



ANTIBIOTIC RESISTANCE PATTERN AMONG STAPHYLOCOCCAL SPECIES ISOLATED FROM TERTIARY CARE HOSPITALS IN KARACHI, PAKISTAN: A CROSS-SECTIONAL STUDY

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Abstract

Background: Antimicrobial resistance among Staphylococcus species, including coagulase-negative staphylococci (CoNS), is a growing global health threat, especially in developing countries like Pakistan, where misuse of antibiotics and poor infection control fuel resistance. These bacteria cause a wide range of infections, from skin conditions to life-threatening bloodstream infections, and their increasing resistance limits treatment options.

Objectives: To isolate and identify Staphylococcus species from clinical samples in tertiary care hospitals, determine their antibiotic susceptibility patterns, and assess their pathogenic potential through multidrug-resistant (MDR) and extensively drug-resistant (XDR) profiles.

Methodology: A cross-sectional study was conducted on 200 clinical samples from two tertiary care hospitals in Karachi. Samples were cultured on blood agar, and Staphylococcus species were identified using Gram staining, catalase, coagulase, and DNase tests. Antibiotic susceptibility was tested using the Kirby–Bauer disc diffusion method on Mueller–Hinton agar, following CLSI guidelines. MDR and XDR were defined using standard criteria, and data were analyzed with SPSS.

Results: Of 200 isolates, resistance was highest to erythromycin (71.5%), ciprofloxacin (66%), and fusidic acid (67.5%), with moderate resistance to amoxicillin-clavulanate (52%) and gentamicin (46%). Linezolid (98% sensitive) and vancomycin (94.5% sensitive) retained excellent activity. A significant proportion of isolates were MDR, with resistance more common in CoPS and in pus and urine samples.

Conclusion: Staphylococcus species in Karachi hospitals show alarming resistance to commonly used antibiotics, though last-resort drugs like linezolid and vancomycin remain effective. The high

prevalence of MDR strains highlights the need for routine susceptibility testing, rational antibiotic use, and stronger infection control and stewardship programs

Keywords: Coagulase-negative Staphylococci (CoNS), Antimicrobial resistance, Multidrug resistance, Extensively drug-resistant bacteria, Antibiotic susceptibility, Tertiary care hospitals

INTRODUCTION:

Antibiotic resistance has emerged as one of the most serious global public health challenges, particularly in developing countries such as Pakistan where antibiotic misuse, over-the-counter availability and inadequate infection control practices are prevalent[1,2]. Among bacterial pathogens, *Staphylococcus* species, especially *Staphylococcus aureus* is the major cause of community-acquired and hospital-associated infections[3]. These organisms are responsible for a wide spectrum of clinical conditions ranging from minor skin and soft tissue infections to severe invasive diseases such as bloodstream infections, pneumonia, and device-associated infections[4-6]. *Staphylococcus* species are among the most common bacterial pathogens implicated in a wide spectrum of human infections ranging from superficial skin and soft tissue infections to life-threatening conditions such as septicemia, endocarditis, and postoperative wound infections[7,8]. Both coagulase-positive staphylococci, particularly *Staphylococcus aureus*, and coagulase-negative staphylococci have emerged as significant causes of community-acquired and healthcare-associated infections[9-12]. The ability of these organisms to adapt to diverse host environments and acquire resistance to multiple antimicrobial agents has made them a major public health concern worldwide. The widespread and often inappropriate use of antibiotics has accelerated the emergence of antimicrobial resistance among staphylococcal species[13]. Resistance to commonly prescribed antibiotics such as beta-lactams, macrolides, fluoroquinolones, and aminoglycosides has been increasingly reported, limiting therapeutic options and leading to prolonged hospital stays, increased healthcare costs, and higher morbidity and mortality rates. Of particular concern is the rise of multidrug-resistant staphylococci, which pose significant challenges in both empirical and definitive antimicrobial therapy.

Coagulase-negative staphylococci, once considered harmless commensals, are now recognized as important opportunistic pathogens, especially in immunocompromised patients and those with indwelling medical devices[14-16]. These organisms have demonstrated a remarkable capacity for biofilm formation and antimicrobial resistance, contributing to persistent and recurrent infections. Similarly, coagulase-positive staphylococci are associated with enhanced virulence due to the production of enzymes such as coagulase and DNase, which facilitate tissue invasion and immune evasion.

