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Original Research Article

Examining Microbial Infections and Antibiotic Resistance in ICU Patients: A Study on Tracheal Aspirates in a Tertiary Care Hospital

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Abstract:
Background: The rise of microbial infections and antibiotic resistance in Intensive Care Units (ICUs) represents a significant challenge in healthcare, with ICUs becoming focal points for nosocomial infections, often complicated by multidrug-resistant organisms. This study aims to explore the patterns of microbial infections and antibiotic resistance in ICU patients, with a focus on tracheal aspirates, to enhance empirical treatment strategies and promote antimicrobial stewardship.
Methods: A retrospective cross-sectional analysis was performed on 100 endotracheal aspirate samples collected from ICU patients at Jawaharlal Nehru Institute of Medical Sciences, Imphal, between November and April 2023. Samples were processed using standard microbiological techniques, including Gram staining, culture, and antimicrobial susceptibility testing, to identify pathogens and assess their resistance profiles.
Results: The study revealed a 75% positive culture rate from the analyzed samples, with a notable predominance of Gram-negative bacilli (70%) over Gram-positive cocci (4%). The majority of isolates displayed multidrug resistance, with significant resistance observed to tetracycline (52.8%), ceftriaxone and ceftazidime (39.9%), amoxicillin-clavulanic acid (40%), and ciprofloxacin (38.6%). Carbapenem-resistant isolates accounted for 31.4% of the total. *Klebsiella* species and *Pseudomonas aeruginosa* were the most frequently isolated pathogens, showing high levels of resistance to commonly used antibiotics.
Conclusion: The study underscores the urgent need for targeted antimicrobial stewardship and the development of empirical antibiotic policies tailored to local microbiological profiles and resistance patterns. Addressing the challenge of antibiotic resistance in ICUs requires a multifaceted approach, including continuous surveillance and the judicious use of antibiotics.
Recommendation: To combat the escalating issue of antibiotic resistance, it is crucial to implement robust infection control measures, promote the rational use of antibiotics, and enhance local surveillance efforts to guide empirical therapy effectively.
Keywords: ICU, Antibiotic Resistance, Tracheal Aspirates, Antimicrobial Stewardship.

Introduction

The escalating challenge of microbial infections and the concurrent crisis of antibiotic resistance within the confines of intensive care units (ICUs) of tertiary care hospitals marks a critical concern in modern healthcare. These ICUs, designed as sanctuaries for the treatment of severe and life-threatening conditions, paradoxically emerge as breeding grounds for nosocomial infections, often exacerbated by the presence of multidrug-resistant organisms. This paradox is central to the study which endeavors to dissect the complex interplay between microbial infections and antibiotic resistance, particularly through the lens of tracheal aspirates [1,2,3].

Tracheal aspirates serve as a crucial diagnostic tool, offering a direct insight into the microbial landscape pervading the ICU. This biological material, obtained from the tracheobronchial tree, is instrumental in identifying the pathogens responsible for infections and their antibiotic susceptibility profiles [4,7]. Given the critical role of the respiratory tract in maintaining pulmonary health and its susceptibility to infections, especially in mechanically ventilated patients, tracheal aspirates provide invaluable data for understanding and combating ICU-acquired infections [5,6].

The phenomenon of antibiotic resistance, a growing global health emergency, is significantly fueled by the indiscriminate and inappropriate use of antibiotics across various sectors, including human medicine, agriculture, and animal husbandry. Within the ICU, the prevalent use of broad-spectrum antibiotics, intended to treat or prevent infections in critically ill patients, inadvertently fosters an environment conducive to the selection and proliferation of resistant microbial strains. This study hypothesizes that a detailed examination of tracheal aspirates from ICU patients will not only unveil the primary microbial agents inciting infections but also illuminate prevailing patterns of antibiotic resistance, thereby guiding the optimization of empiric antibiotic therapy and informing infection control and antibiotic stewardship initiatives[8,9].

The choice of a tertiary care hospital as the setting for this investigation is deliberate, capitalizing on the complex case mix and advanced medical resources characteristic of such institutions. This environment is anticipated to yield a comprehensive dataset reflective of the nuanced challenges inherent in managing ICU infections and navigating the intricacies of antibiotic resistance [10,11].

