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RETROSPECTIVE ANALYSIS OF ANTIBIOTIC RESISTANCE PATTERNS OF *STAPHYLOCOCCUS AUREUS* CLINICAL ISOLATES IN A TERTIARY CARE HOSPITAL

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ABSTRACT

Introduction: Staphylococcus aureus is a common pathogen causing a wide range of infections, from mild skin conditions to severe diseases. The rise of antibiotic resistance, particularly methicillin-resistant Staphylococcus aureus (MRSA), has become a major public health concern. MRSA's resistance is mediated by the mecA gene, making it resistant to β-lactam antibiotics. The misuse of antibiotics, especially in countries like Pakistan, has exacerbated the problem, leading to an urgent need for enhanced surveillance and antimicrobial stewardship programs.

Objective: This study investigates the antibiotic resistance patterns of S. aureus isolates in a tertiary care hospital.

Methodology: This retrospective descriptive study analyzed *Staphylococcus aureus* isolates from clinical samples (respiratory specimens, body fluids, urine, HVS, and blood) collected at Jinnah Postgraduate Medical Centre (JPMC), Karachi, from January to December 2021. Antibiotic susceptibility profiles were evaluated using the Vitek 2 system and the disk diffusion method, following CLSI guidelines. Standard microbiological techniques, including culture on selective media and biochemical tests, were used for identification. Ethical approval was obtained from the Institutional Review Board of JPMC.

Result: A total of 13,470 specimens were analyzed, including 8,087 clinical and 5,383 blood specimens, with 9,604 (71.41%) negative and 3,806 (28.19%) positive. *Staphylococcus aureus* was identified in 955 (25.10%) of positive specimens, with 913 isolates from clinical samples and 42 from blood. Resistance was highest for cloxacillin (93%), erythromycin (85%), and ciprofloxacin

(81%). Vancomycin had the lowest resistance at 2%. These findings highlight the importance of effective antimicrobial strategies to combat increasing resistance.
Conclusion: This study highlights the significant prevalence of *Staphylococcus aureus* and its concerning antibiotic resistance patterns in clinical and blood samples. Ongoing surveillance and prudent antimicrobial management are crucial to combat rising resistance. Future research should prioritize resistance monitoring and optimized treatment strategies to improve patient outcomes.

Key Words: *Staphylococcus aureus*, MRSA, Antibiotic Resistance, Antimicrobial stewardship

INTRODUCTION

Staphylococcus aureus is a versatile pathogen that poses a significant public health threat worldwide (Pidwill et al., 2021). It is a common member of the human skin and mucous membrane flora, colonizing approximately 20-30% of the population without causing harm (Sarmah et al., 2018). However, under certain conditions, such as skin breaches or surgical wounds, *S. aureus* can transition from a harmless commensal organism to a dangerous opportunistic pathogen (Heilbronner & Foster, 2021). It is responsible for a wide range of infections, from mild skin conditions to life-threatening diseases such as pneumonia, endocarditis, osteomyelitis, and toxic shock syndrome (Rihana & Sampson, 2019).

The emergence of antibiotic resistance, particularly methicillin-resistant *Staphylococcus aureus* (MRSA), has become a critical global health concern (Vestergaard et al., 2019). MRSA was first identified shortly after the introduction of methicillin in 1961 (Lee et al., 2018). Today, it is one of the most significant multidrug-resistant pathogens, both in hospitals and the community. Resistance to methicillin in *S. aureus* is mediated by the mecA gene, which encodes the penicillin-binding protein 2a (PBP2a). PBP2a has a low affinity for β-lactam antibiotics, allowing MRSA strains to resist the effects of this important class of drugs. Isolates harboring the mecA gene are resistant to all β-lactam antibiotics, including penicillins, cephalosporins, and carbapenems (Ali et al., 2021; Campanille, 2019; Gajdács, 2019).

The prevalence of antibiotic-resistant *S. aureus*, including MRSA, has been driven by factors such as the over-prescription of antibiotics, inadequate infection control measures, and the misuse of antimicrobial agents (Salamat, 2020). In Pakistan, the situation is particularly alarming, with studies showing a rising trend in antibiotic resistance among *S. aureus* isolates. A study from major hospitals in Pakistan reported that MRSA accounted for a substantial percentage of *S. aureus* infections, underscoring the urgent need for enhanced surveillance and effective infection control strategies (Naimi, 2021). The availability of antibiotics without prescription and the lack of stringent regulations contribute to the misuse and overuse of these agents, further exacerbating the resistance problem (Aitha et al., 2020; Chandra et al., 2021).

