were excluded. Only inpatient isolates were included. Patient age was not consistently available in the retrospective database. Information on prior antimicrobial exposure, treatment duration, route of administration, underlying diseases, and other potential confounding variables was also unavailable; therefore, these factors could not be incorporated into the analysis.

Identification of *S. aureus* followed standard microbiological procedures. Gram staining confirmed Gram-positive cocci arranged in clusters. Catalase and coagulase testing differentiated *S. aureus* from other Gram-positive cocci, and growth on mannitol salt agar with mannitol fermentation supported species identification (18).

3.2. Antimicrobial Susceptibility Testing

Antimicrobial susceptibility testing was performed using the Kirby-Bauer disk diffusion method on Mueller-Hinton agar in accordance with the Clinical and Laboratory Standards Institute (CLSI) 2020 guidelines (19). The antimicrobial panel included cefoxitin (FOX), ciprofloxacin (CIP), clindamycin (CLI), erythromycin (ERY), gentamicin (GEN), doxycycline (DOXY), penicillin (PEN), and trimethoprim-sulfamethoxazole (SXT). After incubation, inhibition zone diameters were measured and interpreted using CLSI breakpoint criteria. Isolates resistant to cefoxitin were classified as MRSA, with cefoxitin serving as the phenotypic surrogate marker for methicillin resistance (20). Molecular confirmation by detection of *mecA* or *mecC* genes was not performed. Inducible clindamycin resistance was not assessed because D-testing was unavailable during the study period. Quality control procedures followed CLSI recommendations using standard reference strains.

3.3. Statistical Analysis

Laboratory records and corresponding clinical information were reviewed retrospectively. Data were entered into a structured database and analyzed using SPSS version 27. Categorical variables are presented as frequencies and percentages, whereas continuous variables are summarized as means and standard deviations, where appropriate. Ninety-five percent CIs were calculated for major resistance estimates. Associations between antimicrobial resistance and categorical variables, including hospital, specimen source, and patient characteristics, were evaluated using the chi-square test or Fisher's exact test when expected cell counts were small. Statistical significance was defined as a two-

sided P value < 0.05 . Resistance patterns were also compared by specimen source, including blood, wound, urine, sputum or respiratory specimens, and body fluids.

Multivariable regression analysis was not performed because the study was primarily descriptive and important clinical variables, including previous antimicrobial exposure, treatment history, and route of antibiotic administration, were unavailable in the retrospective records. Temporal changes in antimicrobial resistance between 2021 and 2024 were evaluated using the Cochran-Armitage trend test. This analysis was conducted in R version 4.3.2 (R Foundation for Statistical Computing, Vienna, Austria) using the DescTools package (21, 22). Resistance data were grouped by calendar year to assess the presence of a linear trend over the study period.

3.4. Ethical Considerations

The study was conducted in accordance with the principles of the Declaration of Helsinki. Ethical approval was obtained from the Research Ethics Committee of Qazvin University of Medical Sciences. Because the study used anonymized retrospective laboratory records, the requirement for informed consent was waived. All patient identifiers were removed before analysis, and study data were stored securely with restricted access.

4. Results

A total of 565 clinical *Staphylococcus aureus* isolates were included in the analysis. Among the patients, 343 (60.8%) were male and 221 (39.2%) were female. No significant association was observed between patient sex and MRSA status ($P = 0.105$). Patient age was not consistently available in the retrospective database and therefore was not analyzed.

Of all isolates, 394 (69.9%) were obtained from Velayat Center and 170 (30.1%) from Bou-Ali Hospital. The distribution of isolates across hospital departments differed significantly between the two institutions ($P < 0.001$). The largest proportion originated from the emergency department (34.3%, $n = 194$), followed by internal medicine (17.3%, $n = 98$) and intensive care units (17.2%, $n = 97$).

Blood cultures were the most common specimen source (30.6%, $n = 173$), followed by wound swabs (23.5%, $n = 133$), urine (13.0%, $n = 73$), sputum (10.1%, $n = 57$), respiratory secretions (9.7%, $n = 55$), and other clinical specimens (12.9%, $n = 73$). Wound specimens were collected more frequently at Bou-Ali Hospital than at Velayat Center (51.2% vs 11.6%).

