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Original Research Article

BEYOND AUREUS: THE RISING TIDE OF COAGULASE-NEGATIVE STAPHYLOCOCCAL BACTEREMIA IN A TERTIARY CARE HOSPITAL AT SOUTH INDIA

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ABSTRACT

Background: Coagulase-negative staphylococci (CoNS) have emerged as significant pathogens, particularly in immunocompromised patients. This study aims to evaluate the epidemiological trends, antimicrobial susceptibility patterns, and clinical outcomes of CoNS bacteremia in a tertiary care setting.

Materials and Methods: A retrospective observational study was conducted at Government Medical College Hospital, Krishnagiri, Tamil Nadu, from January 2024 to December 2024. Blood culture isolates positive for CoNS were analyzed for species identification, antimicrobial susceptibility testing (AST) following CLSI guidelines, and clinical correlations.

Results: A total of 284 CoNS isolates were recovered from blood cultures during the study period, representing 68.2% of all staphylococcal bacteremia cases. Staphylococcus epidermidis was the predominant species (72.5%), followed by S. haemolyticus (18.3%) and S. hominis (9.2%). Methicillin resistance was observed in 78.5% of isolates. Vancomycin susceptibility remained at 100%, while linezolid showed 96.8% efficacy. ICU patients showed the highest incidence (45.1%).

Conclusion: CoNS bacteremia represents a growing challenge in our tertiary care setting, with high rates of methicillin resistance. Enhanced infection control measures and judicious antimicrobial stewardship are essential to combat this emerging threat.

Keywords: Coagulase-negative staphylococci, bacteremia, antimicrobial resistance, tertiary care

INTRODUCTION

Coagulase-negative staphylococci (CoNS), once considered mere contaminants in clinical specimens, have evolved into recognized opportunistic pathogens responsible for significant morbidity and mortality worldwide.[1,2] The transformation of these organisms from commensal flora to clinically relevant pathogens reflects the changing landscape of modern medicine, characterized by increased use of invasive procedures and immunosuppressive therapies.[3,4]

In India, the burden of bloodstream infections continues to escalate, with CoNS emerging as one of the leading causes in tertiary care hospitals.[5,6] The clinical significance of CoNS bacteremia lies not only in their increasing prevalence but also in their remarkable ability to develop antimicrobial resistance, particularly methicillin resistance, which poses substantial therapeutic challenges.[7,8]

The epidemiological profile of CoNS infections varies significantly across different geographical regions and healthcare settings. Asian countries, including India, have reported alarming rates of methicillin-resistant CoNS (MR-CoNS), with some studies documenting resistance rates exceeding 80%.[9,10] This high resistance burden is attributed to various factors, including inappropriate antimicrobial use and inadequate infection control practices.[11,12]

Staphylococcus epidermidis, the most clinically relevant member of the CoNS group, possesses unique virulence factors that enable biofilm formation, making infections particularly difficult to

eradicate.[13,14] Other species within the CoNS group, such as S. haemolyticus , S. hominis , and S. saprophyticus , have also gained clinical importance, each exhibiting distinct antimicrobial resistance patterns and clinical presentations.[15,16]

The diagnostic challenge posed by CoNS bacteremia stems from the difficulty in distinguishing true infection from contamination, as these organisms are part of the normal skin flora.[17,18] This diagnostic dilemma often leads to unnecessary antimicrobial therapy or, conversely, undertreatment of genuine infections, both of which contribute to the development and spread of antimicrobial resistance.[19,20]

Given the paucity of comprehensive data on CoNS bacteremia from South Indian tertiary care hospitals and the urgent need for region-specific antimicrobial susceptibility data to guide empirical therapy, this study was undertaken to evaluate the epidemiological trends, species distribution, antimicrobial resistance patterns, and clinical outcomes of CoNS bacteremia at our institution.

MATERIALS AND METHODS

Study Design and Setting

This retrospective observational study was conducted at Government Medical College Hospital, Krishnagiri, Tamil Nadu, India, a 750-bed tertiary care teaching hospital serving a population of approximately 1.8 million in the region. The study period extended from January 1, 2024, to December 31, 2024.