The burden of antibiotic-resistant *S. aureus* strains, especially MRSA, significantly impacts healthcare systems by increasing treatment costs, prolonging hospital stays, and leading to higher complication rates (Boswihi & Udo, 2018; Gajdács, 2019). Hospital-associated MRSA strains are often resistant to multiple classes of antibiotics, while community-associated MRSA strains typically exhibit resistance to β-lactam antibiotics but remain susceptible to other antimicrobial agents. The presence of resistance genes, such as mecA, complicates treatment and elevates the risk of poor clinical outcomes (Lee et al., 2018; Turner et al., 2019).

To address the growing threat posed by MRSA, infection prevention and control strategies are paramount in reducing its spread, particularly in healthcare environments where vulnerable populations are at increased risk (Henderson & Nimmo, 2018). Effective measures such as improved hygiene practices, regular screening of high-risk patients, and the sensible use of antibiotics can help minimize MRSA transmission. Additionally, the development of novel therapeutic options and vaccines could offer potential long-term solutions to managing antibiotic-resistant S. aureus infections, as current treatment regimens become less effective over time due to the organism's ability to rapidly adapt and develop resistance mechanisms (Clegg et al., 2021).

Given the increasing prevalence of MRSA and its impact on morbidity, mortality, and healthcare costs, it is essential to implement robust antimicrobial stewardship programs and restrict the spread of MRSA within healthcare settings and the community (Garcia Reeves, 2019; Majumder et al., 2020). This study aims to evaluate the antibiotic resistance profiles of *S. aureus* isolates from clinical samples, focusing on the prevalence and resistance trends.

METHODOLOGY

This was a retrospective descriptive study in which data on all clinical isolates included respiratory specimens (such as sputum and tracheal aspirates), body fluids (including pus and tissue) Urine, high vaginal swabs (HVS) and blood samples reported as *Staphylococcus aureus* from January to December 2021 was collected through the electronic medical records system of Jinnah Postgraduate Medical Centre (JPMC), Karachi, Pakistan. The records of antibiotic susceptibility profiles were categorized and analyzed by R software. Ethical approval for the study was obtained from the Institutional Review Board of JPMC.

Microbiological Testing

Identification of Staphylococcus aureus isolates was performed using standard microbiological methods, including culture on selective media and biochemical testing.
clinical samples were inoculated on to Blood agar and Mac Conkey agar for isolation of the pathogens. Those samples yielded the growth Of Staphylococcus aureus that were identified by Standard procedures like catalase test, coagulase test And Vitek 2 ID were further included for the study. Resistance patterns of the isolates were documented From Vitek 2 system.
The antibiotic susceptibility patterns were assessed through the disk diffusion method, in accordance with Clinical and Laboratory Standards Institute (CLSI) guidelines. The antibiotics tested included Cloxacillin, Ciprofloxacin, Erythromycin, Sulfamethoxazole-Trimethoprim (Co-trimoxazole), Daptomycin, Tetracycline, Gentamicin, Fusidic Acid, Vancomycin, Chloramphenicol.

RESULT

This retrospective study analyzed a total of 13,470 specimens, comprising 8,087 clinical specimens (including respiratory specimens, Pus, Sputum, Urine, body fluids, HVS) and 5,383 blood specimens. Among these, 9,604 specimens were negative, accounting for 71.41% of the total, while 3,806 specimens tested positive, representing 28.19%. Within the positive samples, Staphylococcus aureus was identified in 955 specimens, which corresponds to 25.10% of all positive cases. The distribution of positive Staphylococcus aureus isolates indicated that 913 isolates were obtained from clinical specimens, representing 31.13% of the positive clinical samples. Additionally, 42 isolates were detected in blood specimens, accounting for 4.81% of positive blood cases.

The analysis revealed that out of 8,087 clinical specimens, 2,933 were positive (36.28%), while 5,094 were negative (62.98%). In the blood specimen cohort, 873 results were positive (16.24%), compared to 4,510 negative results (83.68%). These findings underscore the notable prevalence of Staphylococcus aureus in both clinical and blood samples, emphasizing the need for continuous monitoring and effective antimicrobial management strategies in combating infections caused by this pathogen (Table.1).

