Regulatory Mechanisms in Biosystems

ISSN 2519-8521 (Print)
ISSN 2520-2588 (Online)
Regul. Mech. Biosyst.

Antibiotic resistance patterns and molecular characterization of *Staphylococcus aureus* in diverse human infections

H. K. Judi, H. H. Naser

University of Al-Qadisiyah, Al-Qadisiyah, Iraq

Article info

Received 02.06.2025
Received in revised form 22.06.2025
Accepted 16.07.2025

Department of Microbiology, College of Veterinary Medicine, University of Al-Qadisiyah, Al-Qadisiyah, Iraq.

Zoonotic Disease Research Unit, College of Veterinary Medicine, University of Al-Qadisiyah, Al-Qadisiyah, Iraq.
E-mail: hawrakaremjudi@gmail.com

Judi, H. K., & Naser, H. H. (2025). Antibiotic resistance patterns and molecular characterization of Staphylococcus aureus in diverse human infections. Regulatory Mechanisms in Biosystems, 16(3), e25103. doi:10.15421/0225103

This study examined the prevalence, antibiotic resistance profiles, and molecular mechanisms of *Staphylococcus aureus* in human clinical infections, including wound, burn, mastitis, and otitis media samples. A total of 137 clinical samples were collected from patients. Samples were cultured on Mannitol Salt Agar and Blood Agar and incubated at 37 °C for 24–48 hours. Antibiotic resistance profiles were determined using VITEK 2 AST-P639 cards, then molecular detection of resistance genes by using the PCR technique. Among 137 clinical specimens, *S. aureus* was isolated at an overall prevalence of 87.6% (120/137), with significant variation across infection types ($\chi^2 = 10.04$, P = 0.018). The highest prevalence was observed in otitis media (94.3%, 33/35) and mastitis (90.4%, 47/52), followed by burn (81.6%, 31/38) and wound infections (75.0%, 9/12). Antibiotic susceptibility testing revealed near-universal resistance to benzylpenicillin (100.0%) and high resistance to oxacillin (57–78%) and erythromycin (57–78%). In contrast, isolates remained fully susceptible to gentamicin, azithromycin, fluoroquinolones (ciprofloxacin, ofloxacin), and doxycycline (100% susceptibility). Multidrug resistance (MDR) was widespread (65.0%, 78/120 isolates), with the highest proportion in wound infections (77.8%, 7/9) and the lowest in mastitis (57.4%, 27/47), though differences were not statistically significant ($\chi^2 = 4.851$, P = 0.183). No extensively drug-resistant (XDR) or pan-drug-resistant (PDR) strains were detected. Molecular analysis identified key resistance genes: mecA (82.1% prevalence in MDR isolates), blaZ (56.4%), NorA (38.5%), and VanA (5.1%). The mecA gene was most prevalent in burn (85.7%, 18/21) and mastitis (81.5%, 22/27) isolates, while VanA was rare across all sources. Statistical analysis showed no significant differences in gene distribution (χ^2 range: 0.89–1.45, P > 0.05). These findings highlight the persistent challenge of antibiotic resistance in *S. aureus* infections and underscore the need for targeted therapeutic strategies.

Keywords: *Staphylococcus aureus*; antibiotic resistance; multidrug resistance (MDR); PCR detection.

Introduction

Staphylococcus aureus is a formidable human pathogen responsible for a wide range of infections, from mild skin conditions to life-threatening systemic diseases such as bacteremia, endocarditis, and toxic shock syndrome (Tong et al., 2015). The bacterium's virulence is compounded by its remarkable ability to develop resistance to multiple antibiotics, rendering treatment increasingly challenging (Lee et al., 2018). The emergence of methicillin-resistant *S. aureus* (MRSA) in the 1960s marked a pivotal moment in the battle against antibiotic resistance, as these strains harbored the mecA gene, encoding penicillin-binding protein 2a (PBP2a), which confers resistance to beta-lactam antibiotics, including penicillins, cephalosporins, and carbapenems (Klein et al., 2020). Since then, MRSA has become a global public health crisis, with both healthcare-associated (HA-MRSA) and community-associated (CA-MRSA) strains contributing to high morbidity and mortality rates (David & Daum, 2017).