4.1. Prevalence of Methicillin-Resistant *Staphylococcus aureus*

Table 1. Antimicrobial Resistance Patterns by Hospital ^a

Antibiotic	Total Resistance	Bou-Ali Resistance	Velayat Resistance	P Value
Cefoxitin (FOX)	138 (24.4)	47 (27.6)	91 (23.0)	0.242
Ciprofloxacin (CIP)	311 (55.1)	99 (58.5)	210 (53.4)	0.315
Clindamycin (CLI)	324 (57.4)	96 (56.3)	228 (57.8)	0.162
Erythromycin (ERY)	345 (61.1)	109 (64.2)	234 (59.4)	0.004 ^b
Gentamicin (GEN)	45 (8.0)	13 (7.9)	32 (8.0)	0.763
Penicillin (PEN)	543 (96.1)	161 (94.7)	381 (96.8)	0.245
Trimethoprim-Sulfamethoxazole (SXT)	177 (31.4)	77 (45.3)	83 (21.1)	< 0.001 ^b
Doxycycline (DOXY)	317 (56.1)	105 (61.5)	215 (54.7)	0.084

^a Values are expressed as No. (%).

^b A P value ≤ 0.05 was considered statistically significant.

Among the 565 isolates, 138 (24.4%) were classified as MRSA (95% CI: 20.9%–28.0%), whereas 427 (75.6%) were methicillin-sensitive *Staphylococcus aureus* (MSSA). The prevalence of MRSA was 27.6% (47/170, 95% CI: 21.0%–34.9%) at Bou-Ali Hospital and 23.0% (91/394, 95% CI: 19.0%–27.4%) at Velayat Center. This difference was not statistically significant ($P = 0.242$).

4.2. Antimicrobial Resistance Patterns

Overall resistance rates are summarized in Table 1. Penicillin showed the highest resistance rate (96.1%), followed by erythromycin (61.1%), clindamycin (57.4%), doxycycline (56.1%), and ciprofloxacin (55.1%). Gentamicin showed the lowest resistance rate (8.0%). Comparisons between the two hospitals showed significant differences in resistance to erythromycin ($P = 0.004$) and trimethoprim-sulfamethoxazole ($P < 0.001$). Resistance rates for the remaining antibiotics were similar between hospitals.

4.3. Antimicrobial Resistance According to Specimen Source

Resistance patterns varied across specimen types. Wound isolates showed the highest resistance to ciprofloxacin (66.1%), erythromycin (69.0%), and trimethoprim-sulfamethoxazole (45.2%). In contrast, blood isolates showed the lowest resistance to gentamicin (3.2%) and trimethoprim-sulfamethoxazole (15.6%). The association between specimen source and resistance was statistically significant for trimethoprim-sulfamethoxazole ($P < 0.001$) and erythromycin ($P = 0.046$). No significant associations were observed for the remaining antimicrobial agents.

4.4. Comparison of MRSA and MSSA Isolates

Resistance profiles differed between MRSA and MSSA isolates. As expected, all MRSA isolates were resistant to cefoxitin, whereas all MSSA isolates were susceptible ($P < 0.001$). Compared with MSSA isolates, MRSA isolates showed significantly higher resistance to ciprofloxacin (73.0% vs 49.6%, $P < 0.001$), erythromycin (72.4% vs 57.5%, $P = 0.007$), gentamicin (30.0% vs 1.1%, $P < 0.001$), and trimethoprim-sulfamethoxazole (47.6% vs 25.6%, $P < 0.001$). Resistance to clindamycin, doxycycline, and penicillin did not differ significantly between the two groups. Detailed susceptibility profiles are presented in Table 2.

4.5. Temporal Trends in Antimicrobial Resistance

Annual resistance rates were evaluated for the period from 2021 to 2024 (2021, $n = 51$; 2022, $n = 104$; 2023, $n = 221$; 2024, $n = 245$). Although resistance rates varied slightly over time, the Cochran-Armitage trend test did not identify statistically significant temporal trends for any of the antimicrobial agents evaluated (all $P > 0.05$). Annual resistance rates are presented in Table 3.

These results illustrate the differential impact of resistance mechanisms between MRSA and MSSA, with MRSA consistently showing higher resistance to key antibiotics.

Overall, MRSA isolates consistently demonstrated higher resistance than MSSA isolates to several clinically important antimicrobial agents. However, no evidence of a significant increase or decrease in resistance was observed during the four-year study period.

