Internal Medicine Section

# A Cross-sectional Study of Ventilatorassociated Pneumonia between Pulmonary and Non pulmonary Indications of Mechanical Ventilation

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#### **ABSTRACT**

**Introduction:** Ventilator-associated Pneumonia (VAP) is defined as pneumonia occurring 48-72 hours after the initiation of invasive Mechanical Ventilation (MV). It is diagnosed based on positive endotracheal tube or tracheostomy secretions culture and new or worsening infiltrates on a chest X-ray after 48 hours of MV. The incidence and severity of VAP may differ between pulmonary and non pulmonary groups due to variations in underlying diseases, immune responses, and duration of ventilation.

**Aim:** To compare the incidence and other parameters of VAP between pulmonary and non pulmonary indications of MV.

Materials and Methods: This cross-sectional study was conducted from April 2023 to December 2024 on 126 VAP patients who were on mechanical ventilation for different indications in the RICU, MICU, and SICU at BLDE (Deemed to be University) Shri BM Patil Medical College, Hospital, and Research Centre, Vijayapura, Karnataka, India. Primarily, this study included all patients who were on MV due to pulmonary and non pulmonary indications during the study period. Inclusion criteria included patients aged over 18 years, of either sex, and willing to provide informed consent. A total of 254 patients who were on MV for more than 48 hours were screened for VAP based on clinical, microbiological, and radiological criteria for diagnosis. Out of these, 126 patients were diagnosed with VAP, 63 due to pulmonary indications and 63 due to non pulmonary indications. A chest X-ray was done immediately after

intubation and repeated after 48 hours of MV for comparison. Endotracheal/tracheostomy tube secretions were sent for culture and sensitivity testing to isolate the organism and determine the resistance pattern. Demographic factors such as age and sex were studied and compared. Predictors of severity, such as the Acute Physiology and Chronic Health Evaluation (APACHE II score) and Sequential Organ Failure Assessment (SOFA) score, were calculated using ROC analysis and compared between pulmonary and non pulmonary indications of MV.

**Results:** The mean age was significantly higher in the pulmonary group (58±16.4 years) compared to the non pulmonary group (49±18.0 years), and both groups showed a male predominance, with 45 (71.4%) in the pulmonary group and 48 (76.2%) in the non pulmonary group. The incidence of VAP in pulmonary indications was 63/134 (47%), whereas for non pulmonary indications, it was 63/120 (52.5%). The most common organisms causing VAP are *Acinetobacter baumannii* complex, followed by *Klebsiella pneumoniae*. Overall mortality and improvement are higher in pulmonary cases compared to non pulmonary cases. SOFA and APACHE II scores are strong predictors of mortality.

**Conclusion:** VAP is one of the most common ICU-acquired infections and is associated with increased mortality and morbidity. The data from this study can provide a reference for the management of VAP and the early detection of high-risk patients.

Keywords: Acute physiology and chronic health evaluation score, Incidence, Solid organ functional assessment score

#### INTRODUCTION

VAP is a significant nosocomial infection in patients undergoing MV, contributing to increased morbidity, mortality, and healthcare burden in Intensive Care Units (ICUs) [1,2]. The incidence of VAP varies from 9% to 27%, depending on patient demographics, ICU type, and diagnostic criteria [3]. MV is utilised for both pulmonary conditionssuch as pneumonia, Acute Respiratory Distress Syndrome (ARDS), and Chronic Obstructive Pulmonary Disease (COPD)-and non pulmonary conditions, including Traumatic Brain Injury (TBI), stroke, and sepsis. Several risk factors may predispose patients to either colonisation of the respiratory tract with pathogenic microorganisms and/or aspiration of contaminated secretions [4-7]. Notably, patients with neurological illnesses are at a higher risk of VAP, with incidence rates reaching up to 61% [2,8]. This susceptibility is attributed to prolonged ventilation, impaired cough reflexes, and altered consciousness. The growing challenge of Multidrug-Resistant Organisms (MDROs), particularly Acinetobacter baumannii and Klebsiella pneumoniae, complicates empirical therapy and increases

mortality risk [9,10]. Identifying resistance patterns is crucial for targeted antibiotic therapy and improved outcomes [11]. Severity scoring systems such as the APACHE II and SOFA are widely employed to assess ICU prognosis and mortality risk [12,13].

