

Occurrence of *ESKAPE* Blood Culture Pathogens Isolated in the Intensive Care Units of a Tertiary Care Teaching Hospital in Delhi: A Descriptive Cross-Sectional Analysis

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Abstract

Background: A comprehensive overview of *ESKAPE* pathogens, highlighting their antibiotic resistance mechanisms and the urgent need to address the clinical impact of these pathogens in bloodstream infections.

Objectives: The aim of the present study was to observe the prevalence and trends of antibiotic susceptibility profiles of *ESKAPE* blood pathogens in Intensive Care Units (ICUs), providing valuable insights for improving patient care and infection control.

Methods: A detailed description of our descriptive cross-sectional study conducted in various ICUs, including blood sample collection, antibiotic susceptibility testing, and data management and statistical analysis.

Results: The findings of the present study reveal insight into the distribution of *ESKAPE* pathogens in different ICUs, with a focus on prevalence, age-specific variations, and antibiotic resistance patterns.

Conclusion: A thorough discussion on the clinical implications of our results, emphasizing the high prevalence of *Acinetobacter baumannii*, *Staphylococcus aureus*, and *Klebsiella pneumoniae*, and the concerning levels of antibiotic resistance observed.

Keywords: Pathogen, Antibiotic Resistance, Intensive Care Units, Bloodstream Infections, Surveillance

1. Background

Bloodstream infections caused by *ESKAPE* pathogens represent a formidable challenge in modern healthcare settings.¹ The acronym *ESKAPE* encompasses a group of bacterial species that have developed alarming levels of antibiotic resistance, rendering conventional treatments increasingly ineffective.² These nosocomial pathogens, consisting of *Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacter species*, have demonstrated the ability to "escape" the bactericidal effects of antibiotics through various mechanisms, including the acquisition of resistance genes and the formation of biofilms.^{2,3}

Recent studies have underscored the urgency of understanding and addressing the clinical impact of *ESKAPE* pathogens in bloodstream infections.¹ As these bacteria continue to evolve and acquire new resistance mechanisms, they pose a significant threat to patient outcomes and healthcare systems worldwide.⁴ In the face of this emerging healthcare crisis, various aspects of *ESKAPE* pathogens, including their epidemiology, antibiotic resistance mechanisms, and clinical outcomes associated with bloodstream infections have been studied extensively.⁵ The increasing prevalence of multidrug-resistant and extensively drug-resistant strains within the *ESKAPE*

group further exacerbates the challenge of managing infections caused by these notorious pathogens.⁶ Surveillance of *ESKAPE* pathogens in ICU settings has become an essential component of infection control and prevention strategies.⁷ The unique environment of ICUs, characterized by critically ill patients, invasive procedures, and a high prevalence of antibiotic usage, presents an ideal breeding ground for *ESKAPE* pathogens.⁸ Hence, monitoring their prevalence and antibiotic susceptibility profiles within these units is vital for implementing targeted interventions, optimizing empiric antibiotic therapy, and curbing the spread of multidrug-resistant strains.⁶⁻⁸

2. Objectives

The aim of the present study was to observe the prevalence and trends of antibiotic susceptibility profile of *ESKAPE* blood pathogens isolated in the ICUs of a tertiary care teaching hospital. This may ultimately provide valuable insight into challenges and opportunities for improving patient care and infection control in ICUs.

3. Methods

This research was a descriptive cross-sectional study conducted in various ICUs and the Department of

Microbiology, UCMS & GTB hospital, Delhi from January to December 2022. Clinical specimens were collected from patients admitted to the Critical Care Unit (CCU), Medicine ICU (MICU), Neonatal ICU (NICU), Paediatric ICU (PICU), and Trauma ICU (TICU) during the study period of one year. A total of 742 *ESKAPE* pathogens were analysed for various parameters.

3.1. Blood Sample Collection

Blood samples were collected aseptically from the study subjects and were subsequently transferred to BactAlert blood culture bottles. The blood culture bottles were immediately transported to the bacteriology laboratory and loaded into the BactAlert system. Samples were aseptically subcultured onto 5% of sheep blood agar and MacConkey agar plates immediately upon the detection of microbial growth as indicated by the BacTAlert system's alert signal. The subsequent processing was done as per the standard protocol.