5. Discussion

In this retrospective surveillance study, MRSA accounted for 24.4% of all *Staphylococcus aureus* isolates recovered from two tertiary healthcare facilities in Qazvin. This prevalence is consistent with reports describing

Table 2. Susceptibility Profiles of MRSA and MSSA Isolates ^a

Antibiotic / Category	MRSA Resistance	MSSA Resistance	P Value
Cefoxitin (FOX) - Resistant	138 (100.0)	0 (0.0)	< 0.001
Sensitive	0 (0.0)	427 (100.0)	
Ciprofloxacin (CIP) - Resistant	84 (73.0)	187 (49.6)	< 0.001
Intermediate	2 (1.7)	14 (3.7)	
Sensitive	29 (25.2)	176 (46.7)	
Clindamycin (CLI) - Resistant	74 (63.8)	199 (55.3)	0.162
Intermediate	0 (0.0)	7 (1.9)	
Sensitive	42 (36.2)	154 (42.8)	
Erythromycin (ERY) - Resistant	76 (72.4)	185 (57.5)	0.007
Intermediate	7 (6.7)	17 (5.3)	
Sensitive	22 (21.0)	120 (37.3)	
Gentamicin (GEN) - Resistant	33 (30.0)	4 (1.1)	< 0.001
Intermediate	3 (2.7)	2 (0.6)	
Sensitive	74 (67.3)	348 (98.3)	
Penicillin (PEN) - Resistant	125 (98.4)	371 (95.4)	0.245
Intermediate	0 (0.0)	1 (0.3)	
Sensitive	2 (1.6)	17 (4.4)	
Trimethoprim-Sulfamethoxazole (SXT) - Resistant	50 (47.6)	75 (25.6)	< 0.001
Intermediate	1 (1.0)	24 (8.2)	
Sensitive	54 (51.4)	194 (66.2)	
Doxycycline (DOXY) - Resistant	34 (59.6)	77 (54.6)	0.084
Intermediate	2 (3.5)	4 (2.8)	
Sensitive	21 (36.8)	60 (42.6)	

^a Values are expressed as No. (%).

moderate MRSA rates in several regional settings, although it is lower than estimates reported from some other areas of Iran and neighboring countries. Differences among studies are expected because of variations in patient populations, specimen sources, study periods, and laboratory methods (1, 9, 23). For example, investigations based on nasal carriage among healthy individuals are not directly comparable with studies of clinical isolates obtained from hospitalized patients (24). Similarly, differences in infection control practices and antimicrobial prescribing policies may contribute to regional variation in MRSA prevalence.

The high prevalence of penicillin resistance (96.1%) observed in this study is consistent with the widespread production of β -lactamase among *S. aureus* isolates worldwide (3). Similar resistance patterns have been reported in previous Iranian and international studies, indicating that penicillin has limited value for the empirical treatment of suspected *S. aureus* infections (7, 16). Resistance to erythromycin (61.1%), clindamycin (57.4%), and ciprofloxacin (55.1%) was also common, suggesting substantial selective pressure from antimicrobial use within healthcare settings. Comparable findings have been

reported in regions where prolonged or inappropriate antibiotic use has contributed to increasing resistance (25, 26). In contrast, gentamicin showed the lowest resistance rate (8.0%) among the antimicrobial agents evaluated. This finding suggests that gentamicin may remain a useful component of combination therapy when clinically appropriate and supported by susceptibility testing. However, treatment decisions should continue to rely on local antibiograms and individual patient characteristics rather than on resistance rates alone.

Although overall resistance patterns were broadly similar between the two participating hospitals, significant differences were observed in resistance to erythromycin and trimethoprim-sulfamethoxazole. These findings may reflect differences in local prescribing practices, patient case mix, referral patterns, or infection prevention strategies. Institution-specific surveillance therefore remains important, as resistance profiles may vary even within the same geographic region. Environmental reservoirs may also contribute to the persistence of resistant organisms within healthcare settings. Recent studies have identified antimicrobial-resistant *S. aureus* in hospital wastewater, supporting the

Table 3. Annual Antimicrobial Resistance Rates ^a

Antibiotic	2021	2022	2023	2024	P Trend
FOX (MRSA)	27.0	27.8	23.5	22.7	0.365
CIP	37.8	50.0	58.6	56.3	0.065
CLI	39.1	51.8	61.6	57.2	0.253
ERY	47.4	53.2	62.6	60.7	0.310
GEN	2.4	9.5	11.9	6.6	0.631
PEN	100.0	95.1	94.8	96.3	0.362
SXT	25.0	26.5	28.1	30.9	0.254
DOXY	50.0	45.8	56.7	58.5	0.250

^a Values are expressed as percentages. Abbreviations: MRSA, methicillin-resistant *Staphylococcus aureus*; FOX, cefoxitin; CIP, ciprofloxacin; CLI, clindamycin; ERY, erythromycin; GEN, gentamicin; PEN, penicillin; SXT, trimethoprim-sulfamethoxazole; DOXY, doxycycline.

possibility that environmental contamination plays a role in maintaining and disseminating resistant strains (14). Although environmental sampling was beyond the scope of the present study, this mechanism should be considered when designing comprehensive infection prevention and antimicrobial stewardship programs.

