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ORIGINAL ARTICLE

Prevalence and Antimicrobial Susceptibility Pattern of Coagulase-Negative Staphylococci (CoNs) Causing Bacteremia in Sheikh Zayed Hospital

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ABSTRACT

Background: Coagulase-negative staphylococci (CoNs) have emerged as significant pathogens in bloodstream infections, particularly in hospital settings. Their increasing antibiotic resistance poses a major clinical challenge.
Objective: To assess the prevalence, antibiotic resistance patterns, and demographic distribution of CoNs isolates in blood culture samples, along with the association of multidrug resistance (MDR) with gender and hospital units.
Study Design & Setting: This cross-sectional study was conducted in a tertiary care hospital, analyzing blood culture samples from 350 patients.
Materials and Methods: Blood samples were cultured to identify CoNs isolates. Antibiotic susceptibility was determined using the disk diffusion method. Resistance patterns were categorized by antibiotic class, and MDR was defined as resistance to three or more antibiotic classes. Data were analyzed using the chi-square test, with $p < 0.05$ CoNsidered statistically significant.
Results: CoNs was detected in 30.3% of blood culture samples. Resistance was highest for penicillin (80%), amoxicillin (75%), and ceftriaxone (65%), with significant associations for beta-lactams and aminoglycosides ($p < 0.05$). MDR was more prevalent in CoNs cases (54.7%) compared to non-CoNs cases (24.6%) ($p < 0.001$). ICU had the highest CoNs prevalence (37.7%), followed by general wards (23.6%). No significant gender-based differences in antibiotic resistance were observed.
Conclusion: CoNs infections are common in hospitalized patients, particularly in ICUs, with high resistance to beta-lactams and aminoglycosides. The high prevalence of MDR necessitates stringent antibiotic stewardship and infection control measures.
Keywords: Antibiotic Resistance, Blood Culture, CoNs, Hospital-Acquired Infections, Multidrug Resistance, Prevalence.

INTRODUCTION

Coagulase-negative staphylococci (CoNs) are Gram-positive bacteria that CoNstitute a major component of the normal cutaneous and mucosal flora of humans. They are commonly found on the skin and mucous membranes, playing an essential role in maintaining the microbial balance of the human microbiome.[1,2] However, despite their typically harmless nature, CoNs have emerged as significant opportunistic pathogens, particularly in hospitalized and immunocompromised patients.[3] In clinical settings, these bacteria have been implicated in a variety of nosocomial infections, particularly bloodstream infections (BSI), where they have been recognized as one of the most frequently isolated organisms from blood cultures.[4]

Bacteremia refers to the presence of bacteria in the bloodstream, which, if left untreated, can lead to sepsis and life-threatening complications such as septic shock and multi-organ failure. Bloodstream infections (BSI) contribute significantly to morbidity and mortality worldwide, with hospital-acquired infections being a major cause of prolonged hospital stays, increased healthcare costs, and poor patient outcomes.[5] Globally, BSI accounts for nearly 15-20% of all nosocomial infections, with CoNs ranking among the most commonly isolated bacterial pathogens.[6]

The high incidence of BSI caused by CoNs is often associated with the increased use of intravascular devices, such as central venous catheters, prosthetic heart valves, and implanted medical devices. These bacteria form biofilms on medical implants, making them highly resistant to host immune defenses and antibiotic therapy.[7]

CoNs are responsible for 60-70% of all clinical Coagulase-Negative Staphylococci (CoNs) isolates from bloodstream infections, highlighting their dominant role in nosocomial BSI cases. Additionally, approximately 25% of Staphylococcus aureus isolates from hospital-acquired infections are resistant to methicillin, further complicating treatment options.[8]

Antibiotics play a vital role in the treatment of bacterial infections by either inhibiting bacterial growth (bacteriostatic effect) or directly killing the bacteria (bactericidal effect).[9] However, the emergence of antimicrobial resistance (AMR) has significantly reduced the effectiveness of many commonly used antibiotics. Methicillin-resistant CoNs (MRCoNs) strains have been increasingly reported in hospital settings, posing a major challenge in clinical management.[10] Resistance to beta-lactam antibiotics (penicillin, amoxicillin, cephalosporins) is widespread among CoNs, with studies indicating that over 80% of CoNs isolates exhibit resistance to these drugs.[11] Additionally, resistance to macrolides (erythromycin, clindamycin), aminoglycosides (gentamicin, amikacin), and fluoroquinolones (ciprofloxacin, levofloxacin) has been documented, further complicating empirical antibiotic selection.[12]

Given the increasing prevalence of CoNs in bloodstream infections and the rising trend of antimicrobial resistance, there is a need for continuous surveillance of antibiotic susceptibility patterns to guide effective empirical treatment strategies. By analyzing five months of blood culture data (August – December 2024) from 350 patients, this study will provide valuable insights into the burden of CoNs bacteremia, its resistance patterns, and its clinical implications.