3.2. Antibiotic Susceptibility Testing

Antimicrobial susceptibility testing of the blood culture isolates was done using the Kirby-Bauer disk diffusion method. This method was carried out on Mueller–Hinton agar plates in accordance with the guidelines outlined in the CLSI 2023 (Clinical and Laboratory Standards Institute, 2023). Vancomycin and Linezolid were tested using gradient diffusion strips. It is worth noting that not all antibiotics were tested for every microorganism, and as part of the quality control process, *Escherichia coli* (ATCC 25922), *Staphylococcus aureus* (ATCC 25923), and *Pseudomonas aeruginosa* (ATCC 27853) control strains were used in the Kirby Bauer disc diffusion method. Each antibiotic was tested with control strain.

Furthermore, each isolate was considered as a single patient.

3.3. Data Management and Statistical Analysis

Data recording was carried out using the MS Excel spreadsheet program. Categorical variables were summarized using frequencies and percentages. To compare groups in terms of categorical data, the Chi-square test was employed. A *p*-value of less than 0.05 was considered as the threshold for statistical significance.

4. Results

According to findings, this study provides insight into the prevalence of *ESKAPE* pathogens, shedding light on the distribution of these clinically significant bacteria in ICU settings. During the study period, 742 were the total *ESKAPE* pathogens. A total of 164 isolates were gram-positive, while 578 isolates were gram-negative *ESKAPE* pathogens. Among the different Intensive Care Units (ICUs), the distribution of isolated organisms varied, with 22 (3%) isolates in the CCU, 178 (30%) in the MICU, 517 (70%) in the NICU, 10 (1.7%) in the PICU, and 5 (0.8%) in the TICU. The highest number of isolates was observed in the NICU (70%), highlighting the unique microbial challenges associated with neonatal care. NICU has more statistically significant prevalent isolated organisms ($p < 0.05$, paired t test).

As depicted in Figure 1, we observed that *Acinetobacter baumannii* (34%) was the most frequently isolated pathogen, accounting for over one-third of the clinical isolates. *Klebsiella pneumoniae* (25%) was the second most prevalent pathogen, followed closely by *Staphylococcus aureus* (20%). The *P*-value was statistically significant amongst the various organisms ($p < 0.03$, chi-square test).

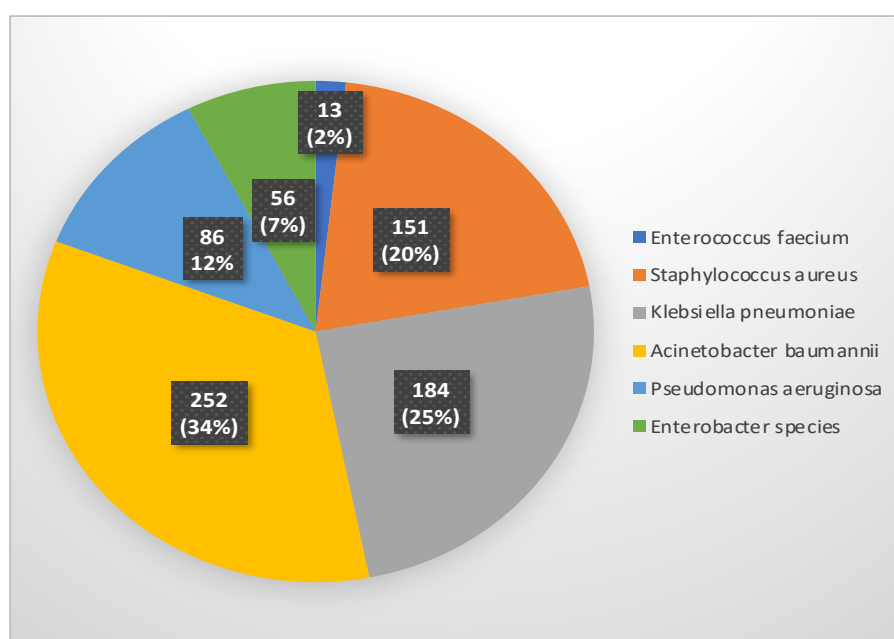


Figure 1. Frequency and Percentage Distribution of *ESKAPE* Pathogens in Various ICUs during the Study Period (n = 742).

