Drug-Resistant *Staphylococcus aureus* in Clinical Samples: A Review of Current Trends and Mechanisms

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Abstract

Staphylococcus aureus remains a formidable human pathogen, characterized by its remarkable ability to evolve resistance against a broad spectrum of antimicrobial agents. This short review examines the current landscape of drug-resistant *S. aureus* (DRSA) in clinical samples, focusing on the sophisticated molecular mechanisms of resistance, the shifting prevalence of methicillin-resistant *S. aureus* (MRSA), and the burgeoning global threat posed by vancomycin-resistant and multidrug-resistant strains. As of the 2024–2026 clinical landscape, the pathogen continues to demonstrate significant genomic plasticity, primarily mediated by the acquisition of the *mecA* gene within the staphylococcal cassette chromosome mec (SCCmec), which renders traditional β-lactam therapies ineffective.

This article provides a comprehensive synthesis of recent clinical data, highlighting how *S. aureus* has transitioned from a primarily healthcare-associated threat to a pervasive community-acquired pathogen. We explore the diagnostic challenges inherent in differentiating between colonized and infected patients, particularly in high-stakes environments such as intensive care units and surgical wards. The review delves into the biochemical pathways of resistance, including target site modification, enzymatic inactivation, and the upregulation of efflux pumps that confer resistance to fluoroquinolones and macrolides.

Furthermore, we evaluate the current gold standards for laboratory identification, contrasting traditional phenotypic assays with rapid molecular techniques like Polymerase Chain Reaction (PCR) and Whole Genome Sequencing (WGS), which have become essential for timely clinical intervention. The discussion concludes by addressing the urgent need for novel therapeutic strategies—such as antimicrobial peptides, phage therapy, and nanoparticle-delivered drugs—as traditional "last-resort" antibiotics like vancomycin and linezolid face increasing resistance. By consolidating recent epidemiological trends and mechanistic insights, this review serves as a critical resource for clinicians and researchers aiming to mitigate the clinical burden of one of the world's most resilient bacterial species.

Introduction

Staphylococcus aureus is a versatile Gram-positive bacterium that exists both as a commensal of the human microbiota and a potent opportunistic pathogen (Al-Saleh et al., 2022). It is a leading

cause of bacterial-associated morbidity and mortality worldwide, capable of causing infections ranging from superficial skin lesions to life-threatening systemic conditions such as bacteremia, endocarditis, and osteomyelitis (Taylor et al., 2025).

The clinical management of *S. aureus* has been perpetually challenged by the emergence of drug resistance. Following the introduction of penicillin, resistant strains appeared within a decade, necessitating the development of methicillin. Today, methicillin-resistant *S. aureus* (MRSA) is classified by the World Health Organization as a high-priority pathogen (Yan et al., 2025; Nalwoga et al., 2016). As of 2024, clinical detection rates for MRSA in some regions remain high; for instance, data from China's Antimicrobial Resistance Surveillance Network (CHINET) indicated an MRSA detection rate of 29.2% (Wei et al., 2025).

Mechanisms of Antimicrobial Resistance

The resistance of *S. aureus* to antibiotics is driven by a combination of horizontal gene transfer via mobile genetic elements and spontaneous chromosomal mutations (Foster, 2017).

1. Beta-lactam Resistance

The primary mechanism for methicillin resistance is the acquisition of the **mecA** gene, located on the staphylococcal cassette chromosome mec (SCCmec) (Tobin et al., 2025). This gene encodes an alternative penicillin-binding protein, **PBP2a**, which possesses a low binding affinity for nearly all beta-lactam antibiotics (Wei et al., 2025). Consequently, the bacterium can continue cell wall synthesis even in the presence of drugs like oxacillin or cephalosporins (Tobin et al., 2025).

2. Vancomycin Resistance

Vancomycin has long been a "last-resort" treatment for MRSA. However, resistance has emerged through two primary pathways, namely:

Vancomycin-Intermediate S. aureus (VISA): Characterized by a thickened cell wall that "traps" the antibiotic, preventing it from reaching its target (Tobin et al., 2025).

Vancomycin-Resistant S. aureus (VRSA): Resulting from the acquisition of the **vanA** gene cluster, typically transferred from vancomycin-resistant *Enterococcus faecalis* (Tobin et al., 2025). This leads to a target modification where the terminal D-Ala-D-Ala of peptidoglycan precursors is replaced by D-Ala-D-Lac, drastically reducing vancomycin affinity (Shao et al., 2025).

3. Other Resistance Mechanisms

Recent clinical isolates demonstrate increasing resistance to non-beta-lactam classes. Resistance to fluoroquinolones often arises from mutations in the **quinolone resistance-determining region (QRDR)** of topoisomerase IV or DNA gyrase, or through the upregulation of efflux

pumps like **NorA** (Shao et al., 2025). Additionally, high resistance rates have been observed for erythromycin (76.4%) and clindamycin (53.8%) in recent clinical cohorts (Wei et al., 2025).