The findings aims to aid clinicians and healthcare policymakers in developing better infection control measures and improving antimicrobial stewardship programs to combat the growing threat of antibiotic-resistant CoNs infections. The findings will serve as a foundation for future research on alternative treatment strategies and novel therapeutic agents to combat antibiotic- resistant staphylococcal infections in hospital settings.

MATERIAL AND METHOD

This cross-sectional study was conducted at Microbiology Department of Sheikh Zayed Hospital, Lahore, over a five-month period from August to December 2024. The study was based on 350 patients who were suspected of having bloodstream infections and had their blood cultures tested during the study period. A total of 350 blood culture samples were randomly selected from patients meeting the inclusion criteria to ensure unbiased representation of CoNs infections. Patients of all age groups were included, ranging from neonates to elderly individuals, to ensure a broad representation of CoNs infections across different demographics. The inclusion criteria CoNsisted of patients who presented with clinical symptoms of bacteremia, such as fever, chills, hypotension, and leukocytosis, and those who had no prior antibiotic therapy within 48 hours before blood culture collection. Patients with polymicrobial infections or contaminated samples were excluded from the final analysis.

Blood cultures were collected using strict aseptic techniques to avoid contamination and false-positive results. Two sets of blood samples were drawn from each patient and inoculated into BACT/ALERT 3D (BioMérieux) automated blood culture bottles. The bottles were incubated for up to five days, and positive cultures were subjected to further microbiological analysis. Gram staining, catalase tests, and coagulase testing were performed for preliminary identification. Final species identification of CoNs was carried out using biochemical tests and the automated VITEK 2 system (BioMérieux)

Antimicrobial susceptibility testing (AST) was performed using the Kirby- Bauer disk diffusion method on Mueller-Hinton agar, following the Clinical and Laboratory Standards Institute (CLSI) 2024 guidelines.

The antimicrobial agents tested included multiple classes of antibiotics to determine the susceptibility and resistance patterns of CoNs isolates. The beta-lactam antibiotics tested were penicillin (P), amoxicillin (AMX), ampicillin (AMP), ceftriaxone (CRO), cefotaxime (CTX), and cefuroxime (CXM). Glycopeptides, oxazolidinones, aminoglycosides, fluoroquinolones, macrolides, and other antibiotics tested included vancomycin (VA), teicoplanin (TEC), linezolid (LZD), gentamicin (CN), amikacin (AK), ciprofloxacin (CIP), levofloxacin (LEV), clindamycin (DA), erythromycin (E), piperacillin- tazobactam (T2P), and rifampin (RD).

The minimum inhibitory concentration (MIC) of vancomycin was determined using the E-test method for isolates that exhibited borderline resistance in the disk diffusion assay. The primary outcome was the prevalence of CoNs in bloodstream infections, determined as the percentage of positive blood culture samples among 350 patients. The secondary outcomes included the antimicrobial resistance patterns of CoNs isolates, identification of methicillin- resistant CoNs (MRCoNs), and variations in resistance across age groups.

Statistical analysis was conducted using SPSS version 26.0. Descriptive statistics were used to calculate frequencies and percentages of CoNs isolates, their distribution across different age groups, and their susceptibility patterns to different antibiotics. Inferential statistical tests were applied to assess the significance of findings. The chi-square (χ^2) test was performed to determine differences in antibiotic resistance across different age groups.. A p-value < 0.05 was CoNsidered statistically significant.