The World Health Organization (WHO) has classified MRSA as a priority pathogen for research and development of new antibiotics due to its widespread resistance and clinical impact (WHO, 2021). Beyond MRSA, *S. aureus* has also developed resistance to other antibiotic classes, including macrolides (e.g., erythromycin), fluoroquinolones, and aminoglycosides, through mechanisms such as efflux pumps (NorA), enzymatic inactivation (blaZ), and target modification (VanA for vancomycin resistance) (Foster, 2017; McGuinness et al., 2017). The rise of multidrug-resistant (MDR) strains, defined as resistance to three or more antibiotic classes, has further limited therapeutic options, particularly in vulnerable populations such as immunocompromised patients and those with chronic infections (Lakhundi & Zhang, 2018).

Recent studies highlight the disproportionate burden of *S. aureus* infections in specific clinical settings, such as burn units, surgical wounds, and otitis media, where biofilm formation and prolonged antibiotic exposure exacerbate resistance (Parker & Prince, 2012; Azimi et al., 2021). For instance, burn wounds provide an ideal environment for *S. aureus* colonization due to compromised skin barriers and immunosuppression, often leading to persistent infections with high MDR rates (Altoparlak et al., 2020). The clinical implications of these resistance patterns are profound, as inappropriate antibiotic use fuels further resistance while increasing healthcare costs and patient mortality (Ventola, 2015).

Molecular diagnostics, such as PCR-based detection of resistance genes (mecA, blaZ, NorA, VanA), have become indispensable tools for surveillance and targeted therapy, enabling rapid identification of high-risk strains (Becker et al., 2020). However, gaps remain in understanding the epidemiological distribution of these genes across diverse infection types and geographic regions. For example, while mecA is well-documented in MRSA, the prevalence of VanA (vancomycin resistance) remains sporadic but concerning due to its potential for horizontal gene transfer. Additionally, the role of efflux pumps (NorA) in fluoroquinolone resistance underscores the complexity of resistance mechanisms, which often coexist in MDR strains (Dashtbani-Roozbehani & Brown, 2021).

This study aims to address these gaps by examining the prevalence, antibiotic resistance profiles, and molecular mechanisms of *S. aureus* in diverse human infections, including wound, burn, mastitis, and otitis media by integrating phenotypic susceptibility testing with genotypic analysis.

Material and methods

A total of 137 clinical samples were collected from patients with wound infections (n = 12), burn infections (n = 38), mastitis (n = 52), and otitis media (n = 35). Samples were obtained using sterile swabs or aspirates, transported in Amies transport medium, and processed within 2 hours of collection to ensure viability.

Samples were cultured on Mannitol Salt Agar (MSA) (Oxoid, UK) and Blood Agar (BA) (HiMedia, India) and incubated at 37 °C

for 24–48 hours. Presumptive *S. aureus* colonies (yellow on MSA, β-hemolytic on BA) were confirmed via Gram staining (Gram-positive cocci in clusters), catalase test (positive), and coagulase test (tube method). Final identification was performed using the VITEK 2 automated system (bioMérieux, France) for biochemical profiling.

Antibiotic resistance profiles determined using VITEK 2 AST-P639 cards included the following antibiotics with clinically relevant concentrations.

Genomic DNA was extracted using the DNA Mini Kit (Geneaid, Tawin) and quantified via NanoDrop (Thermo Fisher, USA).

PCR amplification was performed in a 25 µL reaction mix containing: 12.5 µL of 2X Master Mix (Promega, USA); 1 µL each of forward/reverse primer (10 pmol/µL) (Table 1); 2 µL DNA template (50 ng/µL); 8.5 µL nuclease-free water.