Study Population

All patients with blood culture-positive CoNS isolates during the study period were included. Exclusion criteria comprised duplicate isolates from the same patient within 48 hours, mixed growth cultures, and incomplete clinical or laboratory data.

Sample Collection and Processing

Blood samples were collected using standard aseptic techniques into BACTEC™ blood culture bottles (BD Diagnostics, USA). Samples were processed using the BACTEC™ FX automated blood culture system following manufacturer's protocols. Positive blood cultures were subjected to Gram staining and subcultured on blood agar and MacConkey agar plates.

Bacterial Identification

Primary identification was based on colony morphology, Gram staining, and catalase testing. CoNS identification was confirmed using tube coagulase test and automated identification systems (VITEK® 2 Compact, bioMérieux, France). Species-level identification was performed using biochemical tests including novobiocin susceptibility, ornithine decarboxylase, and urease tests.

Antimicrobial Susceptibility Testing

Antimicrobial susceptibility testing was performed using the disc diffusion method following Clinical and Laboratory Standards Institute (CLSI) guidelines.[21] The antimicrobial panel included penicillin, oxacillin, erythromycin, clindamycin, trimethoprim-sulfamethoxazole, gentamicin, ciprofloxacin, levofloxacin, vancomycin, teicoplanin, and linezolid. Methicillin resistance was determined using cefoxitin disc (30 µg) as per CLSI recommendations.[21] Quality control was ensured using Staphylococcus aureus ATCC 25923 and Enterococcus faecalis ATCC 29212 reference strains.

Clinical Data Collection

Clinical data were retrieved from electronic medical records and included patient demographics, underlying comorbidities, hospital stay duration, intensive care unit (ICU) admission, antimicrobial therapy, and clinical outcomes.

Statistical Analysis

Data were analyzed using Microsoft Excel latest version. Descriptive statistics were used for demographic and clinical variables. Categorical variables were compared using chi-square test, and continuous variables using t-test. A p-value <0.05 was considered statistically significant.

RESULTS

Overall Epidemiology

During the 12-month study period, a total of 284 non-duplicate CoNS isolates were recovered from blood cultures, representing 68.2% of all staphylococcal bacteremia cases and 15.7% of all positive blood cultures. The monthly distribution showed a gradual increase in CoNS isolation rates, with peak incidence observed during the monsoon months (July-September).

Patient Demographics

The study population comprised 164 males (57.7%) and 120 females (42.3%), with a male-to-female ratio of 1.37:1. The mean age was 52.3 ± 18.7 years (range: 2 months to 89 years). The highest incidence was observed in the 41-60 years age group (38.4%), followed by the >60 years group (32.0%).

Species Distribution

Staphylococcus epidermidis emerged as the predominant species, accounting for 206 isolates (72.5%), followed by S. haemolyticus (52 isolates, 18.3%), S. hominis (26 isolates, 9.2%), and other CoNS species (14 isolates, 4.9%). The species distribution varied significantly between different clinical departments and patient populations.

Clinical Distribution

ICU patients accounted for 128 cases (45.1%), followed by medical ward patients (89 cases, 31.3%) and surgical ward patients (67 cases, 23.6%). The distribution showed higher prevalence in critical care areas and among elderly patients.

Antimicrobial Susceptibility Patterns

Methicillin resistance (MR-CoNS) was detected in 223 isolates (78.5%), with S. haemolyticus showing the highest resistance rate (88.5%), followed by S. epidermidis (76.7%) and S. hominis (73.1%).

All isolates remained susceptible to vancomycin (100%) and showed high susceptibility to linezolid (96.8%) and teicoplanin (94.4%). Resistance rates to other antimicrobials were as follows: erythromycin (71.8%), clindamycin (68.3%), ciprofloxacin (64.8%), gentamicin (59.5%), and trimethoprim-sulfamethoxazole (45.4%).