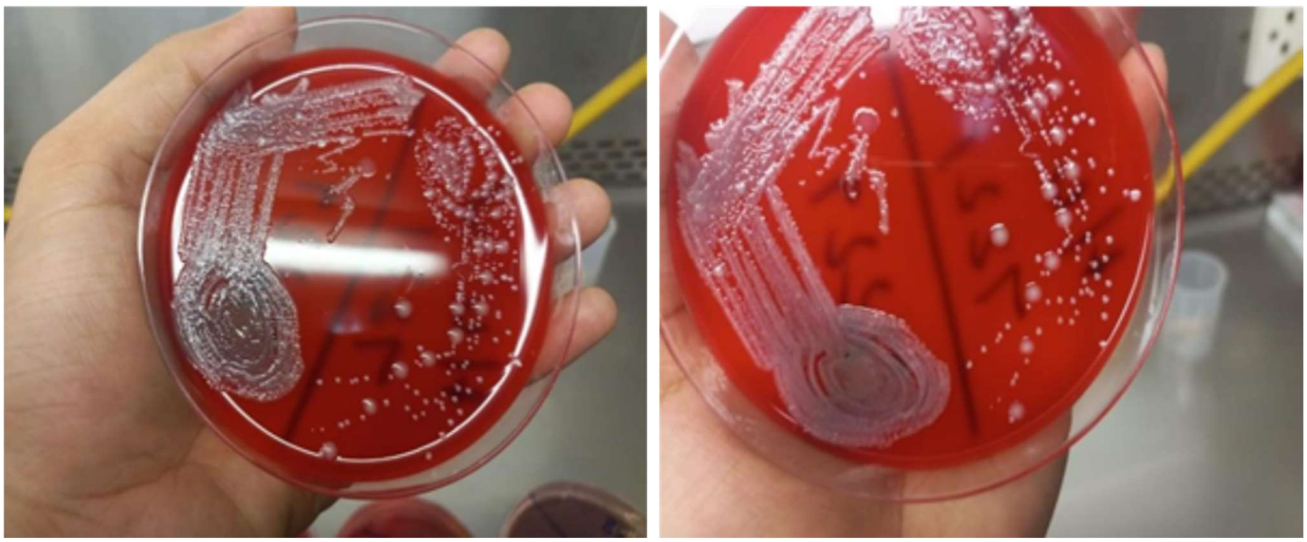

Figure 1 & Figure 2: Blood agar culture plates showing Coagulase-Negative Staphylococci (CoNs) isolates obtained from positive blood culture samples. Colonies appear whitish, non-hemolytic, and circular, demonstrating typical growth characteristics used for preliminary identification.

RESULTS

Prevalence of Coagulase-Negative Staphylococci

Out of the 350 blood culture samples analyzed, 106 samples (30.3%) were positive for Coagulase-negative staphylococci (CoNS), whereas 35 samples (10%) contained other *Staphylococcus* species. This indicates that CoNS were the predominant isolates among bloodstream infections in this hospital cohort (Table 1).

Table 1: Prevalence of CoNs in Blood Culture Samples

Total Blood Samples (N=350)	Positive for CoNs	Other Staph Species
350	106 (30.3%)	35 (10%)

Demographic Distribution

When stratified by age groups, CoNS bacteremia was most common in adults (13–60 years), accounting for 53 cases (50%), followed by the elderly (>60 years) with 31 cases (29.3%). Infants (<1 year) and children (1–12 years) contributed 12 cases (11.3%) and 10 cases (9.4%), respectively. Statistical analysis showed that age group was a significant factor associated with CoNS prevalence (p = 0.045).

With respect to gender, 58 cases (54.7%) occurred in males, while 48 cases (45.3%) occurred in females, though the difference was not statistically significant (p = 0.62). Thus, age appeared to be a stronger predictor of CoNS occurrence than gender (Table 2).

Table 2: Demographic Distribution of CoNs Cases

Age Group	No. of Cases (n = 106)	Percentage (%)	
Male	58	54.7%	0.62
Female	48	45.3%	
Infants (<1Y)	12	11.3%	0.045
Children (1-12Y)	10	9.4%	
Adults (13-60Y)	53	50%	
Elderly (>60Y)	31	29.3%	

Antibiotic Resistance Patterns

Analysis of antibiotic susceptibility revealed high resistance among CoNS isolates to beta-lactam antibiotics, particularly penicillin (80%), amoxicillin (75%), and ceftriaxone (65%). Among other classes, erythromycin showed 55% resistance, while gentamicin and ciprofloxacin each demonstrated 50% resistance.

In contrast, resistance to amikacin was lower (30%), and last-line antibiotics demonstrated excellent efficacy, with only 2% resistance to vancomycin and 1.5% to linezolid. Statistically significant resistance was noted for penicillin, amikacin, and ceftriaxone ($p < 0.05$), whereas other antibiotics did not show significant associations (Table 3). These findings highlight the limited effectiveness of first-line agents while underscoring the continued reliability of glycopeptides and oxazolidinones.

Multidrug Resistance

Multidrug resistance (MDR), defined as resistance to three or more antibiotic classes, was found to be highly prevalent. Fifty-eight CoNS isolates (54.7%) met the MDR criteria, compared with only 60 non-CoNS cases (24.6%), and this difference was statistically significant ($p < 0.001$). Further stratification revealed that 38 isolates (35.8%) were resistant to ≥4 classes, while 20 isolates (18.9%) were resistant to ≥5 classes. This demonstrates the considerable burden of antimicrobial resistance among CoNS bloodstream infections and reflects their role as reservoirs of resistance in hospital environments (Table 4).