Clinical Distribution and Diagnostics

Clinical samples of *S. aureus* are most frequently recovered from pus/wound swabs (25.8%), followed by urine (21.6%) and blood cultures (16.4%) (Mohod et al., 2026). The distinction between Hospital-Acquired (HA-MRSA) and Community-Associated (CA-MRSA) remains vital, as CA-MRSA strains often carry the Panton-Valentine leucocidin (PVL) toxin, which is associated with necrotizing skin infections (Al-Saleh et al., 2022).

Diagnostic standards have shifted toward molecular techniques. While conventional phenotypic methods like the **cefoxitin disk diffusion test** remain common, **Polymerase Chain Reaction (PCR)** for the *mecA* gene is now the gold standard for rapid and accurate MRSA identification (Pillai et al., 2025).

Future Perspectives and Conclusion

The rise of multidrug-resistant *S. aureus* has spurred interest in alternative therapies, including phage therapy, antimicrobial peptides, and the use of nanoparticles to bypass traditional resistance mechanisms (Michalik et al., 2025; Shao et al., 2025). Despite these advances, the clinical burden of *S. aureus* continues to grow, necessitating robust global surveillance and stringent infection control practices, such as active screening and targeted decolonization (Taylor et al., 2025).

References

Al-Saleh, A., Shahid, M., Farid, E., & Bindayna, K. (2022). Trends in methicillin-resistant Staphylococcus aureus in the Gulf Cooperation Council countries: antibiotic resistance, virulence factors and emerging strains. *Eastern Mediterranean Health Journal*, *28*(6), 434–443. https://doi.org/10.26719/emhj.22.042

Wei K., Chen W., Li Y., Xie G., Li F., Zhou J et al (2025). Antimicrobial Resistance Characteristics of *Staphylococcus aureus* Isolated From Both Tertiary Hospitals, One Western Medicine Hospital and One Traditional Chinese Medicine Hospital, in Shanghai, China From 2014-2023. *Infection and Drug Resistance*. 2025 (**18**): 5009-5021 https://www.dovepress.com/antimicrobial-resistance-characteristics-of-staphylococcus-aureus-isol-peer-reviewed-fulltext-article-IDR

Foster, T. J. (2017). Antibiotic resistance in Staphylococcus aureus. Current status and future prospects. *FEMS Microbiology Reviews*, *41*(**3**), 430–449. https://doi.org/10.1093/femsre/fux007

Pillai MM, Latha R, Sarkar G (2025). Detection of Methicillin Resistance in Staphylococcus Aureus by Polymerase Chain Reaction and Conventional Methods: A Comparative Study. *Journal of Laboratory Physicians*. 4(**2**): 83-88 https://jlabphy.org/detection-of-methicillin-

resistance-in-staphylococcus-aureus-by-polymerase-chain-reaction-and-conventional-methods-a-comparative-study/

Michalik, M., Podbielska-Kubera, A., & Dmowska-Koroblewska, A. (2025). Antibiotic Resistance of Staphylococcus aureus Strains—Searching for New Antimicrobial Agents—Review. *Pharmaceuticals*, *18*(1): 81. https://doi.org/10.3390/ph18010081

Mohod SV, Rajan A, Asokan D, Das P, Agrawal G (2026). Changing Battlelines: 12-Month Antimicrobial Resistance Trends at a Tertiary Care Hospital in Nagpur, Maharashtra, India. *Cereus* 18(1): e100797 https://pmc.ncbi.nlm.nih.gov/articles/PMC12874179/

Janet Nalwoga, Michael Tirwomwe, Albert Nyanchoka Onchweri, Josephat Nyabayo Maniga, Cyprian Mose Nyaribo, Conrad Ondieki Miruka (2016). Drug resistant Staphylococcus aureus in clinical samples at Kampala International University-teaching hospital, Bushenyi District, Uganda. American Journal of Biomedical Research 4 (4): 94-98. http://www.sciepub.com/portal/downloads?doi=10.12691/ajbr-4-4-3&filename=ajbr-4-4-3.pdf

Shao, K., Yang, Y., Gong, X., Chen, K., Liao, Z., & Ojha, S. C. (2025). Staphylococcal Drug Resistance: Mechanisms, Therapies, and Nanoparticle Interventions. *Infection and Drug Resistance*, *18*, 1007–1033. https://doi.org/10.2147/idr.s510024

Tobin EH, Jogu P, Koirala J (2025). Methicillin-Resistant Staphylococcus aureus. StatPearls, *NCBI Bookshelf*. https://www.ncbi.nlm.nih.gov/books/NBK482221/

Taylor TA, Tobin EH, Unakal CG (2025). Staphylococcus aureus Infection. StatPearls, *NCBI Bookshelf*. https://www.ncbi.nlm.nih.gov/books/NBK441868/

Yan A, Kus JV, Sant N (2025). The Staphylococcus aureus complex: implications for the clinical microbiology laboratory. *Journal of Clinical Microbiology*. 63(7) e01276-24. https://journals.asm.org/doi/10.1128/jcm.01276-24