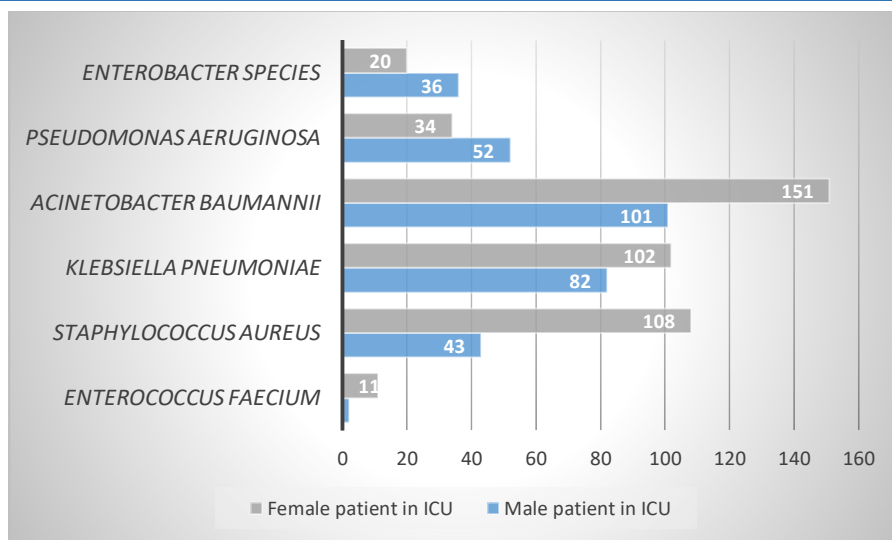


Figure 2. The Distribution of *ESKAPE* Pathogens among Male and Female Patients in ICUs (n = 742).

The distribution of *ESKAPE* pathogens in ICU patients, stratified by age groups, reveals several findings with potential clinical implications (Table 1). The gender-specific variations in *ESKAPE* pathogen distribution is highlighted in Figure 2. Tables 2 and 3 present rates

of susceptibility for gram-positive and gram-negative *ESKAPE* pathogens isolated in various ICUs. Findings depict the antibiotic resistance patterns of these pathogens, which are notorious for their ability to escape the effects of antibiotics.

Table 1. The Distribution of *ESKAPE* Pathogens among ICU Patients (n = 742)

Organism	Newborn	1 month-18 years	19-45 years	46-60 years	>60 years
<i>Enterococcus faecium</i> (n = 13)	5 (38.4%)	0	8 (61.5%)	0	0
<i>Staphylococcus aureus</i> (n = 151)	89 (58.9%)	9 (5.9%)	21 (13.9%)	13 (8.6%)	19 (12.5%)
<i>Klebsiella pneumoniae</i> (n = 184)	163 (88.5%)	0	4 (2.17%)	16 (8.6%)	1 (0.54%)
<i>Acinetobacter baumannii</i> (n = 252)	159 (63.1%)	19 (7.5%)	42 (16.6%)	29 (11.5%)	3 (1.19%)
<i>Pseudomonas aeruginosa</i> (n = 86)	61 (70.9%)	12 (13.9%)	7 (8.13%)	3 (3.48%)	3 (3.48%)
<i>Enterobacter species</i> (n = 56)	34 (60.7%)	0	8 (14.2%)	2 (3.57%)	2 (3.57%)
Statistically significant (Fischer's exact test)	p < 0.02	p = 0.08	p < 0.02	p = 0.06	p = 0.023

Table 2. Rates of Susceptibility for Gram-positive *ESKAPE* Pathogens Isolated ICUs (n = 164)

Antibiotics	<i>Enterococcus faecium</i> (n = 184)	<i>Staphylococcus aureus</i> (n = 86)
Amoxiclav	IR*	57.10%
Vancomycin	100%	100%
Erythromycin	IR*	57.10%
Clindamycin	IR*	53.10%
Gentamicin	IR*	86.80%
Linezolid	100%	100%
Ciprofloxacin	23.07%	32.90%
Teicoplanin	76.90%	90%
Cotrimoxazole	IR*	96%
High-level Gentamicin	84.60%	-
Cefoxitin	-	29.70%

*IR = Intrinsic resistance

Table 3. Rates of Susceptibility for Gram-negative *ESKAPE* Pathogens Isolated in ICUs (n = 578)