Analysis by specimen source identified clinically relevant differences in antimicrobial susceptibility. Wound isolates showed the highest resistance to ciprofloxacin, erythromycin, and trimethoprim-sulfamethoxazole, whereas blood isolates exhibited the lowest resistance to gentamicin and trimethoprim-sulfamethoxazole. These observations suggest that resistance profiles may vary by site of infection. Similar findings have been reported previously and may reflect differences in antimicrobial exposure, tissue microenvironment, bacterial population dynamics, and prescribing practices across clinical settings. The significant association between specimen source and resistance to erythromycin and trimethoprim-sulfamethoxazole further supports the importance of considering the site of infection during empirical antimicrobial selection. Nevertheless, empirical therapy should be guided primarily by local susceptibility data and adjusted once culture and susceptibility results become available.

Comparison of MRSA and MSSA isolates showed that MRSA strains were more frequently resistant to several non- β -lactam antimicrobial agents, including ciprofloxacin, erythromycin, gentamicin, and trimethoprim-sulfamethoxazole. This pattern is consistent with the accumulation of multiple resistance determinants among MRSA lineages and reflects the well-recognized association between methicillin resistance and multidrug resistance (27). These findings reinforce the importance of accurate microbiological diagnosis and antimicrobial susceptibility testing to support appropriate treatment decisions.

5.1. Temporal Trends in Antimicrobial Resistance

No statistically significant temporal trends in antimicrobial resistance were observed between 2021 and 2024. Although resistance rates fluctuated slightly across the study period, these variations did not reach statistical significance. Several factors may explain this finding. The relatively small number of isolates collected during the first study year reduced the statistical power to detect temporal changes. In addition, the unequal distribution of isolates across study years and the retrospective design limited the precision of trend analyses. Changes in healthcare delivery, infection prevention practices, and antimicrobial prescribing during the COVID-19 pandemic may also have influenced resistance patterns. These variables were not available for analysis and therefore could not be evaluated systematically. Consequently, the absence of significant temporal trends should be interpreted cautiously and should not be considered evidence that resistance patterns remained unchanged.

5.2. Clinical Relevance of the Findings

This study provides contemporary antimicrobial resistance data from two major referral hospitals in Qazvin, Iran. These findings contribute to regional surveillance efforts and establish a reference point for future monitoring.

The observed MRSA prevalence indicates that methicillin resistance remains an important concern in hospitalized patients. Continued surveillance is therefore necessary to detect changes in resistance patterns and to support antimicrobial stewardship programs. The consistently low resistance to gentamicin suggests that this agent may remain an appropriate therapeutic option in selected clinical situations when supported by antimicrobial susceptibility testing. Likewise, the

identification of specimen-specific resistance profiles may assist clinicians in selecting empirical therapy before culture results become available.

The differences observed between the participating hospitals also underscore that local resistance data should guide empirical treatment recommendations. Hospital-specific antibiograms are likely to provide more useful information for clinical decision-making than regional estimates alone. An additional finding was the absence of D-testing for inducible clindamycin resistance during the study period. Because inducible resistance may lead to therapeutic failure despite apparent *in vitro* susceptibility, routine implementation of the D-test would improve laboratory reporting and support more appropriate antimicrobial selection.

Overall, these findings add to the available evidence describing antimicrobial resistance among *S. aureus* isolates in Iran and provide data that may assist local infection prevention and antimicrobial stewardship initiatives.

5.3. Strengths and Limitations

Several limitations should be considered when interpreting the findings of this study.

First, the retrospective design limited the availability of clinical information and prevented adjustment for important confounding variables, including previous antimicrobial exposure, duration of hospitalization, severity of illness, and underlying comorbidities. Second, MRSA identification was based on phenotypic cefoxitin resistance without molecular confirmation of *mecA* or *mecC*. Consequently, the study could not evaluate resistance mechanisms, characterize circulating clones, or investigate the molecular epidemiology of MRSA isolates. Third, inducible clindamycin resistance was not assessed because D-testing was unavailable. As a result, the reported clindamycin resistance rates may underestimate the true prevalence of clinically relevant resistance. Fourth, incomplete demographic and clinical data limited the assessment of patient-level risk factors and reduced the ability to explore associations between antimicrobial resistance and clinical characteristics. Finally, the unequal number of isolates collected across study years reduced the statistical power of temporal trend analyses. Therefore, the absence of significant changes over time should be interpreted with caution.

