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Original Research Article

Emerging Diagnostic and Therapeutic Trends in Nosocomial Pneumonia Among ICU Patients: A Focus on Antimicrobial Resistance and Rapid Molecular Testing

Prashant Kumar

Assistant Professor, Department of Anesthesiology & critical care Medicine, Lord Buddha Koshi Medical College and Hospital, Saharsa, Bihar, India

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Corresponding Author: Dr. Prashant Kumar
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Abstract:

Background: Nosocomial pneumonia remains one of the most serious infections acquired in the intensive care unit (ICU) and a major source of morbidity, mortality, and health-care related costs. Thus, it is important to understand emergent microbial trends, resistance patterns, and risk factors associated with managing these diseases for prevention and optimal management. Consequently, this study quantified emergent trends from published literature on nosocomial pneumonia in critically ill patients in the ICU.

Materials and Methods: This study is a type of observational research that looks at future outcomes. It includes 100 adult patients who developed either ventilator-associated pneumonia (VAP) or hospital-acquired pneumonia (HAP) while being treated in a medical intensive care unit at a large teaching hospital. The study describes the results, the patients' clinical features, the infections causing the pneumonia, and how these infections relate to antibiotic resistance and effectiveness.

Results: Of the 100 patients, 30 developed HAP and 70 developed VAP. The overall mortality rate was 64%, with mechanical ventilation being strongly associated with mortality ($p<0.00001$). For the early-onset cases, the predominant organisms were Staphylococcus aureus in 52% of patients and Klebsiella pneumoniae in 43%. In late-onset, K. pneumoniae accounted for 49%, Pseudomonas aeruginosa 26%, and Acinetobacter 12%. The maximum sensitivity was to piperacillin + tazobactam (58%) and carbapenems (45-50%), while maximum resistance was to cefepime (94%) and ceftazidime (90%).

Conclusion: Nosocomial pneumonia had a high rate of morbidity and mortality, particularly in those requiring ventilation. The two most prevalent bacteria, with alarmingly high rates of resistance to widely used antibiotics were Staphylococcus aureus and Klebsiella pneumoniae. Continuous symptom and resistance surveillance, regular reviews of antibiotic use, and adherence to strict infection control measures are paramount to managing the emerging burden seen in the ICU.

Keywords: ICU, ventilator-associated pneumonia (VAP), hospital-acquired pneumonia (HAP), nosocomial pneumonia, risk factors, microbiological trends, antibiotic sensitivity, and multidrug resistance.

Introduction

Although nosocomial pneumonia (NP) is one of the most common infections acquired in hospitals and can be very dangerous, it is hard to detect because it can develop in any patient in the intensive care unit (ICU). NP refers to an infection in the lower part of the lungs that happens within 48 hours after a patient is admitted to the hospital, but not when the infection was already starting before admission. In general, patients who are not on a ventilator and are hospitalized are usually considered to have hospital-acquired pneumonia (HAP). If a patient who has been on a ventilator for more than 48 hours gets an infection related to the ventilator, it is typically classified as NP [1, 2]. It's important to understand the differences between these types because factors like risks, the types of bacteria involved, and how well treatments work can vary a lot. NP can be grouped based on when it occurs during a patient's stay in the hospital. There are two main types: early-onset and late-onset NP. Early-onset NP happens when a patient was intubated or admitted within 2 to 4 days, while late-onset NP occurs after more than 4 days. Patients with late-onset pneumonia are more likely to have infections caused by bacteria that are resistant to many antibiotics, such as Pseudomonas aeruginosa, Acinetobacter baumannii, certain types of bacteria in the Enterobacteriaceae family that produce extended-spectrum beta-lactamases, and methicillin-resistant Staphylococcus aureus (MRSA). These resistant bacteria make it harder to choose the right

treatment early on and can lead to worse outcomes for the patient [3,4,5].

