

An Observational Assessment of Mortality Rates among Intubated and Mechanically Ventilated Subjects with Gram-Negative Pneumonia and to Explore Associated Risk Factors for Mortality

Preeti Kumari¹, Uzma Raihan², Kumar Saurabh³

¹Fellowship Emergency Critical Care, Department of Trauma and Emergency, IGIMS, Patna, Bihar, India

²Fellow SR Emergency Critical Care, Department of Trauma and Emergency, IGIMS, Patna, Bihar, India

³Senior Resident, Department of Anaesthesiology, IGIMS, Patna, Bihar, India

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Corresponding author: Dr. Uzma Raihan

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Abstract

Aim: To describe mortality rates among intubated and mechanically ventilated subjects with Gram-negative pneumonia and to explore associated risk factors for mortality among these subjects.

Methodology: This was a retrospective, observational cohort study conducted in IGIMS, Patna, Bihar, India using hospital records containing information on in-patient care, ambulatory care, and emergency department visits. The databases are derived from administrative data and contain encounter-level, clinical, and nonclinical information including all listed diagnosis and procedures, discharge status, patient demographics, and charges for all patients. The study sample included adults age ≥ 18 y (as of the index date) who were hospitalized with invasive, continuous mechanical ventilation; were discharged between April 1, 2020 and June 30, 2021; and who had a primary or secondary diagnosis of Gram-negative bacterial pneumonia. The study collected demographic, clinical, and admission characteristics. Mortality and risk factors associated with mortality were evaluated in the full study population. All the data was collected and analyzed.

Results: During the study period, a total of 763 patients were admitted who were incubated and mechanically ventilated, out of which approximately 400 subjects were diagnosed with Gram-negative pneumonia. More than half of the included subjects (61.75%) were male, and 52.5% were ≥ 60 years old. Most subjects (80%) utilized the emergency department during their hospitalization. The mortality rate among included subjects during the index hospitalization was 23.25%. 6% patients had previous hospitalization history due to Respiratory Tract Infections (RTI) and 4.5% due to chronic pulmonary diseases. In the present analysis, subjects with concomitant sepsis had the highest risk of mortality followed by subjects age ≥ 60 years and those with any prior hospitalization within 30 days. Comorbidities upon admission with the highest risk of mortality included cancer, liver disease, renal disease, and congestive heart failure. Presence of diabetes (with or without complications) was found to be associated with a lower mortality risk.

Conclusion: From our study, it can be concluded that mortality was high in mechanically ventilated subjects with Gram-negative pneumonia. The main risk factors for mortality identified in this analysis were the presence of sepsis, the presence of cancer, the presence of

liver disease, and age ≥ 60 years. Further prospective research is needed to confirm these findings and to explore potential healthcare intervention strategies that would improve outcomes in this patient population, especially among those at greatest risk.

Keywords: Pneumonia, Ventilators, Gram Negative Bacteria.

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Introduction

Ventilator-associated pneumonia (VAP) is a common infection associated with health care. Incidence of VAP results in prolongation of mechanical ventilation (MV), longer hospitalization time, and higher hospitalization costs [1]. In the 2016 guideline by the American Thoracic Society and the Infectious Diseases Society of America, patients with hospital-acquired pneumonia (HAP) and VAP are classified into 2 distinct groups [2]. Although VAP often has characteristics similar to those of HAP, including the appearance of fever, purulent sputum, leukocytosis, decreased oxygenation, and the identification of new infectious pulmonary infiltrates, treatment depends on many factors such as age and the pathogens involved [2, 3].

Pneumonia is among the top 5 medical conditions associated with the highest 30-d rehospitalization rate among Medicare beneficiaries [4]. Research has shown that the 30-d readmission rate associated with pneumonia was 22.4% in the Medicare population, and 62.6% of these readmissions occurred within 15 d after discharge from the initial hospitalization [5]. VAP incidence has been reported differently in different studies, ranging from 4.5 to 75.5 episodes per 1000 ventilator-days (VD) [3, 6, 7]. VAP often has a high mortality rate varying from 19.4% to 53%, particularly in the intensive care unit [8, 9].