Thermocycling conditions:

1. Initial denaturation: 95 °C for 5 min.
2. 35 cycles:
– denaturation: 95 °C for 30 sec.
– annealing: gene-specific temperature (Table 1) for 30 sec.
– extension: 72 °C for 45 sec.
3. Final extension: 72 °C for 5 min.

Table 1
Antibiotic resistance profiles

Antibiotic class	Antibiotics tested	Concentration range, µg/mL
Penicillins	Oxacillin	0.25–4
	Ampicillin	1–16
Beta-lactamase Inhibitors	Amoxicillin-Clavulanate	1/0.5–16/8
Cephalosporins	Cefoxitin (MRSA screen)	0.5–8
Macrolides	Erythromycin	0.25–4
	Clindamycin	0.25–4
Aminoglycosides	Gentamicin	1–16
Fluoroquinolones	Ciprofloxacin	0.25–4
	Levofloxacin	0.5–8
Tetracyclines	Tetracycline	1–16
	Doxycycline	1–16
Glycopeptides	Vancomycin	1–32
Others	Trimethoprim/sulfamethoxazole	0.5/9.5–4/76
	Linezolid	0.5–8

Table 2
Primers used for PCR amplification of resistance genes were designed in this study and provided by Macrogen (Korea)

Target gene	Primer Sequence (5'→3')	Product size, bp	Annealing temperature, °C	NCBI Accession
mecA	F: TGCAGATAAGGGGTACAGAAAA	516	58	OM574584.1
	R: ACTACATCATCGAAACTTGCCA			
NorA	F: TGGTGGATTATTGGCAGAGT	309	56	AB086042.1
	R: ATACCGCCACCCGTAATAGC			
VanA	F: GGCAAGTCAGGTGAAGATGGA	618	60	MN295031.1
	R: TTCGTTCAGTACATTGCGGC			
blaZ	F: TCAAACAGTTCACATTGCCAAAG	478	57	U58139.2
	R: CGAAGCCAGCAGGTGTTGAA			

PCR products were separated on a 1.5% agarose gel (85 V, 1h.30 min), stained with ethidium bromide, and visualized under UV light. A 100 bp DNA ladder (SolGent, Korea) was used for size comparison. Data were analyzed using SPSS v26 (IBM, USA). Chi-square (χ^2) tests and A p-value < 0.05 was considered statistically significant.

Results

The isolation and identification of *S. aureus* from clinical samples were conducted using standard bacteriological culture techniques. Samples were inoculated onto selective media such as Mannitol Salt Agar (MSA), which is differential for *S. aureus* due to its ability to ferment mannitol, producing yellow colonies. Blood Agar was also used to observe hemolytic patterns, with *S. aureus* typically exhibiting beta-hemolysis. After incubation at 37 °C for 24–48 hours, suspected colonies were subjected to Gram staining and biochemical tests, including catalase (positive for *S. aureus*) and coagulase tests (positive for *S. aureus*). For confirmation, the VITEK 2 automated system was employed, which uses advanced biochemical and enzymatic reactions to accurately identify bacterial species, including *S. aureus*. This method ensures high specificity and reliability in the identification process.

The study analyzed 137 human clinical samples, with an overall *S. aureus* prevalence of 87.6%. The highest prevalence was observed in otitis media infections (94.3%, 33/35 positive samples), followed by mastitis infections (90.4%, 47/52), burn infections (81.6%, 31/38), and wound infections (75.0%, 9/12). Chi-square (χ^2) tests revealed significant differences in prevalence across sample types ($\chi^2 = 10.04$, $P = 0.018$), indicating that *S. aureus* isolation rates vary significantly depending on the type of infection. The high prevalence in otitis media and mastitis infections suggests that these conditions may be particularly susceptible to *S. aureus* colonization or infection in humans.