Table:1 Distribution of Staphylococcus Positive Isolates in Clinical and Blood Samples

Source	Number of Staphylococcus Positive Isolates	Percentage of Total Positive Samples (%)
Clinical Samples	913	95.59%
Blood Samples	42	4.41%
Total	**955**	**100%**

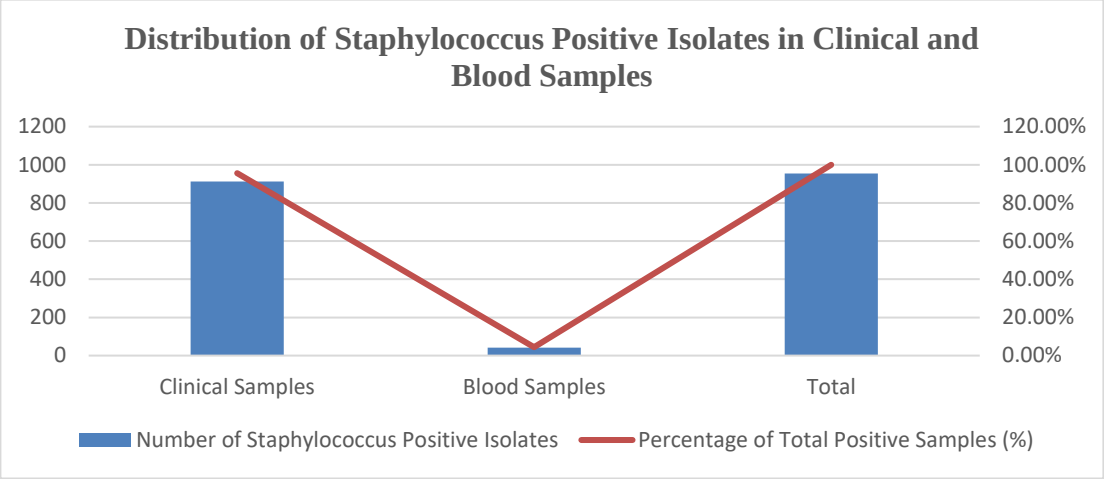

Figure 1: Distribution of Staphylococcus Positive Isolates in Clinical and Blood Samples

Antibiotic Resistance Profiles of *Staphylococcus aureus* Isolates in Blood Samples

The antibiotic resistance profiles of *Staphylococcus aureus* isolates from blood samples revealed a variable pattern of resistance across the tested antibiotics. The highest resistance was observed for tetracycline, with 37% of isolates showing resistance. Sulfamethoxazole-trimethoprim, fusidic acid, and erythromycin each exhibited notable resistance rates of 31%, 28%, and 28%, respectively.

Table:2 Antibiotics Resistance Profiles of Staphylococcus Isolates in Blood Samples

Antibiotic	Number of Resistant Isolates (%)
Cloxacillin	25
Ciprofloxacin	22
Erythromycin	28
Sulfamethoxazole-Trimethoprim	31
Daptomycin	19
Tetracycline	37
Gentamicin	17
Fusidic Acid	28
Vancomycin	1
Chloramphenicol	16