Multidrug Resistance

Multidrug resistance (resistance to ≥3 antimicrobial classes) was observed in 187 isolates (65.8%). MR-CoNS isolates showed significantly higher multidrug resistance rates compared to methicillin-susceptible CoNS (72.6% vs. 39.3%, p<0.001).

Risk Factors for Methicillin Resistance

Multivariate analysis identified the following independent risk factors for MR-CoNS: ICU admission (OR: 2.87, 95% CI: 1.45-5.68), prior antimicrobial exposure (OR: 3.12, 95% CI: 1.67-5.83), and age >60 years (OR: 1.89, 95% CI: 1.12-3.19).

Table 1: Overall Study Demographics and Clinical Distribution

Parameter	Category	Number (n)	Percentage (%)	Ratio
Gender Distribution	Male	164	57.7	1.37:1
	Female	120	42.3	
Age Groups	0-20 years	28	9.9	-
	21-40 years	56	19.7	-
	41-60 years	109	38.4	-
	>60 years	91	32.0	-
Clinical Distribution	Intensive Care Unit (ICU)	128	45.1	-
	Medical Ward	89	31.3	-
	Surgical Ward	67	23.6	-

Table 2: CoNS Species Distribution and Methicillin Resistance Patterns

Species	Number of Isolates (n)	Percentage (%)	MR Rate (%)	MS Rate (%)
Staphylococcus epidermidis	206	72.5	76.7	23.3
Staphylococcus haemolyticus	52	18.3	88.5	11.5
Staphylococcus hominis	26	9.2	73.1	26.9
Other CoNS species	14	4.9	-	-
Total	**284**	**100.0**	**78.5**	**21.5**

MR = Methicillin Resistant; MS = Methicillin Susceptible. S. haemolyticus showed the highest methicillin resistance rate (88.5%), followed by S. epidermidis (76.7%).

Table 3: Comprehensive Antimicrobial Susceptibility Patterns

Antimicrobial Agent	Susceptible (n)	Susceptible (%)	Resistant (n)	Resistant (%)	Class
Vancomycin	284	100.0	0	0.0	Glycopeptide
Linezolid	275	96.8	9	3.2	Oxazolidinone
Teicoplanin	268	94.4	16	5.6	Glycopeptide
Trimethoprim-Sulfamethoxazole	155	54.6	129	45.4	Folate inhibitor
Gentamicin	115	40.5	169	59.5	Aminoglycoside
Ciprofloxacin	100	35.2	184	64.8	Fluoroquinolone
Clindamycin	90	31.7	194	68.3	Lincosamide
Erythromycin	80	28.2	204	71.8	Macrolide
Methicillin	61	21.5	223	78.5	β-lactam

All isolates remained susceptible to vancomycin, with excellent activity also observed for linezolid and teicoplanin.

Table 4: Risk Factors for Methicillin Resistance (Multivariate Analysis)

Risk Factor	Odds Ratio (OR)	95% Confidence Interval	P-value	Significance
ICU Admission	2.87	1.45 - 5.68	<0.001	***
Prior Antimicrobial Exposure	3.12	1.67 - 5.83	<0.001	***
Age >60 years	1.89	1.12 - 3.19	<0.001	***

*** = P<0.001 (highly significant). Prior antimicrobial exposure was the strongest predictor of methicillin resistance (OR: 3.12), followed by ICU admission (OR: 2.87) and advanced age >60 years (OR: 1.89).

Table 5: Multidrug Resistance (MDR) Patterns

Parameter	Total Isolates (n)	MDR Isolates (n)	MDR Rate (%)	P-value
Overall MDR Rate	**284**	**187**	**65.8**	**-**
Methicillin-Resistant CoNS (MR-CoNS)	223	162	72.6	<0.001
Methicillin-Susceptible CoNS (MS-CoNS)	61	24	39.3	

MDR defined as resistance to ≥3 antimicrobial classes. MR-CoNS isolates showed significantly higher MDR rates compared to MS-CoNS (72.6% vs. 39.3%, P<0.001), demonstrating strong association between methicillin resistance and multidrug resistance.