The scourge of ventilator-associated pneumonia (VAP), a predominant nosocomial infection tied to mechanical ventilation and endotracheal intubation, exemplifies the intricate relationship between medical interventions and infection risk. The disruption of normal ciliary function and the formation of biofilms on endotracheal tubes underscore the multifaceted nature of VAP, which predominantly involves both Gram-negative and Gram-positive bacteria, including *Pseudomonas aeruginosa*, *Escherichia coli*, *Acinetobacter baumannii*, *Klebsiella pneumoniae*, and *Staphylococcus aureus*[12-17].

Endotracheal aspiration (ETA) stands out as an essential, yet underutilized, diagnostic practice, capable of identifying the causative agents of fever and pneumonia in ventilated patients with notable simplicity and minimal invasiveness. Despite its clinical value, a notable paucity of data persists regarding the bacterial pathogens implicated in lower respiratory tract infections within the Indian clinical landscape and the resistance patterns exhibited by these pathogens. This variability in resistance patterns, differing markedly across hospital settings, highlights the imperative for continuous research aimed at tailoring antimicrobial strategies to local microbial and resistance profiles. [18,19]

This study seeks to elucidate the colonization patterns of tracheal aspirates in ICU patients and identify the most efficacious antimicrobial agents for managing these infections, thereby furnishing clinicians with vital information to guide empiric antibiotic therapy and inform antibiotic policy revisions. Through its findings, the study aspires to enhance the overall management of respiratory infections in critical care settings, addressing a critical gap in current medical knowledge and practice.

Material and Methodology

Study Design: This investigation was a retrospective cross-sectional study carried out in the bacteriology section of the Department of Microbiology at Jawaharlal Nehru Institute of Medical Sciences, Imphal, spanning from November to April 2023. A collection of 100 endotracheal aspirate samples was analyzed, which were collected from various intensive care units (ICUs) within the hospital. These samples were stored in sterile, leak-proof containers and tubes to ensure their integrity for microbiological examination.

Inclusion and Exclusion Criteria: The study incorporated samples from patients exhibiting symptoms such as cough with purulent sputum, fever with infiltration visible in chest X-rays, or sepsis with multi-organ dysfunction syndrome accompanied by lung infiltration. These symptoms had to persist despite conventional antibiotic treatments for inclusion. Exclusion criteria involved patients who died within two days of the event, those discharged against medical advice within 48 hours of mechanical ventilation, and patients admitted with pneumonia.

Microbiological Processing: Of the total samples, 100 endotracheal aspirates (ETAs) underwent immediate microbiological processing, adhering to standard procedures including microscopy, culture, and antimicrobial susceptibility testing. The initial assessment involved Gram staining to identify pus and epithelial cells, applying the Bartlett criteria to evaluate sample significance based on the presence of inflammatory and Squamous Epithelial Cells (SEC) under a low-power field (LPF). The Q score system was used to determine the specimen's quality, with scores assigned based on the relative counts of White Blood Cells (WBCs) and SECs. Samples were then subjected to semi-quantitative culture techniques, regardless of their Q score.

Samples were liquefied mechanically and homogenized in saline solution before being cultured on various media, including 5% defibrinated sheep Blood Agar (BA), MacConkey agar, and Sabouraud Dextrose Agar (SDA). The cultures were incubated under specific conditions, with colony-forming units per milliliter (cfu/mL) measured to determine clinical significance. Identification and quantification of colonies followed standard biochemical tests, with significant microbial presence defined as ≥10^5 cfu/mL. Antimicrobial susceptibility was assessed using the Kirby Bauer disc diffusion method, in line with the latest Clinical and Laboratory Standards Institute (CLSI) guidelines.

Statistical Analysis: Data was systematically entered into Microsoft Excel, with statistical analyses conducted using SPSS software (Version 27, IBM). Descriptive statistics, including mean, median, mode, and standard deviation, were calculated for continuous variables. Categorical variables were analyzed using frequency, percentage, and the Chi-square test to examine relationships and trends within the data. This comprehensive approach enabled a detailed examination of microbial infections and antibiotic resistance patterns in ICU patients, contributing valuable insights to optimize clinical management and treatment strategies.