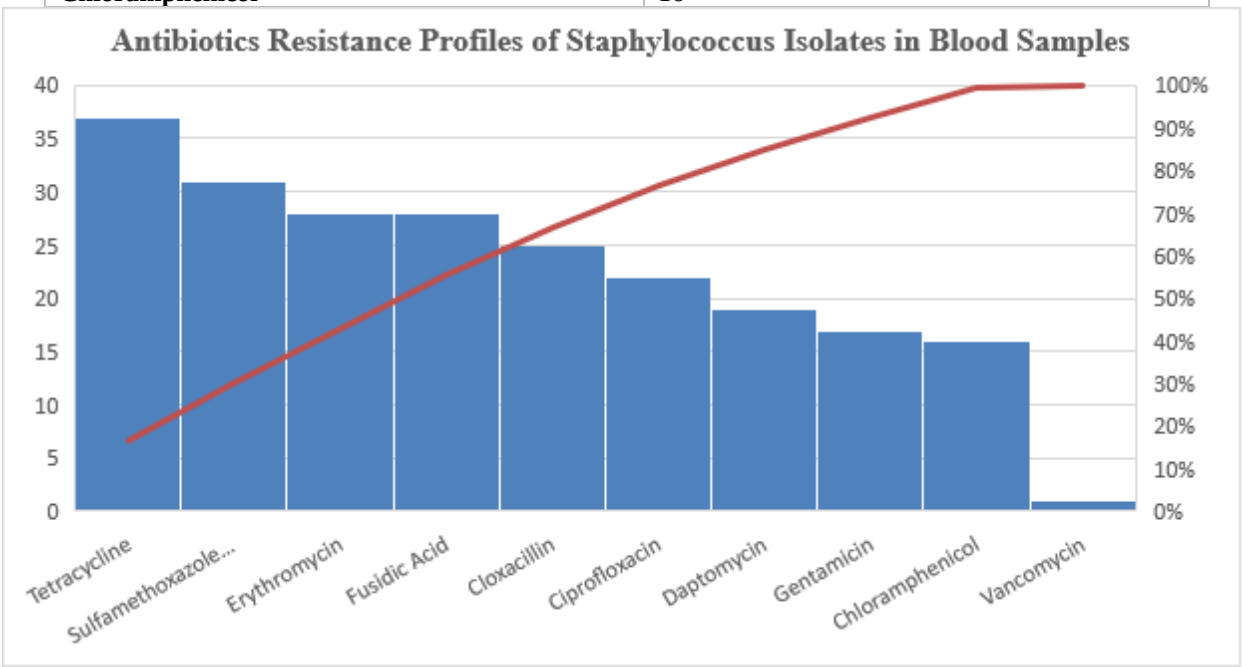

Figure 2: Antibiotics Resistance Profiles of Staphylococcus Isolates in Blood Samples

Resistance to cloxacillin was found in 25% of isolates, while ciprofloxacin showed a resistance rate of 22%. Daptomycin and gentamicin had relatively lower resistance rates, at 19% and 17%, respectively. Chloramphenicol resistance was observed in 16% of isolates. Vancomycin displayed the lowest resistance rate, with only 1% of isolates being resistant. These findings underscore the need for continued monitoring and prudent use of antibiotics to manage *S. aureus* infections effectively.

Antibiotic Resistance Profiles of *Staphylococcus aureus* Isolates in Clinical Samples

The antibiotic resistance profiles of *Staphylococcus aureus* isolates from clinical samples showed a wide range of resistance rates. The highest resistance was observed for cloxacillin, with 68% of isolates being resistant, followed by ciprofloxacin (59%), erythromycin (57%), and fusidic acid (39%).

Table: 3 Antibiotics Resistance Profiles of Staphylococcus Isolates in Clinical Samples

Antibiotic	Percentage of Resistant Isolates (%)
Cloxacillin	68
Ciprofloxacin	59
Erythromycin	57
Sulfamethoxazole-Trimethoprim	13
Daptomycin	16
Tetracycline	37
Gentamicin	31
Fusidic Acid	39
Vancomycin	1
Chloramphenicol	13