Despite these limitations, the study has several strengths. It includes a relatively large number of clinical isolates collected over four consecutive years from two major referral hospitals. Standardized microbiological methods and CLSI susceptibility criteria were used throughout the study period, allowing consistent

assessment of antimicrobial resistance. The inclusion of analyses by specimen source and hospital also provides information that may support local antimicrobial stewardship and empirical treatment recommendations.

The findings provide updated regional surveillance data and may serve as a baseline for future multicenter studies incorporating molecular characterization, comprehensive clinical information, and prospective data collection.

5.4. Clinical Implications

The findings of this study have several implications for clinical practice and antimicrobial stewardship. Given the high resistance rates observed for penicillin, erythromycin, clindamycin, and ciprofloxacin, empirical use of these agents should be guided by local susceptibility data and culture results whenever possible. Hospital antimicrobial stewardship programs should regularly review prescribing practices to reduce unnecessary use of antibiotics associated with high resistance rates.

Gentamicin demonstrated the lowest overall resistance rate and may remain an appropriate treatment option in selected patients, particularly when used as part of combination therapy and supported by antimicrobial susceptibility testing. Because resistance patterns differed by specimen source, hospital-specific antibiograms that incorporate site-specific susceptibility data may improve empirical antibiotic selection. The study also supports continued investment in infection prevention measures, including adherence to hand hygiene, contact precautions for patients colonized or infected with MRSA, environmental cleaning, and surveillance of high-risk patient populations. These measures remain essential for limiting healthcare-associated transmission.

Routine implementation of the D-test for erythromycin-resistant, clindamycin-susceptible isolates should be considered to identify inducible clindamycin resistance and reduce the risk of treatment failure. Continued microbiological surveillance using standardized laboratory methods, together with periodic evaluation of local resistance patterns, will help guide empirical therapy and support evidence-based antimicrobial stewardship within the participating institutions.

5.5. Conclusions

This study found that nearly one-quarter of *Staphylococcus aureus* isolates recovered from hospitalized patients in two referral hospitals in Qazvin were methicillin resistant. Resistance to several commonly prescribed antimicrobial agents, particularly penicillin, erythromycin, clindamycin, and ciprofloxacin, remained

high throughout the study period, whereas gentamicin retained relatively good in vitro activity. Resistance patterns differed by specimen source and between hospitals for selected antibiotics, highlighting the importance of institution-specific surveillance and local antibiograms when selecting empirical therapy. No statistically significant temporal changes in antimicrobial resistance were identified between 2021 and 2024.

These findings support continued antimicrobial stewardship, regular surveillance of resistance patterns, and ongoing infection prevention efforts. Future prospective studies incorporating molecular characterization of MRSA isolates and more detailed clinical data would improve understanding of resistance mechanisms and factors associated with antimicrobial resistance in this setting.

Acknowledgements

This research received no specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Footnotes

AI Use Disclosure: The authors declare that no generative AI tools were used in the creation of this article.

Authors' Contribution: Conceptualization: A. N. and M. S.; Data Curation: A. A. and M. S.; Formal Analysis: A. A.; Investigation: M. S. and A. N.; Methodology: A. N. and A. A.; Project Administration: A. N. and M. S.; Software: A. A. and M. S.; Supervision: A. N. and A. K.; Validation: A. A.; Visualization: A. A.; Writing – Original Draft: A. A., M. S., A. N., and A. K.; Writing – Review & Editing: A. A.

Conflict of Interests Statement: The authors declare that they have no conflict of interest.

Data Availability: The dataset presented in the study is available on request from the corresponding author during submission or after publication.

Ethical Approval: This study was approved by the Ethics Committee of Qazvin University of Medical Sciences with IR.QUMS.REC.1402.416; Date: 2024 - 03 - 17; <https://ethics.research.ac.ir/PortalProposalsList.php?code=IR.QUMS.REC.1402.416&title=&name=&stat=&isAll=&searchmode=exp&searchkey=>

Funding/Support: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Informed Consent: Given the retrospective, laboratory-based design using anonymized archival data and routine diagnostic isolates, the ethics committee waived the requirement for written informed consent. All personal identifiers were removed, and records were coded before analysis. Data were stored securely with access limited to the investigators, and findings were reported only in aggregate to prevent patient identification.

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