Results

During the study period, 100 endotracheal aspirate samples were collected from ICU patients, with a significant majority being male (83%) compared to female (17%). Despite the gender disparity, there was no statistically significant difference in the occurrence of blood culture growths between males and females (p-value=0.3), indicating that gender did not influence the prevalence of microbial growth in this study.

Microbial Growth and Age Distribution: Out of the 100 samples analyzed, 75% showed microbial growth, while 25% had no growth. The majority of patients with microbial growth were above 40 years of age (57%), suggesting that older patients were more susceptible to infections leading to microbial growth in tracheal aspirates. However, the age distribution did not significantly affect the presence of microbial growth (p-value=0.739), pointing to the widespread susceptibility across different age groups.

Microbiological Profile: The microbiological examination revealed a dominance of gram-negative bacteria, constituting 70% of the total isolates. Klebsiella species were the most prevalent (39%), followed by *Pseudomonas aeruginosa* (20%). Other notable pathogens included *Acinetobacter baumannii* (7%), *Escherichia coli* (3%), and *Proteus mirabilis* (1%). A single instance of a fungal species (*Candida*) was also identified, alongside gram-positive cocci (*Staphylococcus aureus,* 4%).

Antibiotic Sensitivity Patterns: Antibiotic sensitivity testing highlighted Imipenem (48.6%) and Piperacillin-Tazobactam (38.6%) as the most effective antibiotics against gram-negative isolates. Conversely, Amoxicillin showed the lowest sensitivity rate (1.4%). The resistance patterns varied among different bacteria, with *Klebsiella species* and *Pseudomonas aeruginosa* showing considerable resistance to a broad spectrum of antibiotics, including Amoxyclavulanic Acid, Ciprofloxacin, and Tetracycline. Acinetobacter baumannii demonstrated high resistance rates to Tetracycline (85.7%) and Gentamicin (42.9%), indicating a challenging resistance profile across common antibiotics.

Resistance Profile of Gram-negative Bacteria: The study further detailed the antibiotic resistance pattern among gram-negative bacteria. Acinetobacter baumannii displayed notable resistance to several antibiotics, with an alarming 85.7% resistance rate to Tetracycline. In contrast, Klebsiella pneumoniae and *Pseudomonas aeruginosa* showed universal resistance to commonly used antibiotics such as Amoxicillin-Clavulanic Acid and Ciprofloxacin. Resistance to Carbapenems (Meropenem and Imipenem) was observed in 28.6% of Acinetobacter baumannii isolates, 23.1% of Klebsiella pneumoniae, and 55% of Pseudomonas aeruginosa, highlighting a concerning trend of resistance against last-resort antibiotics.

This detailed analysis highlights the critical issue of microbial infections and antibiotic resistance in ICU settings, emphasizing the need for vigilant monitoring, effective antimicrobial stewardship, and targeted therapeutic interventions to combat the rising tide of resistant pathogens.

Table-1: Gender distribution among the study population

Growth	Males n (%)	Female n (%)	Total
Present	65 (65%)	10 (10%)	75 (75%)
Absent	18 (18%)	7 (7%)	25 (25%)
Total	83 (83%)	17(17%)	100 (100%)
Chi-square test p value = 0.3*			

Table 2: Age distribution among the study population

Age	Growth present n (%)	Growth absent n (%)	Total n (%)
< 40 years	18 (18%)	6 (6%)	24 (24%)
>41 years	57 (57%)	19 (19%)	76 (76%)
Total	75 (75%)	25 (25%)	100 (100%)
Chi-square test p value = 0.739			

Table 3: Total no of growth

Total growth n (%)	No growth n (%)	Total
75 (75%)	25 (25%)	100(100%)

Table 4: Microbiological profile of tracheal aspirates (N=100)

Organism	n (%)
Klebsiella species	39 (39%)
Proteus mirabilis	1 (%)
Escherichia coli	3 (3%)
Pseudomonas aeruginosa	20 (20%)
Staphylococcus aureus	4 (4%)
Acinetobacter baumannii	7 (7%)
Candida species	1 (1%)
No growth	25 (25%)

Table 5: Antibiotic sensitivity of bacteria (n=70).