The antibiotic susceptibility test results revealed significant resistance patterns in *S. aureus* isolates from wound, burn, mastitis, and otitis media infections. High resistance rates were observed for benzylpenicillin (100% across all sources), oxacillin (57–78%), and erythromycin (57–78%), while gentamicin, azithromycin, fluoroquinolones (e.g., ciprofloxacin), and doxycycline maintained 100% susceptibility. MDR (multidrug-resistant) isolates were prevalent (65% overall), with the highest proportion in wound infections (77.8%) and the lowest in mastitis (57.4%), though statistical analysis ($\chi^2 = 4.851$, $P = 0.183$) indicated no significant difference in MDR distribution across sources. Notably, no XDR (extensively drug-resistant) or PDR (pandrug-resistant) isolates were detected. These findings underscore the persistent challenge of beta-lactam and macrolide resistance while highlighting fluoroquinolones and aminoglycosides as effective alternatives.

Table 3
Prevalence analysis of *S. aureus* isolation from human clinical samples

Type of samples	Tested (n)	Positive (n)	Prevalence, %	χ^2	P-value
Wound infection	12	9	75.00		
Burn infection	38	31	81.58		
Mastitis infection	52	47	90.38	10.04	0.018*
Otitis media infection	35	33	94.29		
Total	137	120	87.59		

The molecular detection of antibiotic resistance genes in multidrug-resistant *S. aureus* isolates was performed using PCR amplification and agarose gel electrophoresis. The study identified four key resistance genes: mecA (conferring methicillin resistance by encoding an altered penicillin-binding protein), blaZ (mediating beta-lactam resistance through beta-lactamase production), NorA (contributing to fluoroquinolone resistance via efflux pumps), and VanA (imparting vancomycin resistance by modifying cell wall precursors) across different clinical sources, including wound, burn, mastitis, and otitis media infections. The mecA gene was the most prevalent, particularly in burn (85.7%) and mastitis (81.5%) infections, while VanA was the least common. Statistical analysis (χ^2 tests) revealed no significant differences in gene distribution across infection sources ($P > 0.05$) as

shown in Table 8. Gel electrophoresis confirmed the presence of these genes, with distinct product sizes (e.g., 516 bp for mecA and 618 bp for VanA) as shown in Figures 1–4.

Table 4
Antibiotic susceptibility test results – wound infection (9 isolates)

Antibiotic	Susceptible (S)	Intermediate (I)	Resistant (R)
Oxacillin	2 (22%)	0 (0%)	7 (78%)
Benzylpenicillin	0 (0%)	0 (0%)	9 (100%)
Gentamicin	9 (100%)	0 (0%)	0 (0%)
Azithromycin	9 (100%)	0 (0%)	0 (0%)
Erythromycin	2 (22%)	0 (0%)	7 (78%)
Tetracycline	8 (89%)	0 (0%)	1 (11%)
Doxycycline	9 (100%)	0 (0%)	0 (0%)
Ofloxacin	9 (100%)	0 (0%)	0 (0%)
Levofloxacin	9 (100%)	0 (0%)	0 (0%)
Moxifloxacin	9 (100%)	0 (0%)	0 (0%)
Ciprofloxacin	9 (100%)	0 (0%)	0 (0%)
Nitrofurantoin	7 (78%)	0 (0%)	2 (22%)
Clindamycin	2 (22%)	0 (0%)	7 (78%)
Rifampin	8 (89%)	0 (0%)	1 (11%)
Trimethoprim	7 (78%)	0 (0%)	2 (22%)

Table 5
Antibiotic susceptibility test results – burn infection (31 isolates)

Antibiotic	Susceptible (S)	Intermediate (I)	Resistant (R)
Oxacillin	10 (32%)	0 (0%)	21 (68%)
Benzylpenicillin	0 (0%)	0 (0%)	31 (100%)
Gentamicin	31 (100%)	0 (0%)	0 (0%)
Azithromycin	31 (100%)	0 (0%)	0 (0%)
Erythromycin	10 (32%)	0 (0%)	21 (68%)
Tetracycline	30 (97%)	0 (0%)	1 (3%)
Doxycycline	31 (100%)	0 (0%)	0 (0%)
Ofloxacin	31 (100%)	0 (0%)	0 (0%)
Levofloxacin	31 (100%)	0 (0%)	0 (0%)
Moxifloxacin	31 (100%)	0 (0%)	0 (0%)
Ciprofloxacin	31 (100%)	0 (0%)	0 (0%)
Nitrofurantoin	23 (74%)	0 (0%)	8 (26%)
Clindamycin	10 (32%)	0 (0%)	21 (68%)
Rifampin	30 (97%)	0 (0%)	1 (3%)
Trimethoprim	23 (74%)	0 (0%)	8 (26%)