Antibiotics	<i>Klebsiella pneumoniae</i> (n = 184)	<i>Acinetobacter baumannii</i> (n = 252)	<i>Pseudomonas aeruginosa</i> (n = 86)	<i>Enterobacter species</i> (n = 56)
Cefotaxime	0%	NT*	IR**	NT*
Ceftriaxone	9.10%	15.06%	IR**	25%
Amoxiclav	7.10%	IR**	IR**	NT*
Ceftazidime	15.80%	27.80%	37%	25%
Ciprofloxacin	29.30%	35.30%	66.60%	32.50%
Imipenem	27.60%	33.70%	49.30%	57.50%
Piperacillin-tazobactam	24.90%	24.80%	79.60%	10%
Gentamicin	31.50%	31.10%	52.30%	75%
Aztreonam	21.50%	IR**	34.10%	12.50%
Tobramicin	NT*	50.10%	54.70%	NT*

*NT = Not tested, **IR = Intrinsic resistance

5. Discussion

Antimicrobial Resistance (AMR) poses a growing and significant challenge in the majority of healthcare institutions. Hospital-Acquired Infections (HAIs) that are resistant to multiple drugs significantly contribute to inpatient morbidity and mortality. Notably, the ICUs are the primary hotspot for HAIs.⁹ Thus; this study was conducted to assess the prevalence and trends of antibiotic susceptibility profile of ESKAPE blood pathogens isolated in the ICUs of a tertiary care hospital.

The results presented in this study provided data regarding the isolation frequency and percentage of various ESKAPE pathogens. These findings are significant and bear implications for both clinical practice and public health. The isolation frequency of *Acinetobacter baumannii* (34%) is strikingly high, indicating its dominance among the ESKAPE pathogens. These bacteria are notorious for their ability to thrive in healthcare settings, causing difficult-to-treat infections, especially in critically ill patients. A study done in an ICU of Mexico also reported *A. baumannii* (15.8%) to be the most frequently isolated organism, similar to our findings.⁷

The relatively high prevalence of *Staphylococcus aureus* (20%) in our study is concerning, due to its ability to acquire antibiotic resistance, including methicillin-resistant *Staphylococcus aureus* (MRSA). The isolation of *Klebsiella pneumoniae* (25%) at a significant frequency highlights its prevalence and potential clinical impact, as they are notorious for their multidrug resistance, particularly to carbapenems, which are often considered last-resort antibiotics. Although *Pseudomonas aeruginosa* was isolated at a moderate frequency (12%) in our study, its clinical significance should not be underestimated. Another study carried out in Romania on ESKAPE pathogens revealed *Pseudomonas aeruginosa* to be the most frequently isolated ESKAPE pathogen, contrast to our study findings.¹⁰

Enterococcus faecium is most prevalent in patients aged 19-45 years (61.5%), while *Staphylococcus aureus* dominates in new-borns (58.9%) and those aged 1 month to 18 years (55.9%). *Klebsiella pneumoniae* overwhelmingly affects new-borns (88.5%) and diminishes in prevalence with age, highlighting neonatal susceptibility. *Acinetobacter baumannii* exhibits a relatively uniform distribution across age groups, emphasizing its broad impact, while *Pseudomonas aeruginosa* is prominent in new-borns (70.9%) with a declining trend in older age groups.

In our study, *Enterococcus faecium* has shown complete susceptibility to Vancomycin and Linezolid, indicating the efficacy of these antibiotics. A similar pattern of sensitivity has been observed in a study conducted in Italy on *Enterococcus* species on isolated from various clinical samples.¹¹ *Staphylococcus aureus*, especially Methicillin-Resistant *Staphylococcus aureus* (MRSA), exhibits a concerning level of resistance to Co-Amoxiclav, Erythromycin, Clindamycin, and Ciprofloxacin, with resistance

rates exceeding 50%, indicating a substantial challenge in treating infections caused by these strains. Various studies which have been globally conducted have also reported similar findings.^{12,13} This resistance poses a serious threat to conventional treatment strategies, leading to the need for alternative therapeutic approaches. However, it is highly susceptible to Vancomycin and Linezolid. *Klebsiella pneumoniae* in our study shows alarmingly high resistance to most antibiotics listed, with susceptibility rates often below 10%. This includes complete resistance to Cefotaxime, Co-Amoxiclav, and Ceftazidime. The limited susceptibility to antibiotics like Gentamicin and Piperacillin-tazobactam suggests a challenging scenario in the treatment of *Klebsiella pneumoniae* infections in ICUs. A similar pattern of resistance has been observed in a study conducted in ICU patients in North India.¹⁴ *Acinetobacter baumannii* exhibits variable resistance patterns in our study. Notably, it shows high resistance to Ciprofloxacin and significant resistance to Imipenem. However, it demonstrates intrinsic resistance to several antibiotics, highlighting the importance of selecting appropriate antibiotics and monitoring resistance trends for this pathogen. *Pseudomonas aeruginosa* is highly resistant to most antibiotics, with complete resistance to Cefotaxime and Ceftriaxone. The resistance levels for Ciprofloxacin and Piperacillin-tazobactam are also concerning. This emphasizes the critical need for alternative treatment strategies when dealing with *Pseudomonas aeruginosa* infections in ICUs. *Enterobacter species* have varying susceptibility patterns, with resistance to some antibiotics but susceptibility to others. Gentamicin and Imipenem show effectiveness against these pathogens. However, Tobramycin and Ceftriaxone demonstrate limited success.