The recognition of nosocomial pneumonia (NP), especially in the intensive care unit (ICU) setting, as a significant public health problem comes from the serious complications to patient outcomes. NP has been shown, in every study, to lengthen the length of stay in, intensive care unit (ICU) and even overall hospital time. NP increases the length of mechanical ventilation, as well as morbidity and mortality [1,2,3,4,5]. The longer hospital days and ventilator days are burdens to the patient and to the healthcare system, as well as the healthcare system's resources and effort. These adverse outcomes are associated with the growing burden of healthcare and associated dollar costs; NP is a clinical and economic problem [2,4]. Overall, the burden associated with nosocomial pneumonia in the documented ICU setting has a very large range of incidence rates, ranging from 9% to greater than 58%, which can be affected by patient factors, types of ICUs, comorbidities, and the methods utilized to diagnose NP [1,2,3,6,7,8]. The variability of numbers is also reflective of the variability of the surveillance systems, infection prevention practices, and reporting across institutions and countries. The associated mortality remains unacceptably high (30% to 70%), and this underscores the urgent need to improve approaches to prevent and manage NP [1,2,6,7,8].

NP management in the ICU is complicated. One of the most challenging aspects of NP is its nonspecific clinical presentation. Patients in the ICU often have fever, leukocytosis, and radiological findings due to their primary illness, prompting the NP to diagnose. Subsequently, separating colonization from infection adds to the difficulties. Further complicating matters, the microbial spectrum of pneumonia in a hospital setting is not static and changes by time, place, and patient population. The resistance and susceptibility profiles significantly vary between hospitals, and even the different ICU units in the same hospital [5,6,9]. This variation has been documented all over the world, emphasizing the need for local epidemiological surveillance of pathogens and their antibiotic susceptibility patterns to inform empirical and targeted antimicrobial therapy [6,9,10]. Not accounting for variation negatively affects therapeutic efficacy and contributes to the rising global emergency of antimicrobial resistance, identified by the WHO as one of the greatest threats to global health.

A lot of research is showing that bacteria and viruses that are resistant to many drugs are playing a big part in the development of hospital-acquired pneumonia. Many common pneumonia-causing germs, like Streptococcus pneumoniae, Haemophilus influenzae, and Staphylococcus aureus that are sensitive to methicillin, have been studied before (3, 5, 8). Recent studies also show that drug-resistant bacteria, such as MRSA (methicillin-resistant Staphylococcus aureus) and gram-negative bacteria like Pseudomonas and Acinetobacter, are becoming more common. When it comes to late-onset ventilator-associated pneumonia, the types of germs causing it to have changed over time, and factors like how long someone is on a ventilator, how serious their illness is, and whether they've used antibiotics before are the strongest indicators. The development of E. coli, other fast-growing E. coli, and carbapenem-resistant bacteria has changed the environment, thereby making empirical antibiotic selection extremely difficult, if not impossible. Clinical outcomes, treatment options, and costs associated with health care continue to be negatively impacted (6, 8). Given this reasoning, it is apparent that antibiotic stewardship and appropriate use in the intensive

The presence of rapidly evolving organisms is another important current trend in the ICU - the realization of current ICU-related risk factors. The entire area of ICU practice, based on physical grounds and moral grounds, encourages risk. The use of invasive procedures, prolonged sedation, immunosuppressive therapy, and intensive life-support measures can be clinically life-saving while simultaneously placing patients at risk for NP. Elderly patients, patients with various comorbidities (e.g., diabetes or chronic kidney disease), and impeded immunoreactivity are all exemplary examples of patients warranting consideration when the introduction of NP is contemplated. In the ICU, there are not just patients presenting variable degrees of health instability; the ICU has a disparate and frequently shifting membership of patient population, also frequently employing broad-spectrum antibiotics. All of these factors create a compromised disease state system that really introduces substantial chances for new resistant pathogens to arise [4,6,7]. This dictates that potential prevention measures cannot be general but must embrace the uniqueness of the ICU, and they must constantly develop prevention measures as new and evolving risk factors present themselves.

The ongoing evolution of diagnosis is also an issue. Chest radiography, clinical scores, and microbiological cultures are some diagnostic methods that have become standards, but more recent methods, including polymerase chain reaction (PCR)-based assays, next-generation sequencing, and rapid biomarker assays (procalcitonin (PC) and C-reactive protein (CRP)), are all being used and explored for diagnostic ability in early and accurate diagnosis. Unfortunately, the burgeoning technologies are expensive, and it is important to note that these diagnostic (and therapeutic) advances are not uniformly available in different healthcare settings, particularly resource-limited settings. Certainly, there will be differences between high-income and low-income countries that

have obtained unique differential capabilities for diagnosis and treatment that require the introduction of different global patterns in NP [5,9].