Data suggest VAP occurs in 9–27% of all intubated patients [10, 11]. Among intubated patients, the risk of acquiring VAP is estimated to be between 1.2 and

8.5 cases per 1,000 ventilator days [12]. Patients with a higher sequential organ failure assessment (SOFA) score [9] and psychiatric diseases [13] usually have higher attributable mortality. Given that routine blood examination and blood biochemical tests have been commonly used for inpatients, clinicians should be interested in taking full advantage of these tests. Although neutrophil-to-lymphocyte ratio (NLR) and BUN/ALB levels had been considered as prognostic markers for mortality in community-acquired pneumonia [14, 15], there has been a lack of evidence to use tests as prognostic markers in cases of VAP.

The underlying etiology of pneumonia is important for the effective treatment of VAP. Gram-negative bacteria is estimated to cause 55–85% of hospital-acquired pneumonia [16, 17]. With the potential public health crisis posed by resistant Gram-negative bacteria, understanding the epidemiology of Gram-negative VAP is increasingly important [18, 19]. To address this gap in the literature, we sought to describe mortality rates among intubated and mechanically ventilated subjects with Gram-negative pneumonia and to explore associated risk factors for mortality among these subjects.

Methodology:

This was a retrospective, observational cohort study conducted in IGIMS, Patna, Bihar, India using hospital records containing information on in-patient care, ambulatory care, and emergency department visits. The databases are derived from administrative data and

contain encounter-level, clinical, and nonclinical information including all listed diagnoses and procedures, discharge status, patient demographics, and charges for all patients.

The study sample included adults age ≥ 18 y (as of the index date) who were hospitalized with invasive, continuous mechanical ventilation; were discharged between April 1, 2020 and June 30, 2021; and who had a primary or secondary diagnosis of Gram-negative bacterial pneumonia. Subjects with index hospitalizations with a primary or secondary discharge diagnosis of viral pneumonia, fungal pneumonia, atypical organisms, Gram-positive bacterial pneumonia, or pneumonia occurring secondary to infectious disease were excluded. The pre-index baseline period included the 30 d prior to admission for the index event, and the post-index follow-up period included the 30 d after discharge for the index event.

The study collected demographic, clinical, and admission characteristics. Subject characteristics included age, gender, and payer source. Clinical characteristics included the severity of illness classification, the presence of sepsis, and

an indicator of hospitalization within 30 d prior to index due to chronic pulmonary disease, lower respiratory tract infection, or any cause. Admission characteristics included the presence or absence of an emergency department visit and discharge disposition. Mortality and risk factors associated with mortality were evaluated in the full study population. Mortality rate was defined as the number of pneumonia admissions with discharge disposition of death divided by the total number of subjects included in the study population. All the data was collected and analyzed.

Results

During the study period, a total of 763 patients were admitted who were incubated and mechanically ventilated, out of which approximately 400 subjects were diagnosed with Gram-negative pneumonia. More than half of the included subjects (61.75%) were male, and 52.5% were ≥ 60 years old. Most subjects (80%) utilized the emergency department during their hospitalization. The mortality rate among included subjects during the index hospitalization was 23.25%. 6% patients had previous hospitalization history due to Respiratory Tract Infections (RTI) and 4.5% due to chronic pulmonary diseases.

Table 1: Demographic, hospitalization, and discharge details.

Variables		Number (n=400)	%
Age	18-30	32	8.0
	31-60	158	39.5
	>60	210	52.5
Gender	Male	247	61.75
	Female	153	38.25
Sepsis at admission	Yes	171	42.75
	No	229	57.25
Previous hospitalizations	Due to RTI	24	6.0
	Due to Chronic pulmonary diseases	18	4.5
Discharge position	Discharged	105	26.25
	Referred	77	19.25
	LAMA	87	21.75
	Died in hospital	93	23.25
	Unknown	38	9.5

The final multivariate model identified several statistically significant risk factors associated with mortality. In the present analysis, subjects with concomitant sepsis had the highest risk of mortality followed by subjects age ≥ 60 years and those with any prior hospitalization within 30 days.