Antimicrobial susceptibility testing plays a crucial role in guiding appropriate antibiotic therapy and in monitoring local resistance patterns. Knowledge of prevailing resistance trends is essential for clinicians to select effective empirical treatment and for institutions to develop evidence-based antibiotic stewardship policies[17]. Regular surveillance of antimicrobial resistance also aids in early detection of emerging resistance to last-line agents such as vancomycin and linezolid.

In this context, the present study was undertaken to evaluate the antimicrobial resistance patterns of clinical *Staphylococcus* isolates obtained from various specimens in a tertiary care hospital. The study aims to assess the extent of multidrug resistance and to determine the effectiveness of commonly used and reserve antibiotics, thereby providing valuable data to support rational antibiotic use and strengthen infection control strategies.

Objectives

The primary objective of this study is to isolate and identify *Staphylococcus* species from clinical and nosocomial samples obtained from tertiary care hospitals. The objectives include determining the antibiotic susceptibility pattern of the isolated Staphylococcal species and assessing their pathogenic potential in terms of multidrug resistance (MDR) and extensive drug resistance (XDR).

This help to understand the prevalence and resistance patterns of Staphylococcus species in the hospital setting, informing infection control strategies and antibiotic treatment options.

METHODOLOGY

The study was a cross-sectional laboratory-based investigation conducted at two tertiary care hospitals in Karachi, Pakistan: Al-Tibri Hospital, Isra University, and Bahria Hospital. The researchers collected 200 clinical samples from outpatient department (OPD) settings. The study isolated 200 Staphylococcus species from various clinical samples, including HVS (66, 33%), blood (50, 25%), pus (51, 25.5%), ear swab (2, 1%), sputum (3, 1.5%), urine (27, 13.5%), and ascitic fluid (1, 0.5%). The samples were cultured on blood agar with 5% sheep blood at 37°C for 24 hours, and Staphylococci were identified based on morphology and Gram staining. The study received ethical approval from the institutional ethics committees, and informed consent was exempted since no patient clinical data were used.

. Colonies suggestive of *Staphylococcus* species were identified based on colony morphology, Gram staining, and biochemical tests. Gram-positive cocci arranged in clusters were subjected to catalase testing for preliminary identification. Species differentiation was performed using coagulase testing to classify isolates into coagulase-positive and coagulase-negative staphylococci. DNase testing was carried out where required to support species identification and assess virulence characteristics.

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) guidelines. A standardized inoculum equivalent to 0.5 McFarland turbidity was prepared for each isolate. Antibiotic discs used in the study included amoxicillin-clavulanate, ciprofloxacin, clindamycin, erythromycin, linezolid, tetracycline, trimethoprim-sulfamethoxazole, gentamicin, vancomycin, doxycycline, and fusidic acid. After incubation at 37°C for 16–18 hours, zones of inhibition were measured and interpreted as sensitive or resistant based on CLSI breakpoints.

Quality control of antimicrobial susceptibility testing was ensured by using standard reference strains as recommended by CLSI. Multidrug resistance was defined as resistance to three or more classes of antimicrobial agents. Data were recorded systematically and entered into Microsoft Excel for analysis. Descriptive statistical analysis was performed, and results were expressed as frequencies and percentages.

Ethical considerations

The study was approved by the institutional IRB of Al tibri medical college and Hospital, Karachi.

STATISTICAL ANALYSIS

All laboratory and antimicrobial susceptibility data were entered and analyzed using SPSS version 22.0. Descriptive statistics were used to summarize the distribution of Staphylococcal species isolated from various clinical samples, expressed as frequencies and percentages. Antibiotic susceptibility results were categorized as sensitive, intermediate, or resistant according to CLSI guidelines, and resistance rates for each antibiotic were calculated.

The prevalence of methicillin-resistant Staphylococcus aureus (MRSA), multidrug-resistant (MDR), and extensively drug-resistant (XDR) isolates was determined using standard operational definitions. Comparative analysis between coagulase-positive Staphylococci (CoPS) and coagulase-negative Staphylococci (CoNS) was performed using the Chi-square test or Fisher's exact test, where appropriate, to assess differences in resistance patterns. A p-value of <0.05 was considered statistically significant. The results were presented in the form of tables and figures to clearly demonstrate resistance trends and distribution patterns among the isolates.