While all these complexities have been discussed, most new evidence supports timely diagnosis, the appropriate use of antimicrobials, and strong preventive and therapeutic initiatives to reduce mortality and improve outcomes in the ICU [1,2,3,4,5,6,7,8,9,10]. Preventive strategies (e.g., compliance with vented care bundles, hand hygiene, head of bed elevation, oral decontamination with chlorhexidine, avoiding/early withdrawal of sedatives etc.), have consistently demonstrated a reduction in the rates of VAP, whereas good stewardship of antimicrobials (e.g., short duration of therapy, rotating antimicrobials, narrow spectrum agent if possible) is essential to minimize resistance [7,9]. We are also seeing increased use of infection control measures (e.g., surveillance cultures, cohorting of infected patients, isolation of resistant organisms) to assist in infection control/prevention in the ICU.

The changing environment also captures both local and national epidemiological studies. It is well documented that resistance patterns of microbial flora can be so disparate between institutions that it may, on occasion, be reasonable to take same-day data to inform empiric therapy. This will be an exceptionally large issue in developing countries, where same-day data can be even more disparate from any international association data. Surveillance data has the potential to not only improve empiric therapy locally but also to explore resistance trends over time and ideas for population health issues [6,10].

Considering the aforementioned local and global concerns, nosocomial pneumonia in the intensive care unit has a complicated interaction with host risk factors, practice variables, shifting microbial patterns, and systemic difficulties (such as antibiotic resistance). To aid in the development of pertinent preventative and therapeutic methods at the institutional and regional levels, it is imperative to comprehend the epidemiology, clinical spectrum, and microbiological etiology of HAP and VAP in patient-specific cohorts. These needs led to the study's primary goal in the intensive care unit (ICU) of a public-sector tertiary care teaching hospital: to describe the clinical profile and outcome of patients who developed nosocomial pneumonia. The secondary goals were to identify the aetiological organisms of HAP and VAP, assess their patterns of antibiotic sensitivity and resistance, and correlate these findings with patient outcomes [3,6,7,9,10]. In order to better understand and manage this complicated infection globally, this research should ideally shed more light on the burden of nosocomial pneumonia in local contexts as well as the wider evolving patterns of nosocomial pneumonia in the intensive care unit.

Methodology

Study Design: This prospective observational cohort study aimed to evaluate the developing trends of nosocomial pneumonia in ICU patients regarding its incidence, clinical profile, causative microorganisms, and antimicrobial patterns among hospitalized patients in a tertiary hospital.

Study Area: The study was carried out at the Lord Buddha Koshi Medical College and Hospital, Saharsa, Bihar, India, in the Department of Anesthesiology & Critical Care Medicine

Study Duration: The study was carried out over a period of one year.

Study Population: All adult patients who were 18 years old or older and were admitted to a medical intensive care unit (MICU) at a tertiary care teaching hospital were considered for this study. The patients included in the study were those who stayed in the ICU for at least 48 hours and were later diagnosed with nosocomial pneumonia.

Sample Size: This study utilized a sample of 100 adult patients admitted to the Medical ICU (MICU) of the tertiary care teaching public hospital who met the inclusion and exclusion criteria for nosocomial pneumonia (HAP/VAP). The total of 100 cases in this study represented the sample of the study in examining emerging trends of nosocomial pneumonia in the ICU, including incidence, clinical characteristics, microbial etiology, antibiotic susceptibility, and antibiotic resistance patterns.

Inclusion criteria

- Adults (≥18 years), either sex, admitted to MICU for ≥48 h.
- New/progressive pulmonary infiltrate plus compatible clinical features (e.g., fever, leukocyte abnormality, purulent secretions) meeting HAP/VAP definitions.

Exclusion criteria

- Pneumonia present or incubating within 48 h of hospital admission (community-acquired or aspiration at admission).
- Non-infectious pulmonary conditions mimicking pneumonia (e.g., pulmonary edema, ARDS without infection, pulmonary hemorrhage) when confirmed.
- Patients transferred with ongoing HAP/VAP already diagnosed elsewhere before MICU day 0.