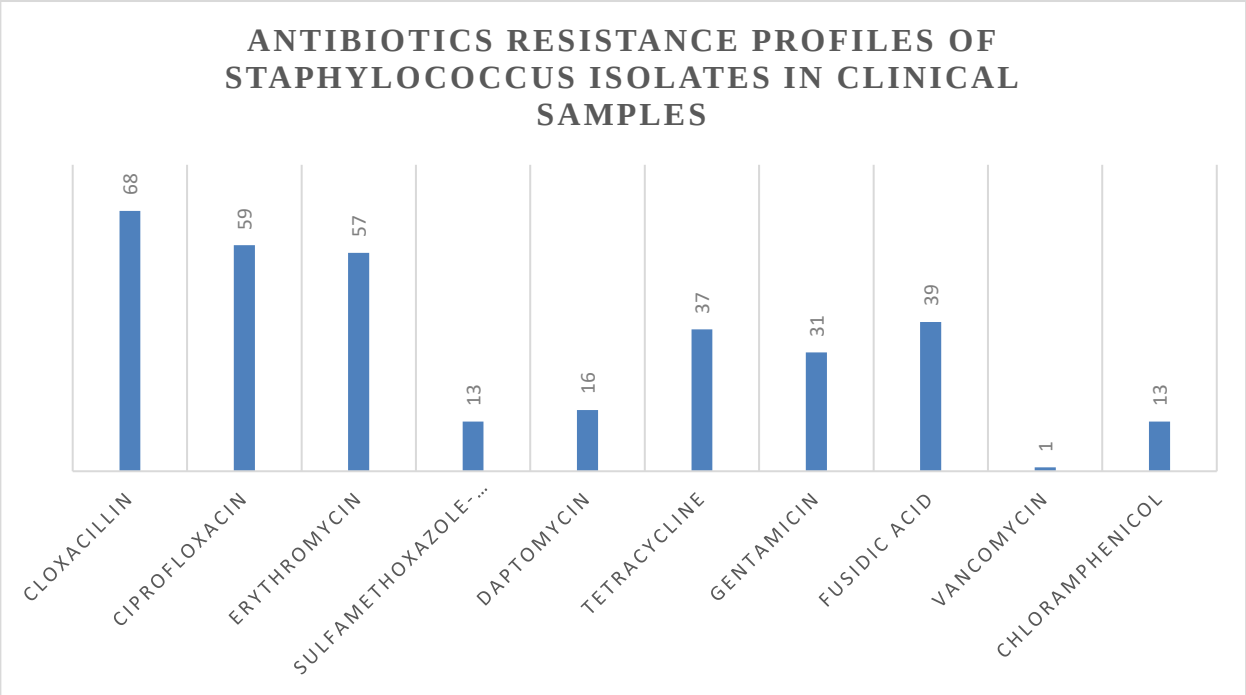

Figure 3: Antibiotics Resistance Profiles of Staphylococcus Isolates in Clinical Samples

Tetracycline and gentamicin resistance rates were 37% and 31%, respectively. Daptomycin and sulfamethoxazole-trimethoprim exhibited lower resistance, at 16% and 13%, respectively. Chloramphenicol also showed a resistance rate of 13%. Vancomycin displayed the lowest resistance, with only 1% of isolates being resistant. These results highlight significant antibiotic

resistance in *S. aureus* isolates, particularly to cloxacillin, ciprofloxacin, and erythromycin, emphasizing the importance of optimizing antibiotic use in clinical practice.

Overall Antibiotic Resistance Profiles of *Staphylococcus aureus* Isolates

The highest resistance was observed for cloxacillin, with 93% of isolates being resistant. Erythromycin and ciprofloxacin followed, showing resistance rates of 85% and 81%, respectively. Fusidic acid and tetracycline exhibited significant resistance rates of 67% and 74%, while gentamicin and sulfamethoxazole-trimethoprim showed resistance rates of 48% and 44%, respectively.

Table.4 Total Antibiotics Resistance Profiles of Staphylococcus Isolates in Blood and Clinical Samples

Antibiotic	Number of Resistant Isolates (%)
Cloxacillin	93
Ciprofloxacin	81
Erythromycin	85
Sulfamethoxazole-Trimethoprim	44
Daptomycin	35
Tetracycline	74
Gentamicin	48
Fusidic Acid	67
Vancomycin	2
Chloramphenicol	29