RESULTS

A total of 200 clinical isolates of *Staphylococcus* species were analyzed in the present study. The isolates were recovered from a variety of clinical specimens including high vaginal swabs, pus,

blood, urine, sputum, ear swabs, and ascitic fluid, representing both superficial and invasive infections. Both coagulase-negative staphylococci (CoNS) and coagulase-positive staphylococci (CoPS) were included. Catalase positivity was observed in all isolates, confirming their classification as *Staphylococcus* species, while DNase positivity was predominantly observed among coagulase-positive isolates.

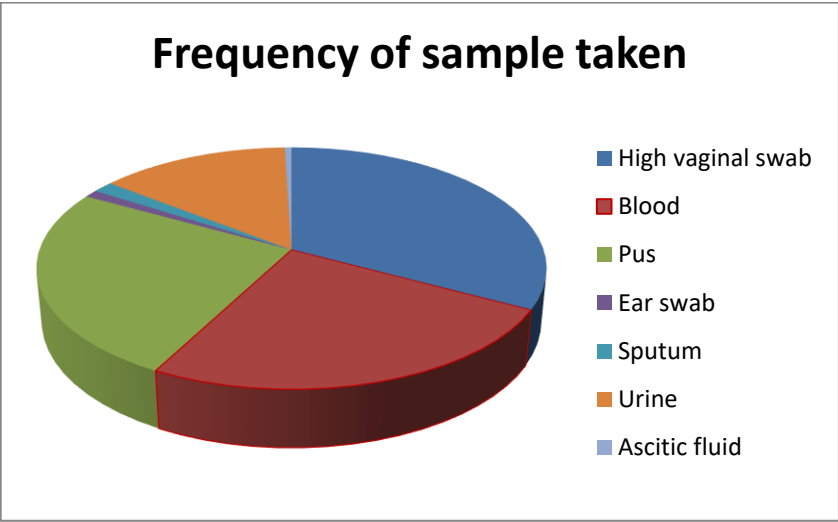


Figure 1 Showed the frequency and Percentages among Isolates

The antibiotic susceptibility profile revealed a high burden of resistance to several commonly used antimicrobial agents. Resistance to erythromycin was the most frequent finding, observed in more than two-thirds of the isolates, followed closely by ciprofloxacin and fusidic acid. More than half of the isolates were resistant to amoxicillin-clavulanate, indicating reduced effectiveness of beta-lactam antibiotics in empirical therapy. Moderate resistance rates were observed for gentamicin, doxycycline, and trimethoprim-sulfamethoxazole, suggesting partial preservation of activity for these agents. Clindamycin showed comparatively better sensitivity, although resistance was still present in a notable proportion of isolates.

Table 1: Antibiotic Susceptibility Pattern of Staphylococcal Isolates (n = 200)

Antibiotic	Resistant (n)	Resistant (%)	Sensitive (n)	Sensitive (%)
Amoxicillin–Clavulanate	104	52.0%	96	48.0%
Ciprofloxacin	132	66.0%	68	34.0%
Clindamycin	74	37.0%	126	63.0%
Erythromycin	143	71.5%	57	28.5%
Linezolid	4	2.0%	196	98.0%
Trimethoprim–Sulfamethoxazole	65	32.5%	135	67.5%
Gentamicin	92	46.0%	108	54.0%
Vancomycin	11	5.5%	189	94.5%
Doxycycline	65	32.5%	135	67.5%
Fusidic Acid	135	67.5%	65	32.5%

In contrast, linezolid demonstrated excellent in-vitro activity, with resistance detected in only a very small fraction of isolates. Vancomycin also retained high efficacy, with low levels of resistance, highlighting its continued role as a reliable therapeutic option for serious staphylococcal infections.