Data Collection: An established proforma was used for data collection, which included demographic information, clinical history, comorbid conditions, length of ICU stay, justification for ventilator use, laboratory tests, radiological results, and severity scores. To identify the bacteria responsible for the infection and their resistance to antibiotics, we col-

lected microbiological samples (sputum, endotracheal aspirates, and bronchoalveolar lavage) and cultured them. Methodical documentation of clinical outcomes (i.e., ventilation duration, intensive care unit stay duration, and mortality) was carried out.

Procedure: Patients who met the inclusion criteria were assessed and followed carefully from the moment they were admitted to the intensive care unit until their discharged from the intensive care unit. The clinical assessment involved symptoms, vital signs, and laboratory tests. Radiological tests involved a chest X-ray or, more often, a CT scan if the patient had new or worsening pulmonary infiltrates. Microbiological tests involved collecting sputum, endotracheal aspirates, or bronchoalveolar lavages (BAL) to attempt to culture organisms and antibiotic sensitivities. All samples were collected under sterile conditions. Patients were managed according to usual intensive care unit management, and all tests and management strategies were documented in detail, including the prescription of antibiotics, ventilatory support, and supportive care (for mechanically ventilated patients, according to the clinical protocol). Patient data on clinical outcome and ventilator days, as well as length of stay, were obtained for correlation with the identifiable organisms and resistance patterns.

Statistical Analysis: We analyzed the data and input it into Microsoft Excel using SPSS. They used descriptive statistics, including means, standard deviations, frequencies, and percentages, to describe the baseline demographic and clinical features. For categorical data, we applied for either a chi-square test or Fisher's exact test. For continuous data, we used an independent t-test or a Mann-Whitney U test. A p-value less than 0.05 was considered statistically significant. To better understand the trends in hospital-acquired pneumonia in the intensive care unit, we looked at trends in antibiotic resistance, patient outcomes, and the causes of the infection.

Result

Table 1 shows the distribution of risk factors and mortality amongst ICU patients with nosocomial pneumonia. Mechanical ventilation had the highest rate of mortality, with 53 of 70 patients (75.7%) dying. This was statistically significant, $p < 0.00001$. Deaths were recorded in elderly (> 60 years), COPD & diabetes patients as well (>0.6%; 83.3% & 66.7%), but were not statistically significant. Smoking, CKD, cardiac diseases, and a history of recent surgery had varying mortalities and were not significantly proven lethal. Overall, mechanical ventilation was cited as the most serious risk factor of mortality, thus allowing for early detection & monitoring with preventative working strategies to generate theoretically lower mortality rates from nosocomial pneumonia in the ICU.

Table 1: Risk factors for nosocomial pneumonia in Intensive Care Units

Risk Factor	Number of Patients	Mortality (%)	Survived (%)	P value
Age > 60 years	25	18 (72.0)	7 (28.0)	0.241
Smoking	20	12 (60.0)	8 (40.0)	0.840
Requirement of mechanical ventilation	70	53 (75.7)	17 (24.3)	<0.00001
COPD	6	5 (83.3)	1 (16.7)	0.475
Diabetes mellitus (DM)	18	12 (66.7)	6 (33.3)	0.653
Chronic kidney disease (CKD)	4	1 (25.0)	3 (75.0)	0.241
Cardiac diseases	10	6 (60.0)	4 (40.0)	0.574
Recent surgical intervention	2	1 (50.0)	1 (50.0)	1.000

Table 2 highlights the emerging microbial trends in nosocomial pneumonia among ICU patients. Staphylococcus aureus (52%) and Klebsiella pneumoniae (43%) were the most commonly implicated organisms, paralleling their predominance in both HAP and VAP. Pseudomonas (32%) also made up a significant proportion, especially in ventilated patients, which is worth noting as a pathogen in the ICU. Mixed infections (7%) and multi-drug-resistant organisms such as Acinetobacter (3%) in VAP cases almost certainly forebode a disturbing trend of resistance. E. coli (11%) and Streptococcus pneumoniae (16%) were less prevalent than the previously cited pathogens, but their role should not be overlooked. Overall, resistant gram-negative pathogens and mixed infections appear to be emerging, chiefly in VAP, posing potential threats. An important action point is the need for ongoing surveillance in tandem with rational antibiotic utilization to optimize ICU outcomes.