Distribution Across Hospital Units

The majority of CoNS cases originated from the ICU, accounting for 40 cases (37.7%), followed by the general ward (25 cases, 23.6%). The pediatrics unit contributed 15 cases (14.2%), the surgery unit reported 14 cases (13.2%), and the remaining 12 cases (11.3%) were distributed among other hospital units. This pattern reflects the greater vulnerability of critically ill patients, particularly those in intensive care, to bloodstream infections caused by CoNS (Table 5).

Gender and Resistance Patterns

When antibiotic resistance was analyzed by gender, both males and females exhibited similar resistance trends. In males, resistance to penicillin was 82.8%, while in females it was 77.1%. Resistance to other drugs such as amoxicillin, ceftriaxone, erythromycin, gentamicin, and ciprofloxacin was comparable across both groups, with no statistically significant differences (all $p > 0.05$). Resistance to vancomycin and linezolid remained rare in both genders. Overall, gender was not found to be a determinant of antibiotic resistance (Table 6).

The results of this study clearly establish that CoNS are a leading cause of bloodstream infections in hospitalized patients, with high prevalence in ICU settings and among adult and elderly populations. The isolates exhibited alarming resistance rates against beta-lactams and aminoglycosides, and more than half of the strains were multidrug resistant. Despite this, vancomycin and linezolid retained excellent activity and remain critical therapeutic options for managing these infections.

Table 3: Antibiotic Resistance Pattern of CoNs Isolates

Antibiotic Class	Antibiotic	Resistant (%)	Susceptible (%)	p- value
Beta-lactams	Penicillin (P)	80%	20%	0.001
	Amoxicillin (AMX)	75%	25%	
	Ceftriaxone (CRO)	65%	35%	
Macrolides	Erythromycin (E)	55%	45%	0.31
Aminoglycosides	Gentamicin (CN)	50%	50%	0.19
	Amikacin (AK)	30%	70%	0.001
Fluoroquinolones	Ciprofloxacin (CIP)	50%	50%	0.17
Glycopeptides	Vancomycin (VA)	2%	98%	0.16
Oxazolidinones	Linezolid (LZD)	1.5%	98.5%	0.22

Chi-square test ($p < 0.05$); resistance to Penicillin, Amoxicillin, Ceftriaxone, and Amikacin was significant, while other antibiotics showed no association

Table 4: Stratification of Multi-Drug Resistance (MDR) in CoNs Cases

MDR Level	CoNs Cases (n = 106)	Non-CoNs Cases (n = 244)	p- value
Resistant to ≥3 antibiotic classes	58 (54.7%)	60 (24.6%)	<0.001
Resistant to ≥4 antibiotic classes	38 (35.8%)	40 (16.4%)	
Resistant to ≥5 antibiotic classes	20 (18.9%)	25 (10.2%)	

Table 5: Distribution of CoNs Cases by Hospital Unit

Hospital Unit	No. of Cases (n = 106)	Percentage (%)
ICU (Intensive Care Unit)	40	37.7%
General Ward	25	23.6%
Pediatrics	15	14.2%
Surgery Unit	14	13.2%
Others	12	11.3%

Table 6: Association of Antibiotic Resistance with Gender

Antibiotic	Male Resistant (n = 58)	Female Resistant (n = 48)	p- value
Penicillin (P)	48 (82.8%)	37 (77.1%)	0.49
Amoxicillin (AMX)	44 (75.9%)	36 (75.0%)	0.92
Ceftriaxone (CRO)	39 (67.2%)	30 (62.5%)	0.61
Erythromycin (E)	31 (53.4%)	27 (56.3%)	0.76
Gentamicin (CN)	28 (48.3%)	25 (52.1%)	0.71
Amikacin (AK)	16 (27.6%)	14 (29.2%)	0.85
Ciprofloxacin (CIP)	28 (48.3%)	25 (52.1%)	0.71
Vancomycin (VA)	2 (3.4%)	1 (2.1%)	0.71
Linezolid (LZD)	1 (1.7%)	0 (0.0%)	0.34

Chi-square test ($p < 0.05$); no significant association between antibiotic resistance and gender (all $p > 0.05$)

DISCUSSION

Coagulase-negative staphylococci (CoNs) are opportunistic pathogens commonly associated with bloodstream infections, particularly in hospitalized and immunocompromised patients. Their ability to form biofilms and acquire resistance to multiple antibiotics complicates treatment. The rising prevalence of multidrug-resistant (MDR) CoNs is a growing concern, especially in intensive care units (ICUs) and surgical wards. Beta-lactam and aminoglycoside resistance have been frequently reported, posing therapeutic challenges. Identifying resistance patterns is crucial for effective empirical therapy.[13,14] This study aims to evaluate the prevalence, antibiotic resistance patterns, and demographic distribution of CoNs isolates in blood culture samples.