Table 6
Antibiotic susceptibility test results – mastitis infection (47 isolates)

Antibiotic	Susceptible (S)	Intermediate (I)	Resistant (R)
Oxacillin	20 (43%)	0 (0%)	27 (57%)
Benzylpenicillin	0 (0%)	0 (0%)	47 (100%)
Gentamicin	47 (100%)	0 (0%)	0 (0%)
Azithromycin	47 (100%)	0 (0%)	0 (0%)
Erythromycin	20 (43%)	0 (0%)	27 (57%)
Tetracycline	47 (100%)	0 (0%)	0 (0%)
Doxycycline	47 (100%)	0 (0%)	0 (0%)
Ofloxacin	47 (100%)	0 (0%)	0 (0%)
Levofloxacin	47 (100%)	0 (0%)	0 (0%)
Moxifloxacin	47 (100%)	0 (0%)	0 (0%)
Ciprofloxacin	47 (100%)	0 (0%)	0 (0%)
Nitrofurantoin	35 (74%)	0 (0%)	12 (26%)
Clindamycin	20 (43%)	0 (0%)	27 (57%)
Rifampin	47 (100%)	0 (0%)	0 (0%)
Trimethoprim	35 (74%)	0 (0%)	12 (26%)

Table 7
Antibiotic susceptibility test – otitis media infection (33 isolates)

Antibiotic	Susceptible (S)	Intermediate (I)	Resistant (R)
Oxacillin	10 (30%)	0 (0%)	23 (70%)
Benzylpenicillin	0 (0%)	0 (0%)	33 (100%)
Gentamicin	33 (100%)	0 (0%)	0 (0%)
Azithromycin	33 (100%)	0 (0%)	0 (0%)
Erythromycin	10 (30%)	0 (0%)	23 (70%)
Tetracycline	29 (88%)	0 (0%)	4 (12%)
Doxycycline	33 (100%)	0 (0%)	0 (0%)
Ofloxacin	33 (100%)	0 (0%)	0 (0%)
Levofloxacin	33 (100%)	0 (0%)	0 (0%)
Moxifloxacin	33 (100%)	0 (0%)	0 (0%)
Ciprofloxacin	33 (100%)	0 (0%)	0 (0%)
Nitrofurantoin	25 (76%)	0 (0%)	8 (24%)
Clindamycin	10 (30%)	0 (0%)	23 (70%)
Rifampin	29 (88%)	0 (0%)	4 (12%)
Trimethoprim	25 (76%)	0 (0%)	8 (24%)

Table 8
Antibiotic resistance pattern by source of sample (120 isolates)

Resistance Pattern	Wound Infection (9)	Burn Infection (31)	Mastitis Infection (47)	Otitis Media Infection (33)	Total (120)
Non-MDR	2 (22%)	10 (32%)	20 (43%)	10 (30%)	42 (35%)
MDR	7 (78%)	21 (68%)	27 (57%)	23 (70%)	78 (65%)
XDR	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
PDR	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Table 9
Comparison of MDR antibiotic resistance pattern by source of sample

Source of sample	MDR isolates	Total isolates	Percentage	χ^2	P-value
Wound infection	7	9	77.8%	4.851	0.183
Burn infection	21	31	67.7%		
Mastitis infection	27	47	57.4%		
Otitis media infection	23	33	69.7%		
Total	78	120	65.0%	–	–