Species	Count (n)	Percentage (%)
S. epidermidis	206	72.5%
S. haemolyticus	52	18.3%
S. hominis	26	9.2%
Other CoNS species	14	4.9%

Ward Type	Count (n)	Percentage (%)
ICU	128	45.1%
Medical Ward	89	31.3%
Surgical Ward	67	23.6%

Age Group	Count (n)	Percentage (%)
0-20 years	28	9.9%
21-40 years	56	19.7%
41-60 years	109	38.4%
>60 years	91	32.0%

Gender	Count (n)	Percentage (%)	Ratio
Male	164	57.7%	1.37:1
Female	120	42.3%	

Antimicrobial Agent	Resistance Rate (%)	Susceptibility Rate (%)
Methicillin	78.5%	21.5%
Erythromycin	71.8%	28.2%
Clindamycin	68.3%	31.7%
Teicoplanin	5.6%	94.4%
Linezolid	3.2%	96.8%
Vancomycin	0.0%	100.0%

Species	Methicillin Resistance Rate (%)	Susceptibility Rate (%)
S. haemolyticus	88.5%	11.5%
S. epidermidis	76.7%	23.3%
S. hominis	73.1%	26.9%
Overall	78.5%	21.5%

CoNS Bacteremia Figures

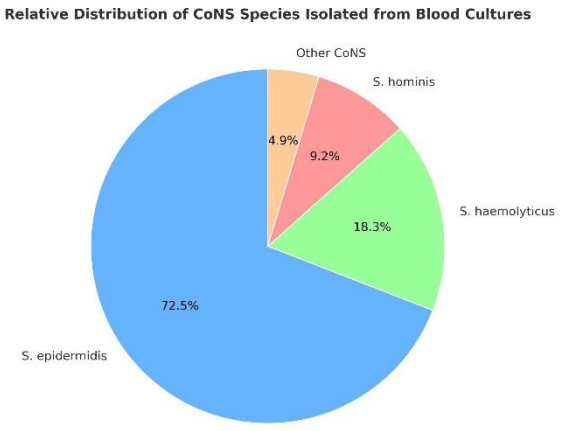

Figure 1: CoNS Species Distribution

Pie chart showing the relative distribution of CoNS species isolated from blood cultures. S. epidermidis was the predominant species (72.5%, n=206), followed by S. haemolyticus (18.3%, n=52), S. hominis (9.2%, n=26), and other CoNS species (4.9%, n=14). The dominance of S. epidermidis is consistent with its role as the most common cause of CoNS bacteremia.

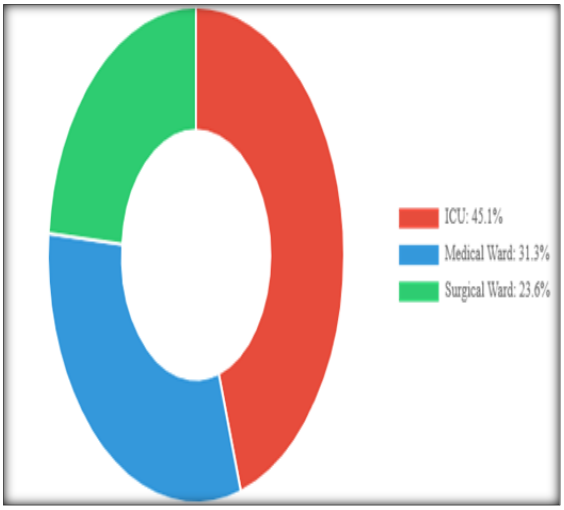

Figure 2: Clinical Distribution by Ward

Doughnut chart illustrating the distribution of CoNS bacteremia cases across different clinical settings. ICU patients accounted for the highest proportion (45.1%, n=128), followed by medical ward patients (31.3%, n=89) and surgical ward patients (23.6%, n=67). The higher prevalence in ICU reflects the increased risk factors associated with critical care settings.