Antibiotics	Sensitive	Antibiotics	Sensitive
Amoxy-clavulanic Acid	3(4.3%)	Vancomycin	4(5.7%)
Ciprofloxacin	25(35.7%)	Ceftriaxone	7(10%)
Imipenem	34 (48.6%)	Amoxicillin	1(1.4%)
Azithromycin	16 (7.4%)	Piperacillin -Tazobactam	27(38.6%)
Cefepime	12 (22.9%)	Clindamycin	10(14.3%)
Cotrimoxazole	6(8.6%)	Polymyxin B	7 (10%)
Tetracycline	10(14.3)	Amikacin	9 (12.9%)
Amikacin	9(12.9%)	Cefotaxime	2 (2.9%)
Meropenem	18(25.7%)	Colistin	2(2.9%)
Gentamicin	3(4.3%)	Levofloxacin	3(4.3%)
Ceftazidime	11(15.7%)		

Table 6: Antibiotic resistance pattern of gram-negative bacteria

Antibiotics	***Klebsiella* species (n = 39)**	***Proteus mirabilis* (n = 1)**	***Escherichia Coli* (n = 3)**	***Pseudomonas aeruginosa* (n = 20)**	***Acinetobacter baumannii* (n = 7)**
Amoxyclavulanic Acid (Betalactam + Betalactamase Inhibitor Combination)	21 (53.8%)	0 (0%)	0 (0%)	6 (30%)	1 (14.2%)
Ciprofloxacin (Fluoroquinolone)	18(46.1%)	0(0%)	1(33.3%)	5(25%)	3(42.9%)
Imipenem (Carbapenem)	1(2.6%)	0(0%)	0(0%)	5(25%)	1(14.2%)
Meropenem (Carbapenem)	8(20.5%)	0(0%)	0(0%)	6(30%)	1(14.2%)
Azithromycin (Macrolides)	21(53.8%)	2(50%)	2(66.6%)	0(0%)	0(0%)
Cotrimoxazole (Sulphur or sulfonamides)	30 (76.9%)	1(100%)	1(33.3%)	11(55%)	0(0%)
Tetracycline (Glycylcycline)	20(51%)	0(0%)	2(66.6%)	9(45%)	6(85.7%)
Gentamicin (Aminoglycoside)	2(5.1%)	0(0%)	0(0%)	4(20%)	3(42.9%)
Piperacillin Tazobactam	1(2.6%)	0(0%)	0(0%)	2(10%)	3(42.9%)

(Penicillin and Beta Lactamase Inhibitor)					
Ampicillin (Penicillin)	5(15.8%)	0(0%)	0(0%)	4(20%)	0(0%)
Cefazolin (2nd Generation Cephalosporin)	7(18%)	0(0%)	0(0%)	3(15%)	1(14.2%)
Ceftazidime (3rd Generation Cephalosporin)	10(25.6%)	1(100%)	0(0%)	0(0%)	0(0%)
Ceftriaxone (3rd Generation Cephalosporin)	11(28.2%)	0(0%)	0(0%)	0(0%)	1(14.2%)

Discussion

The misuse of antibiotics has significantly contributed to the emergence of resistant bacteria in therapeutic environments, posing a considerable challenge in the management of nosocomial infections. Patients in intensive care units (ICUs) are especially vulnerable due to the high incidence of invasive treatments, such as mechanical ventilation, which amplify the risk of acquiring hospital-acquired infections like ventilator-associated pneumonia (VAP). [20-23] The severity of untreated VAP emphasizes the need for an effective empirical antibiotic policy tailored to the specific pathogens prevalent in the ICU setting. The variation in etiological agents across different studies reflects the influence of the research population and the specifics of the ICU environment.

Our study demonstrated a positive culture rate of 75%, indicating a substantial prevalence of microbial growth in collected samples. This rate varies when compared to findings from other studies, such as Pallavi Chitrans et al. [24] with a 55.3% positive rate, Sanjana Rajkumari et al. [25] with 100%, and Prajapati BK et al. [1]with 88.4%, suggesting that factors like the diversity of the study population or colonization of the endotracheal (ET) tube could account for these differences. Notably, gram-negative bacilli constituted the majority (70%) of pathogens identified in our study, which is comparable to but slightly lower than the 77% reported by Akshata Uppar et al.[3]

In our research, predominant pathogens included *Pseudomonas aeruginosa* (20%), Escherichia coli (3%), Acinetobacter species (7%), and Klebsiella species (39%). This distribution aligns with findings from Ghanshani et al., [26] though with some variation in the prevalence of specific organisms like *Acinetobacter baumannii* and *Klebsiella pneumoniae*.