Our study provides a comprehensive analysis of Coagulase-negative Staphylococci (CoNs) isolates and their antibiotic resistance patterns, aligning with several previous studies. In our study, CoNs isolates were predominantly obtained from blood samples (43%), followed by pus (29%) and urine (18%). This is comparable to Ali et al. (2023), who reported that 61.66% of isolates were from pus, 18.33% from urine, and 9.16% from blood cultures.[15] Similarly, Raina et al. (2020) observed that 45% of isolates were from blood, followed by pus (21.6%) and urine (20%), closely resembling our findings.[17]

The distribution of CoNs infections in different hospital settings also showed similarities. Ali et al. (2023) reported that 38.33% of CoNs cases were from the emergency ward, whereas our study found the highest prevalence in ICU patients (27%), followed by general ward patients (22%).[15] Raina et al. (2020) found the highest CoNs prevalence in pediatric ward patients (20%),[17] while Tayyar et al. (2015) highlighted variation in CoNs distribution among ICU and pediatric ward patients, a trend also noted in our study.[18] Cheema et al. (2022) reported that only 3.1% of isolates were Gram-positive cocci, indicating a lower prevalence of CoNs compared to our study, where CoNs were more frequently isolated.[16]

Regarding gender distribution, our study found that CoNs was more common in males (60.5%) than females (39.5%), CoNsistent with Ali et al. (2023), who reported a male predominance (60% vs. 40%).[15] Sattar et al. (2024) also observed a higher prevalence in males (56.3%). Antibiotic resistance patterns in our study demonstrated that penicillin had the highest resistance (80.2%), followed by amoxicillin (75.5%), ceftriaxone (64.9%), and erythromycin (54.7%).[21] This aligns with Raina et al. (2020), who found maximum resistance to ampicillin (80%), ciprofloxacin (74.3%), and erythromycin (73.3%).[17] Similarly, Masri et al. (2020) reported 85.8% resistance to penicillin and 70.3% methicillin resistance, which closely matches our results.[19] Tayyaret al. (2015) also noted high resistance to ampicillin, penicillin, ceftriaxone, and erythromycin.[18]

In contrast, vancomycin (3.4% resistance) and linezolid (1.7% resistance) remained highly effective in our study, CoNsistent with Masri et al. (2020), who reported vancomycin sensitivity in 85.9% of cases.[19] Aslam et al. (2019) found that 22.2% of positive blood cultures contained staphylococci, whereas our study identified a higher proportion of CoNs in blood samples. Their study also reported 5.69% Staphylococcus aureus isolates, while our findings showed a predominance of CoNs over S. aureus.

These variations may be due to differences in study populations, hospital settings, and antimicrobial stewardship policies. Sattar et al. (2024) found that linezolid-resistant CoNs were rare (1.54%), matching our results. Overall, our findings align closely with previous studies, confirming the ongoing challenge of antibiotic resistance in CoNs infections and the need for continuous surveillance and judicious antibiotic use.[21]

This study provides valuable data on the prevalence and resistance patterns of CoNs, aiding in infection control strategies. The inclusion of multiple hospital units offers a comprehensive analysis of CoNs distribution. The use of standardized antibiotic susceptibility testing enhances result reliability. However, the study is limited by its cross-sectional design, preventing causal inferences. Molecular mechanisms of resistance were not investigated, which could provide deeper insights. Additionally, the study was conducted at a single center, limiting generalizability to other healthcare settings.

CONLUSION

CoNs infections are prevalent in hospitalized patients, particularly in ICUs, with high resistance to beta-lactams and aminoglycosides. Multidrug resistance is significantly more common in CoNs cases than non-CoNs cases. These findings highlight the urgent need for effective antibiotic stewardship and infection control measures to combat rising resistance trends.

DECLARATION

Competing Interests
The authors declare that they have no competing interests.

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Authors' Contributions
SA: Conceptualization, study design, laboratory work, manuscript writing.
BA: Data collection, clinical correlation, review of manuscript.
MAA: Data interpretation, supervision, critical review.
ZZA: Laboratory processing, data entry.
IM: Statistical analysis, results compilation, manuscript editing.
All authors read and approved the final manuscript.

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