Table 10
Antibiotic resistance genes in MDR *Staphylococcus aureus* isolates

Source of sample	mecA gene	blaZ gene	NorA gene	VanA gene	Total (120)
Wound infection	5 (71.4%)	3 (42.9%)	2 (28.6%)	0 (0%)	7 (100%)
Burn infection	18 (85.7%)	12 (57.1%)	9 (42.9%)	1 (4.8%)	21 (100%)
Mastitis infection	22 (81.5%)	15 (55.6%)	11 (40.7%)	2 (7.4%)	27 (100%)
Otitis media infection	19 (82.6%)	14 (60.9%)	8 (34.8%)	1 (4.3%)	23 (100%)
χ^2 value	0.98	1.12	0.89	1.45	–
P-value	0.81 (NS)	0.77 (NS)	0.83 (NS)	0.69 (NS)	–

Note: NS – not significant (P > 0.05); χ^2 tests compared the distribution of each gene across infection sources (degrees of freedom = 3).

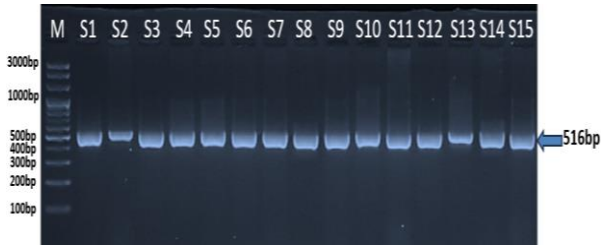

Fig. 1. PCR amplification of antibiotic resistance methicillin (mecA) gene in *Staphylococcus aureus* isolates from different clinical sources using 1.5% agarose gel electrophoresis: *M* – marker ladder (3000–100 bp); the positive amplification of some *S. aureus* isolates at 516 bp product size

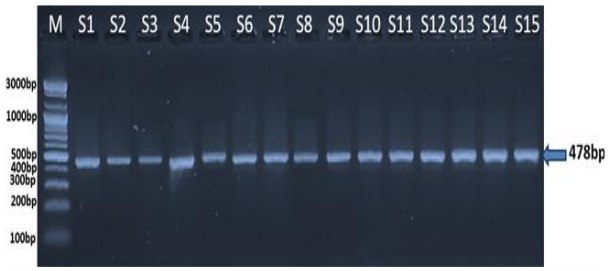

Fig. 2. PCR amplification of antibiotic resistance methicillin (blaZ) gene in *Staphylococcus aureus* isolates from different clinical sources using 1.5% agarose gel electrophoresis: *M* – marker ladder (3000–100 bp); the positive amplification of some *S. aureus* isolates at 478 bp product size

Discussion

The findings of this study highlight the alarming prevalence of *Staphylococcus aureus* (87.6%) across diverse human infections, with otitis media (94.3%) and mastitis (90.4%) exhibiting the highest colonization rates, consistent with prior reports of *S. aureus* tropism for mucosal and wound environments (Kwiecinski et al., 2020). The

near-universal resistance to benzylpenicillin (100%) and high resistance to oxacillin (57–78%) and erythromycin (57–78%) underscore the global crisis of β-lactam and macrolide resistance, driven by decades of antibiotic misuse (Klein et al., 2020). Notably, the absence of resistance to gentamicin, fluoroquinolones, and doxycycline (100% susceptibility) aligns with recent clinical guidelines recommending these as first-line alternatives for MRSA infections (Hassoun et al., 2020).

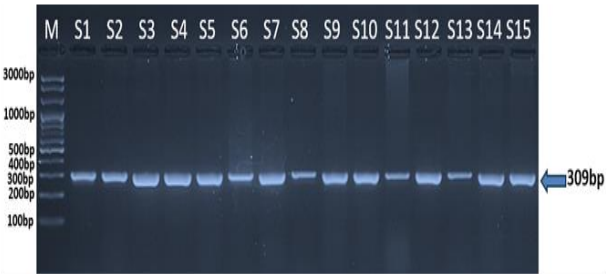

Fig. 3. PCR amplification of antibiotic resistance methicillin (NorA) gene in *Staphylococcus aureus* isolates from different clinical sources using 1.5% agarose gel electrophoresis: *M* – marker ladder (3000–100 bp); the positive amplification of some *S. aureus* isolates at 309 bp product size