Comorbidities upon admission with the highest risk of mortality included cancer, liver disease, renal disease, and congestive heart failure. Presence of diabetes (with or without complications) was found to be associated with a lower mortality risk

Table 2: Risk factors associated with in-hospital mortality among intubated and mechanically ventilated subjects with Gram-negative pneumonia

Risk Factor	Odds Ratio estimate (95% CI)
Sepsis	2.33–2.90
Cancer	2.11–2.78
Liver diseases	1.66–2.08
Age>60	1.61–2.07
Prior hospitalizations	1.18–1.51
Renal diseases	1.19–1.42
CHF	1.12–1.21
Diabetes	0.69–0.90

Discussion

Mechanical ventilation is an effective intervention method to save the life of critically ill patients and is widely used in intensive care units (ICUs). Ventilator-associated pneumonia (VAP) is a type of nosocomial infections and occurs after more than 48 h of mechanical ventilation. There are several strategies used to prevent and control VAP in clinic, such as prevention bundles and drugs including chlorhexidine, β -lactam antibiotics and probiotics. Although the prevalence of VAP has declined in recent years due to the implementation of therapeutic strategies, it remains one of the most common causes of nosocomial infections and death of critically ill patients during hospitalization in ICUs.

Given the limited number of studies on burden of illness involving subjects with VAP due to Gram-negative bacteria, we sought to describe mortality rates and associated risk factors for each outcome among intubated and mechanically ventilated subjects with Gram-negative pneumonia using data from the IGIMS Hospital. Overall, the incidence of mortality was found to be considerable in

this study of adult intubated and mechanically ventilated subjects with Gram-negative pneumonia. One fourth of subjects in this study died during the index hospitalization, and even higher mortality rates were observed among subjects with sepsis, cancer, liver disease, and increased age. Of note, more than half of the subjects in the study were ≥ 60 years old and male, and almost one fourth of subjects had experienced a previous hospitalization. The mortality rates observed in this study among intubated and mechanically ventilated subjects with Gram-negative pneumonia are largely consistent with other studies that examined mortality in subjects with pneumonia of varying etiologies requiring intubation or mechanical ventilation.

Similarly, a retrospective hospital database study noted that the mortality rate among mechanically ventilated subjects with pneumonia was 25.5% [20]. Mortality estimates among subjects with VAP who require intubation range from 24% to 50% and up to 76% in some high-risk settings [21]. The populations found to be at greatest risk for mortality in this study were also largely similar to previous analyses. Elderly subjects and subjects

with septic shock were previously reported to be at an increased risk of mortality [22]. While previous studies reported that subjects with diabetes were at an increased risk [22], the presence of diabetes was associated with a lower mortality risk in this analysis. It is important to note that the majority of subjects in our analyses had diabetes without complications, and this probably reflects a patient population with less severe disease as opposed to a true protective effect.

VAP can cause patients to have difficulty to get off the ventilator and to stay in the hospital longer, which cause a huge financial burden to patients and a huge demand for medical resources. Therefore, it is very important to clarify the risk factors of VAP to know more and get better prevention and control of VAP. There are various risk factors for VAP occurrence. Each factor is not only an independent risk factor of VAP, but also has an influence on each other. Due to the decline of the physiological and immune functions, elderly patients often have more than one comorbidity, which can lead to an increase in hospital length of stay and mechanical ventilation time, increasing the susceptibility to VAP. In a 2017 retrospective study, it was reported that ventilation time and ICU length of stay were significantly longer in patients with VAP than in those without VAP [23]. Patients with chronic diseases had longer mechanical ventilation time and hospital stay [24, 25] further showed that patients with chronic obstructive pulmonary disease (COPD) were 2.35 times more likely to develop VAP than patients without COPD. COPD could be an independent predictor of VAP.

Conclusion:

From our study, it can be concluded that mortality was high in mechanically ventilated subjects with Gram-negative pneumonia. The main risk factors for mortality identified in this analysis were the presence of sepsis, the presence of

cancer, the presence of liver disease, and age ≥ 60 years. Further prospective research is needed to confirm these findings and to explore potential health care intervention strategies that would improve outcomes in this patient population, especially among those at greatest risk.

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