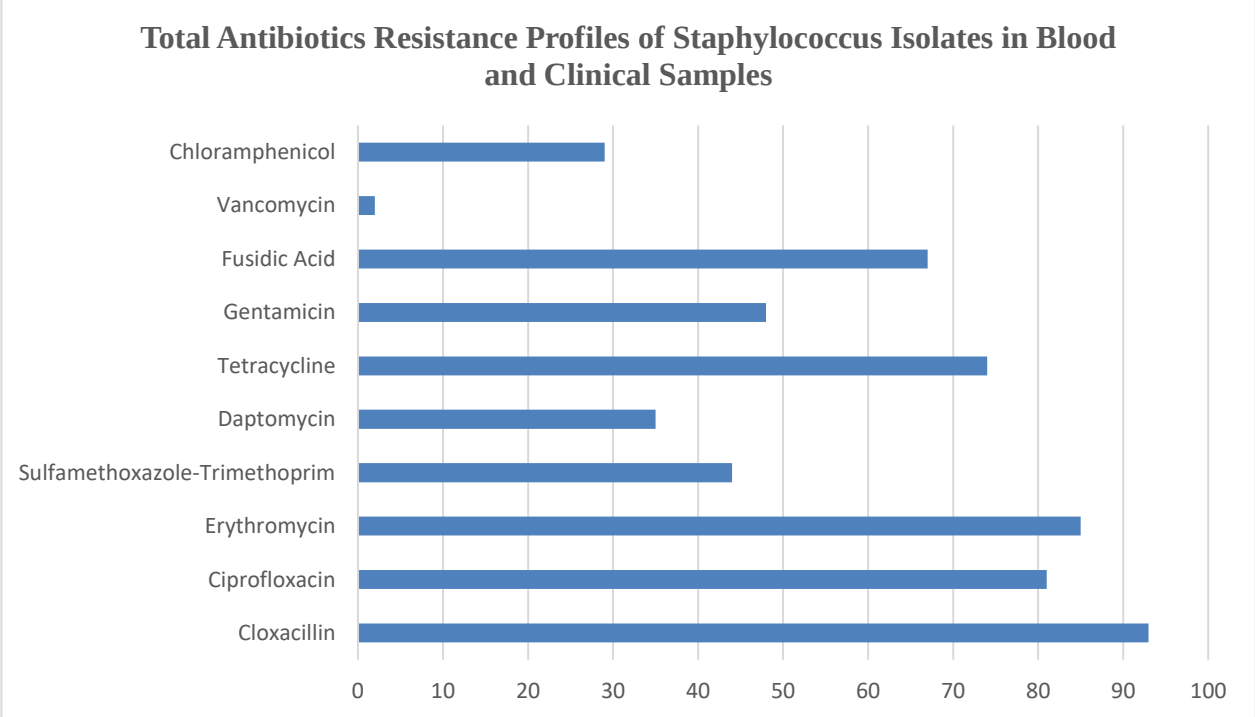

Figure 4: Total Antibiotics Resistance Profiles of Staphylococcus Isolates in Blood and Clinical Samples

Daptomycin resistance was reported in 35% of isolates, while chloramphenicol showed a resistance rate of 29%. Vancomycin had the lowest resistance rate, with only 2% of isolates being resistant. These results indicate widespread resistance among *S. aureus* isolates to multiple antibiotics, underscoring the necessity for vigilant antibiotic management and targeted treatment strategies.

DISCUSSION

This retrospective study provided a comprehensive analysis of 13,470 specimens, including 8,087 clinical samples and 5,383 blood samples, revealing significant insights into the prevalence of *Staphylococcus aureus* in our healthcare setting. The findings indicated that *S. aureus* was identified in 955 specimens, accounting for 25.10% of all positive cases. This substantial proportion highlights the importance of this pathogen as a common cause of infection in both clinical and bloodstream specimens.

The distribution of *S. aureus* isolates demonstrated that 913 of these were obtained from clinical specimens, constituting 31.13% of the total positive clinical samples. This suggests that *S. aureus* is a prevalent pathogen in various infections, particularly those associated with respiratory and body fluid specimens. Conversely, only 42 isolates were identified from blood specimens, making up 4.81% of positive blood cultures. The higher detection rate in clinical specimens may reflect the various routes of infection that *S. aureus* can take, such as skin, respiratory tract, or other bodily fluids. In contrast, the lower prevalence in blood samples may indicate a more stringent selection for systemic infections, where *S. aureus* must overcome significant host defenses to establish infection (Brás, 2020).

These findings underscore the critical need for continuous monitoring of *S. aureus* prevalence and antibiotic resistance patterns, particularly in light of rising rates of methicillin-resistant *Staphylococcus aureus* (MRSA). The ability of *S. aureus* to develop resistance to multiple antibiotics poses a significant challenge for treatment strategies, necessitating the implementation of effective antimicrobial management protocols. Additionally, our results align with previous studies that have reported similar prevalence rates of *S. aureus* in clinical specimens, reinforcing the need for heightened awareness among healthcare professionals regarding this pathogen's impact on patient health (Popovich et al., 2019).

The analysis of antibiotic resistance profiles of *Staphylococcus aureus* isolates from both blood and clinical samples reveals concerning patterns of resistance, underscoring significant challenges in treating infections caused by this pathogen.