This study sheds light on the clinical implications of antibiotic resistance patterns among ESKAPE pathogens, emphasizing the challenges faced by clinicians in selecting appropriate empirical antibiotic therapy. The observed resistance, particularly in key pathogens such as *Acinetobacter baumannii* and *Klebsiella pneumoniae*, poses a considerable threat to the effectiveness of conventional treatments. This fact is particularly concerning in critically ill patients who may have limited alternative therapeutic options.

The practical consequences of antibiotic resistance extend beyond the choice of antibiotics. Prolonged hospital stays, increased healthcare costs, and elevated mortality rates are among the significant outcomes associated with infections caused by multidrug-resistant strains. Our findings underscore the urgency of implementing and strengthening antibiotic stewardship programs to ensure the judicious use of antibiotics, minimize the development of resistance, and optimize patient outcomes

6. Conclusion

The findings of the present study highlights the critical

issue of antibiotic resistance among *ESKAPE* pathogens in ICUs. It underscores the need for stringent antibiotic stewardship programs to ensure the appropriate use of antibiotics and the development of alternative treatment strategies to combat these resistant pathogens effectively. Additionally, ongoing surveillance and monitoring of resistance patterns are essential to adapt treatment protocols and preserve the effectiveness of antibiotics in ICU settings.

6.1. Limitations and Future Directions

The study was conducted in a single tertiary care teaching hospital in Delhi, limiting the generalizability of the findings to broader geographical locations or diverse healthcare settings.

The antibiotic susceptibility testing focused on a specific panel, and not all antibiotics were tested for every microorganism. This could influence the comprehensiveness of the resistance profiles.

However, conducting multi-centric studies across diverse healthcare settings would enhance the generalizability of findings and provide a more comprehensive understanding of *ESKAPE* pathogens on a broader scale. Future research should explore the longitudinal trends of *ESKAPE* pathogens over extended periods to capture potential variations and emerging patterns in prevalence and resistance. Future studies could delve deeper into the clinical outcomes

associated with infections caused by *ESKAPE* pathogens, providing a more holistic understanding of the impact on patient morbidity and mortality.

Addressing these limitations and pursuing these future directions would contribute to a more robust understanding of *ESKAPE* pathogens, aiding in the development of effective strategies for their management and control in healthcare settings.

Author Contributions

KN and KS conceptualized the study, formulated the protocol, participated in data collection, performed statistical analyses, interpreted the findings, and drafted the manuscript. DC contributed to data collection, while SD provided consultation and collaborated on the study design. The final version of the manuscript received approval from all authors for submission.

Conflict of Interest Disclosures

All authors declared that they have no conflict of interest.

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Research Highlights

What Is Already Known?

- The acronym *ESKAPE* encompasses a group of bacterial species, including *Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacter* species.
- These pathogens are notorious for their ability to "escape" the effects of antibiotics through various mechanisms, posing a significant challenge in modern healthcare settings.
- The global prevalence of multidrug-resistant strains within the *ESKAPE* group has heightened concerns regarding the efficacy of conventional treatments and has spurred extensive research on their clinical impact.

What Does This Study Add?

- This study contributes a comprehensive analysis of the occurrence and antibiotic susceptibility profiles of *ESKAPE* pathogens in the ICUs of a tertiary care teaching hospital in Delhi.
- This study not only adds to the existing knowledge on *ESKAPE* pathogens but also provides a localized perspective, enhancing our understanding of the prevalence and antibiotic resistance patterns in a specific healthcare setting.
- The findings call for continuous surveillance, targeted interventions, and a holistic approach to infection control in ICUs to mitigate the growing threat of multidrug-resistant *ESKAPE* pathogens and improve patient outcomes.

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