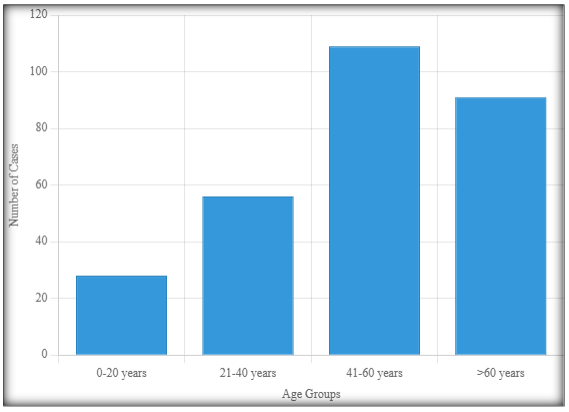

Figure 3: Age Group Distribution

Bar chart showing the age distribution of CoNS bacteremia cases. The 41-60 years age group had the highest incidence (38.4%, n=109), followed by >60 years (32.0%, n=91), 21-40 years (19.7%, n=56), and 0-20 years (9.9%, n=28). The bimodal distribution peaks in middle-aged and elderly populations, reflecting increased susceptibility with advancing age.

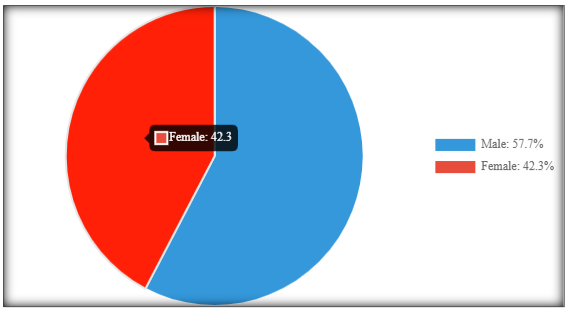

Figure 4: Gender Distribution

Pie chart depicting gender distribution among CoNS bacteremia cases. Males predominated with 164 cases (57.7%) compared to 120 females (42.3%), resulting in a male-to-female ratio of 1.37:1. This male predominance may reflect differential exposure to healthcare settings or underlying risk factors.

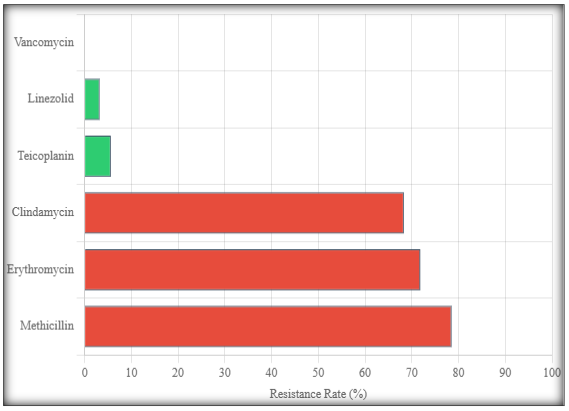

Figure 5: Antimicrobial Resistance Rates

Horizontal bar chart displaying resistance rates for nine antimicrobial agents, arranged from highest to lowest resistance. Methicillin showed the highest resistance (78.5%), followed by erythromycin (71.8%) and clindamycin (68.3%). Excellent susceptibility was maintained to vancomycin (100%), linezolid (96.8%), and teicoplanin (94.4%), representing crucial therapeutic options.

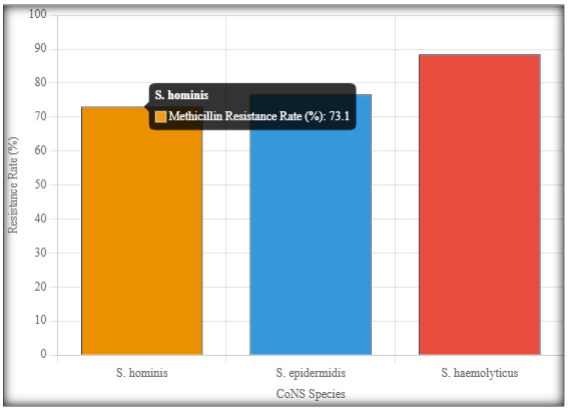

Figure 6: Methicillin Resistance by Species

Bar chart comparing methicillin resistance rates among the three major CoNS species. S. haemolyticus exhibited the highest resistance rate (88.5%), followed by S. epidermidis (76.7%) and S. hominis (73.1%). The overall resistance rate was 78.5%. These species-specific differences have important implications for empirical therapy selection.