In clinical samples, the resistance profiles were more severe. Cloxacillin exhibited the highest resistance rate (68%), followed by ciprofloxacin (59%) and erythromycin (57%), indicating a high level of resistance among isolates obtained from general clinical settings. These rates are significantly higher than those observed in the blood isolates, suggesting that *S. aureus* strains in clinical settings might be exposed to more antibiotic pressure, leading to higher resistance. The resistance to fusidic acid (39%) and tetracycline (37%) was also substantial, and gentamicin showed resistance in 31% of isolates, which is considerably higher than in blood samples. Notably, sulfamethoxazole-trimethoprim and chloramphenicol had relatively lower resistance rates (13%), and vancomycin remained highly effective with only 1% resistance. The elevated resistance rates in clinical isolates highlight the need for stringent antibiotic policies and regular susceptibility testing to prevent further escalation of resistance (Dietvorst et al., 2020).

In the blood samples, *S. aureus* demonstrated the highest resistance to tetracycline (37%), followed by sulfamethoxazole-trimethoprim, fusidic acid, and erythromycin (31%, 28%, and 28%, respectively). Resistance to other commonly used antibiotics like cloxacillin and ciprofloxacin was also notable, with resistance rates of 25% and 22%, respectively. Gentamicin and daptomycin had lower resistance rates (17% and 19%), suggesting these may still be viable treatment options for bloodstream infections. Vancomycin exhibited the lowest resistance (1%), which aligns with its continued effectiveness against methicillin-resistant *Staphylococcus aureus* (MRSA). These findings highlight the need for prudent antibiotic use in treating bloodstream infections and emphasize the potential value of gentamicin and daptomycin, alongside vancomycin Consistent with previous study (Jorge et al., 2019; Ramos et al., 2019), for severe infections where resistance to other antibiotics is prevalent.

When combining the data from both blood and clinical samples, the resistance trends become even more concerning. Cloxacillin had an alarming resistance rate of 93%, followed closely by

erythromycin (85%) and ciprofloxacin (81%). These results reflect a widespread resistance issue, with many first-line antibiotics showing diminished efficacy. Fusidic acid (67%) and tetracycline (74%) also had high resistance rates, indicating that they may no longer be reliable options for treating *S. aureus* infections in many cases. Resistance to daptomycin (35%) and gentamicin (48%) was moderate, but the relatively lower resistance to sulfamethoxazole-trimethoprim (44%) and chloramphenicol (29%) suggests these may still be viable treatment options in certain cases. Vancomycin remained highly effective, with only 2% of isolates showing resistance across both sample types.

The overall findings demonstrate that *S. aureus* is developing resistance to a broad spectrum of antibiotics, with particularly high resistance rates observed for commonly used agents like cloxacillin, erythromycin, and ciprofloxacin. These data stress the urgent need for antimicrobial stewardship programs to manage antibiotic use more effectively, particularly in clinical settings where resistance rates are significantly higher. Furthermore, the continued effectiveness of vancomycin suggests that it should remain a cornerstone of treatment for severe *S. aureus* infections, particularly MRSA, but its use should be monitored to prevent the development of vancomycin-resistant strains (Cong et al., 2020; Kest & Kaushik, 2019).

Future strategies should focus on routine resistance monitoring, infection control practices, and the development of novel antibiotics to combat the rising resistance in *S. aureus*. Additionally, incorporating combination therapies that include lower resistance antibiotics like sulfamethoxazole-trimethoprim or chloramphenicol may provide alternative therapeutic avenues (Liu et al., 2019).

Moreover, the presence of *S. aureus* in both clinical and blood samples emphasizes the necessity for robust infection control measures within healthcare settings. These measures should focus on early detection and appropriate treatment strategies to mitigate the risk of transmission and the development of resistance. Our study contributes valuable data to the growing body of literature on *S. aureus* in the region and highlights the urgency of addressing the public health implications of this pathogen.

CONCLUSION

In conclusion, this study provides critical insights into the prevalence of *Staphylococcus aureus* in clinical and blood samples, emphasizing the need for ongoing surveillance and the establishment of effective infection prevention and control strategies. Future research should focus on elucidating the specific antibiotic resistance patterns of *S. aureus* isolates to inform empirical treatment guidelines and ensure better patient outcomes.

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