Table 2: Distribution of the Organisms Found in the ICU with Early-Onset Nosocomial Pneumonia

Organisms Isolated	Hospital-Acquired Pneumonia (HAP) n (%)	Ventilator-Acquired Pneumonia (VAP) n (%)	Total n (%)
Klebsiella pneumoniae	17 (17.0)	26 (26.0)	43 (43.0)
Staphylococcus aureus	43 (43.0)	9 (9.0)	52 (52.0)
Pseudomonas	17 (17.0)	15 (15.0)	32 (32.0)
Mixed Infections	0 (0.0)	7 (7.0)	7 (7.0)
Escherichia coli	9 (9.0)	2 (2.0)	11 (11.0)
Streptococcus pneumoniae	13 (13.0)	3 (3.0)	16 (16.0)
Acinetobacter	0 (0.0)	3 (3.0)	3 (3.0)
Total	**100 (100)**	**65 (100*)**	**100 (100)**

Table 3 Late-onset nosocomial pneumonia in the ICU is primarily due to Klebsiella pneumoniae (49%) and Pseudomonas (26%), and most cases occurred in ventilated patients. Acinetobacter (12%) and E. coli (9%) were also important late-onset pathogens and reflect the growing danger of multidrug resistance for patients who are in the ICU for long periods of time. Mixed infections occurred in 6% of cases, and Staphylococcus aureus (4%) and Streptococcus pneumoniae (2%) were listed as less prevalent isolates in cases of VAP and new infections. The findings support the idea that resistant gram-negative organisms are primarily involved in late-onset VAP, and that they pose a significant challenge for infection control in ICUs and the appropriate use of antimicrobials.

Table 3: Distribution of the Organisms Found in the ICU with Late-Onset Nosocomial Pneumonia

Organisms Isolated	Hospital-Acquired Pneumonia (HAP) n (%)	Ventilator-Acquired Pneumonia (VAP) n (%)	Total n (%)
Klebsiella pneumoniae	4 (4.0)	45 (45.0)	49 (49.0)
Pseudomonas	3 (3.0)	23 (23.0)	26 (26.0)
Acinetobacter	0 (0.0)	12 (12.0)	12 (12.0)
Escherichia coli	0 (0.0)	9 (9.0)	9 (9.0)
Mixed Infections	0 (0.0)	6 (6.0)	6 (6.0)
Staphylococcus aureus	0 (0.0)	4 (4.0)	4 (4.0)
Streptococcus pneumoniae	0 (0.0)	2 (2.0)	2 (2.0)
Total	**7 (7.0)**	**101 (101*)**	**100 (100)**

Discussion

This study presents novel data and new insights into nosocomial pneumonia (NP) within ICU settings, as well as into the relationships between clinical risk factors, microbial etiology, and antimicrobial resistance pathways. The authors have established that mechanical ventilation is the most powerful predictor of NP-related mortality. This is presumably due to the patients with mechanical ventilation having a very poor prognosis with mortality reported in excess of 75.7%, as opposed to previously reported mortality rates of 30%-70% for ventilator-associated pneumonia (VAP) [1,2]. The huge association with mechanical ventilation and mortality ($p < 0.00001$) nevertheless indicates that VAP remains the most concerning NP alternative. It is known that prolonged intubation can inhibit host defenses, facilitate the development of biofilm, and allow the bacteria to establish multidrug-resistant (MDR) colonization; each dramatically complicates the illness.

In our cohort, older age, smoking, diabetes, COPD, and cardiac comorbidities were other risk factors for mortality, but did not reach significance. Seventy-two percent of older patients (>60) died, and 83.3% of patients who had COPD (Table 4). These findings fit well with the literature that has identified both those who are elderly and those with comorbidities at greater risk of mortality due to immunocompromise, decreased pulmonary reserve, and one of the risk factors for antibiotic exposure [5,6]. It is possible that the lack of significance when looking at some risk factors was due to the small sample size; still, the trends presented here are clinically important and emphasize the need for individual risk assessment and close follow-up in high-risk populations.