DISCUSSION

This comprehensive study provides valuable insights into the epidemiology and antimicrobial resistance patterns of CoNS bacteremia in a South Indian tertiary care setting. Our findings demonstrate that CoNS have indeed moved "beyond aureus" to become major pathogens, accounting for more than two-thirds of all staphylococcal bloodstream infections at our institution.

The predominance of S. epidermidis (72.5%) in our study aligns with global trends, where this species consistently emerges as the leading cause of CoNS bacteremia (22,23). The significant representation of S. haemolyticus (18.3%) is particularly noteworthy, as this species has gained recognition for its remarkable ability to develop antimicrobial resistance and its association with severe infections in immunocompromised hosts.[24]

Our methicillin resistance rate of 78.5% is concerning but consistent with reports from other Indian tertiary care centers, where MR-CoNS rates ranging from 65% to 85% have been documented.[7,8] This high resistance burden reflects the selective pressure exerted by widespread β-lactam use in hospital settings and highlights the urgent need for antimicrobial stewardship programs.[25]

The universal susceptibility to vancomycin observed in our study is reassuring and consistent with most Indian reports.[11,12] However, the emergence of vancomycin-intermediate and vancomycin-resistant

CoNS has been reported from various parts of the world, necessitating continued vigilance and appropriate susceptibility testing.[16]

The high susceptibility to linezolid (96.8%) and teicoplanin (94.4%) provides important therapeutic options for treating MR-CoNS infections. However, the increasing use of these agents may lead to resistance development, as evidenced by reports of linezolid-resistant CoNS from various centers globally.[15]

The significant association between multidrug resistance and methicillin resistance observed in our study has important clinical implications. MR-CoNS isolates not only showed resistance to β-lactam antibiotics but also exhibited co-resistance to multiple other antimicrobial classes, limiting therapeutic options and potentially leading to worse clinical outcomes.[19,20]

The higher mortality observed in ICU patients and those with MR-CoNS infections highlights the need for prompt recognition, appropriate antimicrobial therapy, and aggressive supportive care in these high-risk populations.

Clinical Implications

Our findings have several important clinical implications. First, the high prevalence of MR-CoNS necessitates empirical antimicrobial therapy that covers methicillin-resistant organisms in patients with suspected CoNS bacteremia. Second, the association with critical care areas emphasizes the importance of strict infection control measures in ICU settings.

Limitations

This study has several limitations. As a single-center retrospective study, the generalizability of findings may be limited. The distinction between true infection and contamination in CoNS bacteremia can be challenging, although we used strict criteria to minimize inclusion of contaminants. Additionally, molecular characterization of isolates and detection of specific resistance genes were not performed due to resource constraints.

CONCLUSION

CoNS bacteremia represents a significant and growing challenge in our tertiary care setting, with S. epidermidis being the predominant species. The alarmingly high rate of methicillin resistance (78.5%) underscores the urgent need for comprehensive infection prevention and control strategies.

The universal susceptibility to vancomycin and high susceptibility to linezolid provide valuable therapeutic options, but judicious use is essential to preserve their efficacy. The significant mortality associated with CoNS bacteremia, particularly in ICU patients and those with resistant isolates, emphasizes the clinical importance of these infections.

Enhanced surveillance systems, robust antimicrobial stewardship programs, strict infection control measures, and continued research into novel therapeutic approaches are essential to combat the rising tide of CoNS bacteremia. Future studies incorporating molecular epidemiology and resistance mechanisms will provide deeper insights into the pathogenesis and spread of these emerging pathogens.

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