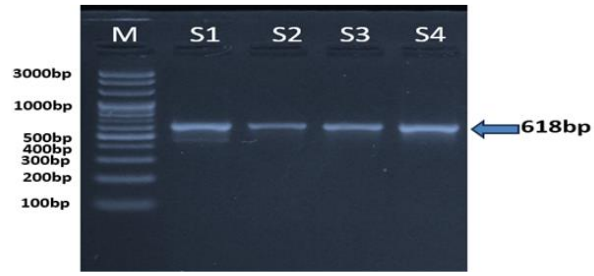

Fig. 4. PCR amplification of antibiotic resistance methicillin (VanA) gene in *Staphylococcus aureus* isolates from different clinical source using 1.5% agarose gel electrophoresis: *M* – marker ladder (3000–100 bp); the positive amplification of only *S. aureus* isolates at 618 bp product size

The predominance of multidrug-resistant (MDR) strains (65%) mirrors global trends, with wound infections showing the highest MDR prevalence (77.8%), likely due to biofilm formation and chronic antibiotic exposure. The molecular data reveal mecA as the most prevalent resistance gene (82.1% in MDR isolates), corroborating its role in methicillin resistance via PBP2a modification, while the low VanA prevalence (5.1%) suggests vancomycin remains a last-resort option, though sporadic cases demand vigilance (Viana et al., 2025). The widespread blaZ (56.4%) and NorA (38.5%) genes reflect enzymatic and efflux-mediated resistance mechanisms, respectively, emphasizing the need for combinatorial therapies. The lack of significant differences in gene distribution across infection types ($P > 0.05$) implies that horizontal gene transfer may homogenize resistance traits, complicating targeted interventions. These results align with studies linking *S. aureus* resistance to hospital-acquired infections and livestock-associated strains, highlighting One Health implications. The high susceptibility to fluoroquinolones contrasts with rising resistance in *Pseudomonas* and *E. coli*, suggesting *S. aureus* may lag in developing these resistances (Tomazi et al., 2015). However, the persistence of MDR strains in burns (68%) and otitis media (70%) underscores the urgency of antibiotic stewardship (Ventola, 2015), especially in low-resource settings where empirical prescribing is common (Altoparlak et al., 2020). The study's limitations include a modest sample size and geographic restriction, warranting broader surveillance. Future research should explore genomic epidemiology to track resistance evolution and evaluate novel agents like teixobactin. Clinically, these findings advocate for rapid molecular diagnostics and tailored regimens, such as fluoroquinolones for otitis media (Laxminarayan et al., 2022) and gentamicin for mastitis. Public health strategies must prioritize vaccine development and infection control in high-risk settings like burn units (Ling et al., 2015). In conclusion, this study reinforces *S. aureus* as a persistent threat with evolving resistance patterns, necessitating integrated approaches combining surveillance, stewardship, and innovation to curb the AMR crisis (Kaur et al., 2022).

Conclusion

These results emphasize the ongoing issue of antibiotic resistance in *S. aureus* infections and underscore the need for targeted therapeutic strategies.

References

Altoparlak, U., Erol, S., Akcay, M. N., Celebi, F., & Kadanali, A. (2020). The time-related changes of antimicrobial resistance patterns and predominant bacterial profiles of burn wounds and body flora of burned patients. Burns, 30(7), 660–664.

Azimi, T., Nasiri, M. J., Chirani, A. S., Pouriran, R., & Dabiri, H. (2021). The role of antibiotics in chronic otitis media with effusion. Infection and Drug Resistance, 14, 1713–1721.

Becker, K., Both, A., Weißelberg, S., Heilmann, C., & Rohde, H. (2020). Emergence of coagulase-negative staphylococci. Expert Review of Anti-Infective Therapy, 18(4), 349–366.