Microbiological analysis in our study indicates a troubling shift in the etiologic profile of NP. Early onset NP was predominantly from Staphylococcus aureus (52%) and Klebsiella pneumoniae (43%). Traditionally, and predominantly when speaking of early-onset NP in trauma ICU patients, NP has been attributed to community-type flora such as Streptococcus pneumoniae or Haemophilus influenzae. Our data suggests that even early infections of ICU patients are repeatedly occurring with hospital-acquired organisms; perhaps not surprising given the extensive prior antibiotic exposures and/or the

length of hospital stay before ICU admission experienced by patients. The considerable proportion of Pseudomonas (32%) and mixed infections (7%) of patients with early onset NP also supports that resistant gram-negative bacilli have now infiltrated the earlier phases of ICU [7,8].

The issue is even more critical in late-onset NP. With late-onset NP, our data showed that Klebsiella pneumoniae (49%) and Pseudomonas (26%) were the most common organisms we identified, and Acinetobacter (12%) and E. coli (9%) or enterobacter species show very substantial antimicrobial resistance, also established to have very high levels of carbapenem resistance with Acinetobacter and ESBL production with Enterobacteriaceae (includes Klebsiella and E. coli). Signs of mixed infections (6%), resistant gram-negative pathogens contribute to poor outcomes with treatment of late-onset NP infections in critical patients. Other work in Indian ICUs indicates that similar events are taking place with the continued historical predominance of gram-negative bacilli, increasing multidrug resistance and treatment failure, leading to poorer outcomes for patients [3,4,9].

These organisms have important clinical implications. The dominance of resistant pathogens would imply that the use of the authors' interpretation of the old guideline is now totally inappropriate for empirical therapy. Local antibiograms and ongoing active surveillance must be viewed as mandatory. Antimicrobial resistance resulting from infection management must be managed delicately, as must stewardship principles with antibiotic use and infection control practices. Otherwise, the rates of resistance development and the loss of several common antibiotics will only increase.

Our results also contribute to the larger worldwide discussion related to prevention. While mechanical ventilation is high-level life support, the relationship to NP mortality emphasizes the need to elucidate the clear and structured ventilator care processes, including elevation of the head of bed, daily sedation interruption, chlorhexidine oral care, and early weaning [10]. Since resistant organisms are so important to the NP burden, it is evident that prevention efforts must extend beyond ventilator care and that there must be a strong focus on hand hygiene, environmental cleaning, and either cohorting or isolating infected patients for health care workers.

As well as the conclusion that nosocomial pneumonia in the ICU is no longer limited to only a few pathogens, our conversation now supports that, for example, regardless of initial treatment with piperacillin-tazobactam, pneumonia may still be complicated by resistant gram-negative bacilli, mixed infections in early onset infections. Certainly, mechanical ventilation was still the strongest predictor of mortality; however, so was older age and other comorbidities. They remain optimistic that our data can help contribute to further understanding of the complicated clinical presentation of NP, with its continued microbial resistance feature in its pathophysiology. Our summary of the observational data showed indicated changes over time, which require ongoing vigilance for the execution of appropriate local prevention, ongoing surveillance efforts, and prudent antimicrobial stewardship if we want to change mortality and mortality-related outcomes for patients in the post-ICU experience.

Conclusion

Nosocomial pneumonia continues to be a topic of discussion in ICU practice, and mechanical ventilation is the strongest predictor of mortality. Older age, younger age, and chronic conditions such as COPD and diabetes also predispose to pneumonia, highlighting its multifactorial risk factors. Late-onset pneumonia often had multidrug-resistant gram-negative organisms, including Klebsiella pneumoniae, Pseudomonas aeruginosa, and Acinetobacter species, usually as mixed infections. The challenge posed by antimicrobial resistance for empirical therapy has been significant and requires severe treatment options, although the best approach is to continue local surveillance and diagnostics as quickly as possible. Routine preventative strategies, which include compliance with ventilator bundles, policies on effective infection control, and what constitutes effective antimicrobial stewardship, will help minimize both incidence and resistance. Importantly, managing the causative factors contributing to these emerging trends, together with prudent empirical prediction, rational therapy, and continued surveillance, will optimize outcomes for patients and the health care burden associated with pneumonia acquired in the ICU.

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