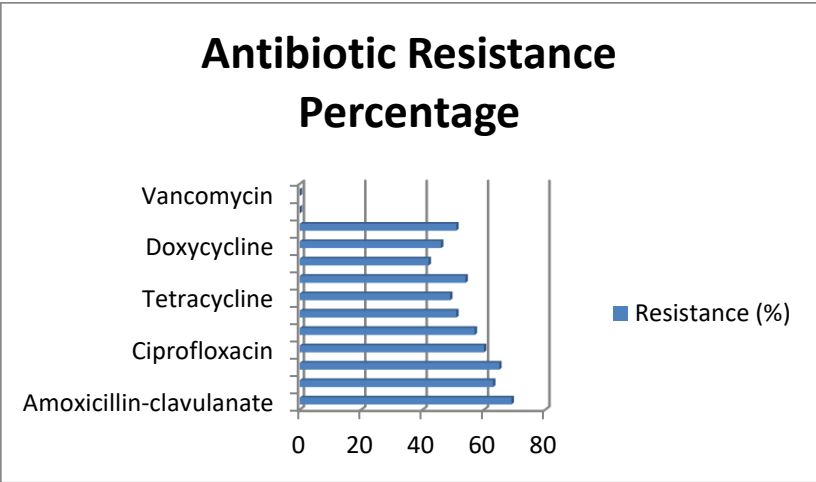


Figure 2 Showed the Antibiotic Resistance Percentage among Isolates

These findings emphasize the importance of reserving these agents for severe or multidrug-resistant infections to prevent further emergence of resistance. A significant proportion of the isolates fulfilled the criteria for multidrug resistance, exhibiting resistance to three or more classes of antibiotics.

Table 2: High- and Low-Resistance Antibiotics Among Isolates

Resistance Category	Antibiotics
High resistance (>60%)	Erythromycin, Fusidic Acid, Ciprofloxacin
Moderate resistance (30–60%)	Amoxicillin-Clavulanate, Gentamicin, Clindamycin, Doxycycline, SXT
Low resistance (<10%)	Linezolid, Vancomycin

Multidrug resistance was more commonly observed among coagulase-positive staphylococci and isolates obtained from pus and urine samples

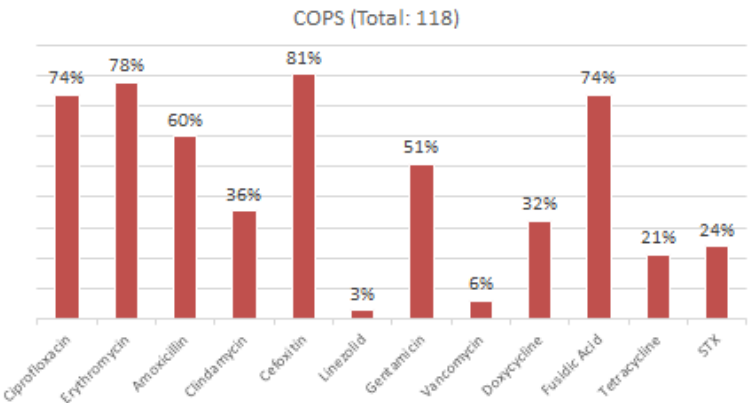


Figure 3. Antibiotic Susceptibility Assay

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The coexistence of virulence factors such as coagulase and DNase production with multidrug resistance further underscores the pathogenic potential of these isolates, , indicating a higher resistance burden in infections associated with tissue invasion and healthcare exposure.

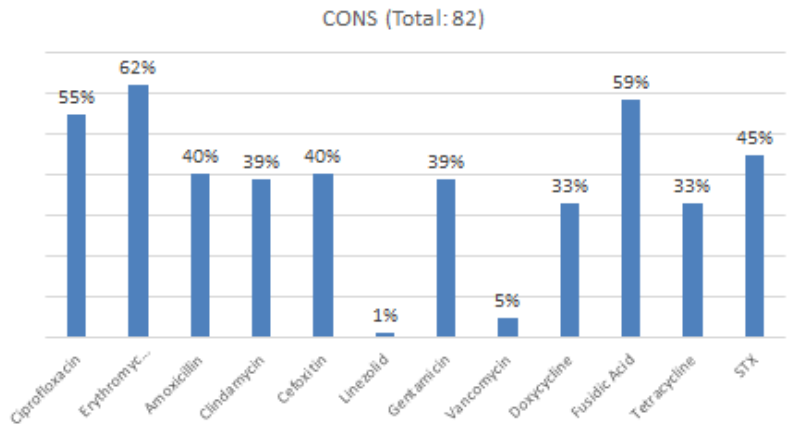


Figure 4. Antibiotic Susceptibility Assay

17

Table 3: Effectiveness of Reserve Antibiotics

Antibiotic	Sensitivity (%)	Clinical Interpretation
Linezolid	98.0%	Highly effective
Vancomycin	94.5%	Highly effective
Clindamycin	63.0%	Moderately effective

Overall, the study demonstrates a high prevalence of antimicrobial resistance among clinical *Staphylococcus* isolates, particularly against commonly prescribed oral antibiotics, while preserving susceptibility to last-line agents such as linezolid and vancomycin. These findings highlight the need for routine antimicrobial susceptibility testing, rational antibiotic use, and strengthened antimicrobial stewardship programs to limit the spread of resistant staphylococcal strains.