Dashtbani-Roozbehani, A., & Brown, M. H. (2021). Efflux pump mediated antimicrobial resistance by staphylococci in health-related environments: Challenges and the quest for inhibition. Antibiotics, 10(12), 1502.

David, M. Z., & Daum, R. S. (2017). Community-associated methicillin-resistant *Staphylococcus aureus*: Epidemiology and clinical consequences of an emerging epidemic. Clinical Microbiology Reviews, 23(3), 616–687.

Foster, T. J. (2017). Antibiotic resistance in *Staphylococcus aureus*: Current status and future prospects. FEMS Microbiology Reviews, 41(3), 430–449.

Hassoun, A., Linden, P. K., & Friedman, B. (2017). Incidence, prevalence, and management of MRSA bacteremia across patient populations-a review of recent developments in MRSA management and treatment. Critical Care, 21(1), 211.

Kaur, D. C., Chate, S. S., & Ghadage, D. P. (2022). Antibiotic susceptibility of *S. aureus* in otitis media. Journal of Global Infectious Diseases, 14(1), 12–16.

Klein, E. Y., Van Boeckel, T. P., Martinez, E. M., Pant, S., Gandra, S., Levin, S. A., & Laxminarayan, R. (2020). Global antibiotic consumption trends. Proceedings of the National Academy of Sciences, 115(15), E3463–E3470.

Kwiecinski, J. M., Horswill, A. R., & Jenul, C. (2020). *S. aureus* adhesion in infections. Virulence, 11(1), 265–277.

Lakhundi, S., & Zhang, K. (2018). Methicillin-resistant *Staphylococcus aureus*: Molecular characterization, evolution, and epidemiology. Clinical Microbiology Reviews, 31(4), e00020-18.

Laxminarayan, R., Van Boeckel, T., & Teillant, A. (2022). The economic costs of antimicrobial resistance. OECD Food, Agriculture and Fisheries Papers, 78, 1–40.

Lee, A. S., de Lencastre, H., Garau, J., Kluytmans, J., Malhotra-Kumar, S., Peschel, A., & Harbarth, S. (2018). Methicillin-resistant *Staphylococcus aureus*. Nature Reviews: Disease Primers, 4, 18033.

Ling, L. L., Schneider, T., Peoples, A. J., Spoering, A. L., Engels, I., Conlon, B. P., ... & Lewis, K. (2015). A new antibiotic kills pathogens without detectable resistance. Nature, 517(7535), 455–459.

McGuinness, W. A., Malachowa, N., & DeLeo, F. R. (2017). Vancomycin Resistance in *Staphylococcus aureus*. The Yale Journal of Biology and Medicine, 90(2), 269–281.

Parker, D., & Prince, A. (2012). Immunopathogenesis of *Staphylococcus aureus* pulmonary infection. Seminars in Immunopathology, 34(2), 281–297.

Tomazi, T., Gonçalves, J. L., Barreiro, J. R., Arcari, M. A., & dos Santos, M. V. (2015). Bovine subclinical intramammary infection caused by coagulase-negative staphylococci increases somatic cell count but has no effect on milk yield or composition. Journal of Dairy Science, 98(5), 3071–3078.

Tong, S. Y., Davis, J. S., Eichenberger, E., Holland, T. L., & Fowler Jr., V. G. (2015). *Staphylococcus aureus* infections: Epidemiology, pathophysiology, clinical manifestations, and management. Clinical Microbiology Reviews, 28(3), 603–661.

Ventola, C. L. (2015). The antibiotic resistance crisis. Part 1: Causes and threats. Pharmacy and Therapeutics, 40(4), 277–283.

Viana, G. G. F., Cardozo, M. V., Pereira, J. G., & Rossi, G. A. M. (2025). Antimicrobial resistant *Staphylococcus* spp., *Escherichia coli*, and *Salmonella* spp. in food handlers: A global review of persistence, transmission, and mitigation challenges. Pathogens, 14(5), 496.

WHO (2021). Global antimicrobial resistance and use surveillance system. World Health Organization, Geneva.