The resistance patterns observed in our study highlight a significant challenge in managing infections caused by gram-negative organisms. For instance, Klebsiella sp. isolates exhibited high resistance to amoxyclavulanate and ciprofloxacin, similar to the patterns reported by Akshata Uppar et al. [3]However, these isolates retained sensitivity to aminoglycosides, imipenem, and tigecycline. In a study by Goel and Hogade et al., a concerning percentage of Acinetobacter sp. isolates were resistant to all tested antibiotics, including carbapenems. Our findings echo this resistance, especially against ciprofloxacin, gentamicin, and imipenem, with Acinetobacter sp. showing considerable resistance rates. Nonetheless, a significant portion of Acinetobacter sp. in our study was sensitive to levofloxacin and ceftazidime, offering some avenues for effective treatment.

The study's limitations stem from its single-center design, which may affect the generalizability of the results to broader populations. The specific resistance patterns and pathogen distribution observed here underline the critical need for local surveillance data to inform empirical antibiotic choices in ICUs. Addressing the challenge of antibiotic resistance requires a multifaceted approach, including the development of robust antibiotic stewardship programs, continuous monitoring of resistance trends, and adherence to infection control practices to mitigate the spread of resistant pathogens within healthcare settings.

Conclusion

Ventilator-associated pneumonia (VAP) continues to pose significant morbidity and mortality risks in the realm of nosocomial infections despite ongoing advancements in medical treatment and prevention strategies. The critical aspect of combating VAP lies in the early and accurate administration of empirical treatments, tailored to the unique microbiological landscape and resistance patterns prevalent within each hospital setting. An essential component of effective antimicrobial stewardship involves a comprehensive understanding of the local bacteriology and susceptibility profiles, aiming to curtail antibiotic misuse and resistance proliferation.

In this prospective observational study, the predominance of Gram-negative organisms in culture samples highlights a substantial challenge in managing VAP. Notably, a significant portion of these Gram-negative isolates exhibited multidrug resistance (MDR), presenting a concerning resistance profile:

- 52.8% of the isolates displayed resistance to tetracycline.
- Resistance to ceftriaxone and ceftazidime was observed in 39.9% of isolates.
- Amoxicillin-clavulanic acid and ciprofloxacin encountered resistance in 40% and 38.6% of cases, respectively.
- Additionally, 31.4% of the patients harbored pathogens resistant to carbapenems, including meropenem and imipenem.

Among the Gram-negative bacteria, Klebsiella species and *Pseudomonas aeruginosa* were the most frequently isolated pathogens. Other less frequently identified species included *Acinetobacter*, *Escherichia coli*, and *Proteus mirabilis*. A notable resistance pattern emerged among Klebsiella organisms, exhibiting resistance to a wide array of antibiotics such as amoxicillin, clavulanate, ampicillin, gentamicin, cotrimoxazole, azithromycin, ceftazidime, ceftriaxone, cefazolin, tetracycline, piperacillin-tazobactam, and ciprofloxacin.

The study highlights the significant susceptibility of Gram-negative bacteria to develop resistance to third-generation cephalosporins. Conversely, antibiotics such as imipenem, amikacin, and piperacillin-tazobactam demonstrated effectiveness against these pathogens. Gram-positive cocci showed an increased resistance pattern to penicillin and cefazolin, indicating a shifting resistance landscape that necessitates vigilant antimicrobial stewardship.

The inappropriate or inadequate use of antibiotics in treating VAP can lead to poor patient outcomes and the escalation of multi-drug resistance. The timely isolation of bacterial pathogens and their antibiotic susceptibility testing becomes paramount in orchestrating an effective response to infections caused by multi-drug resistant bacteria. Continuous observation and analysis of the varying patterns of organism species and their antimicrobial susceptibilities can significantly contribute to the optimization of treatment strategies for lower respiratory tract infections, particularly in settings plagued by the challenges of VAP.

This study emphasizes the importance of localized, data-driven approaches in managing VAP, advocating for the tailored use of antimicrobials based on current and accurate bacterial resistance profiles to enhance patient outcomes and mitigate the spread of resistant pathogens.

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