DISCUSSION

This study highlights a concerning burden of antimicrobial resistance among Staphylococcal species isolated from clinical samples in tertiary care hospitals in Karachi, Pakistan. The present study demonstrates a high prevalence of antimicrobial resistance among clinical *Staphylococcus* isolates obtained from diverse specimen types, highlighting the growing therapeutic challenge posed by these organisms in routine clinical practice[18,19]. The predominance of resistance to commonly prescribed antibiotics such as erythromycin, ciprofloxacin, amoxicillin-clavulanate, and fusidic acid reflects extensive and often empirical use of these agents, both in community and hospital settings. Such resistance trends are consistent with global and regional surveillance reports that identify macrolides and fluoroquinolones as antibiotics with rapidly diminishing efficacy against staphylococcal species.

Many researches showed that Erythromycin exhibited the highest resistance rate in this study, indicating widespread macrolide resistance among both coagulase-positive and coagulase-negative staphylococci. This finding is clinically significant, as macrolides are frequently used for skin, soft tissue, and gynecological infections[20]. The high resistance observed may be attributed to the presence of erm-mediated methylation of ribosomal targets or active efflux mechanisms, which have been well documented in staphylococcal isolates. Similarly, the elevated resistance to ciprofloxacin

suggests selective pressure from frequent fluoroquinolone use, leading to chromosomal mutations in DNA gyrase and topoisomerase IV[21-22].

Resistance to amoxicillin-clavulanate was observed in more than half of the isolates, underscoring the limited reliability of beta-lactam/beta-lactamase inhibitor combinations in treating staphylococcal infections[23]. This may be explained by altered penicillin-binding proteins and hyperproduction of beta-lactamases. The substantial resistance to fusidic acid further raises concern, as this agent is often used topically and systemically for staphylococcal infections, particularly in dermatological practice[24]. Unregulated and prolonged use of fusidic acid may have contributed to the high resistance rates observed.

In contrast, linezolid and vancomycin retained excellent in-vitro activity against the majority of isolates. The very low resistance to linezolid emphasizes its continued effectiveness as a reserve drug for multidrug-resistant staphylococcal infections. Similarly, vancomycin remained highly effective, reinforcing its role as a cornerstone in the management of serious staphylococcal infections[25]. However, the detection of even a small proportion of vancomycin-resistant isolates is alarming and warrants continuous surveillance, as resistance to glycopeptides significantly limits therapeutic options.

Moderate resistance rates to clindamycin, doxycycline, gentamicin, and trimethoprim-sulfamethoxazole suggest that these agents may still have a role in targeted therapy when guided by susceptibility testing. Clindamycin, in particular, showed comparatively better sensitivity and remains a valuable option for skin and soft tissue infections. However, the possibility of inducible clindamycin resistance highlights the importance of performing D-tests prior to its clinical use[26].

A notable finding of this study is the high prevalence of multidrug resistance, defined as resistance to three or more antibiotic classes. Multidrug-resistant isolates were more frequently recovered from pus and urine samples, indicating a higher resistance burden in invasive and healthcare-associated infections[27]. The coexistence of virulence factors such as coagulase and DNase production with multidrug resistance further enhances the pathogenic potential of these organisms and complicates infection management[28].

Overall, the findings of this study underscore the urgent need for rational antibiotic prescribing practices, routine antimicrobial susceptibility testing, and the implementation of robust antimicrobial stewardship programs. Continuous monitoring of resistance patterns is essential to guide empirical therapy and to preserve the effectiveness of last-line antibiotics such as vancomycin and linezolid. Strengthening infection control measures and limiting the indiscriminate use of broad-spectrum antibiotics are critical steps in mitigating the rising threat of antimicrobial resistance among *Staphylococcus* species.

CONCLUSION

The study reveals a problem of antimicrobial resistance among *Staphylococcus* species in Karachi, Pakistan, with significant MRSA, MDR, and XDR profiles. Overall, the study underscores the urgent need for rational antibiotic prescribing, strengthened antimicrobial stewardship programs, and continuous surveillance of resistance patterns. The coexistence of resistance with virulence factors further increases the clinical significance of these pathogens and complicates treatment outcomes. These findings reinforce the necessity of routine antimicrobial susceptibility testing to guide targeted therapy rather than reliance on empirical treatment alone. Prudent use of last-line antibiotics, adherence to infection control practices, and regular monitoring of emerging resistance are essential to preserve the effectiveness of existing antimicrobial agents and to mitigate the escalating threat posed by resistant *Staphylococcus* species.

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