Studies are lacking in comparisons of different parameters among various indications of MV that develop VAP. The rationale of this study is to compare the incidence, microbial profile, antibiotic resistance, clinical outcomes, and predictive utility of APACHE II and SOFA scores in VAP among patients ventilated for pulmonary versus non pulmonary indications. The aim of the study is to compare Ventilator-Associated Pneumonia between pulmonary and non pulmonary indications of MV.

The primary objectives of the study are to compare the incidence of VAP between pulmonary and non pulmonary indications for MV, to identify the organism and its resistance pattern causing VAP in the ICU, and to compare the outcomes of VAP between pulmonary and non pulmonary indications for MV. The secondary objectives of the study are to determine the predictive value of the following at

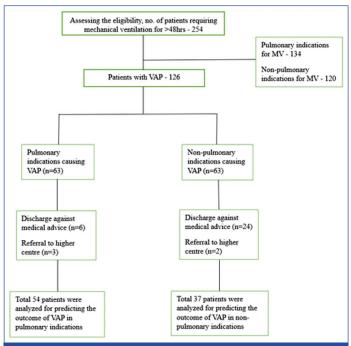
diagnosis towards outcome and prognosis:

- APACHE-II
- SOFA score

# **MATERIALS AND METHODS**

This cross-sectional study was conducted from April 2023 to December 2024 on 126 VAP patients who were on mechanical ventilation for different indications in the RICU, MICU, and SICU at BLDE (Deemed to be University) Shri BM Patil Medical College, Hospital, and Research Centre, Vijayapura, Karnataka, India. Ethical clearance was obtained, with the IEC number BLDE (DU)/IEC/871/2022-23.

Sample size calculation: Based on the expected VAP rates of 9% to 27% [3] in India, the study required 63 participants per group (totaling 126) with a 95% level of confidence and 5% absolute precision [4]. A p-value of <0.05 will be considered statistically significant. All statistical tests will be performed as two-tailed. Randomisation was done using a lottery system, and the study included 126 patients: 63 mechanically ventilated patients due to pulmonary indications and 63 mechanically ventilated patients due to non pulmonary indications. To calculate the incidence of VAP and reach the sample size of 126 VAP cases, 254 patients who were on MV for more than 48 hours were screened for VAP [Table/Fig-1].



**[Table/Fig-1]:** Flowchart of patient screening, grouping by MV indications, and evaluation for Ventilator-Associated Pneumonia (VAP).

**Inclusion and Exclusion criteria:** This study included patients over the age of 18, regardless of gender, who provided informed consent. Patients who were on MV for less than 48 hours, pregnant women, and those younger than 18 years were excluded from the study.

All patients were monitored on a daily basis. A baseline chest X-ray was taken at intubation and repeated after 48 hours. Any new pulmonary infiltrates after 48 hours of MV, along with clinical and microbiological findings, were considered diagnostic for VAP according to the American Thoracic Society (ATS)/Infectious Diseases Society of America (IDSA) guidelines [14]. Respiratory samples from endotracheal tube or tracheostomy aspirates were collected in suspected VAP cases and sent for culture. A positive quantitative or qualitative bacterial culture resulting from endotracheal aspirate (with a threshold growth of >10<sup>5</sup>×CFU/mL taken as the cut-off for endotracheal aspirate [15]) along with new-onset or worsening infiltrates on chest X-ray after 48 hours of MV confirms the diagnosis of VAP. Only patients meeting both radiological and

microbiological criteria were classified as having VAP. Patients were followed up until hospital discharge or death.

Demographic data (age, sex, smoking/alcohol history), clinical characteristics, duration of MV, primary diagnosis, VAP occurrence, and culture sensitivity patterns were recorded. Outcomes (death or improvement) were noted. The APACHE II and SOFA scores were calculated on admission and used to assess severity and predict mortality. The APACHE II score includes age, temperature, mean arterial pressure, heart rate, respiratory rate, oxygenation, pH, sodium, potassium, creatinine, hematocrit, white cell count, and GCS score, as well as any history of immunocompromise or organ failure [Table/Fig-2] [12]. The SOFA score incorporates the PaO<sub>2</sub>/FiO<sub>2</sub> ratio, platelet count, bilirubin, mean arterial pressure (or vasopressor use), Glasgow Coma Scale (GCS) score, serum creatinine, and urine output [Table/Fig-3] [13].

Score	Mortality
0-4	4%
5-9	4%
10-14	15%
15-19	25%
20-24	40%
25-29	55%
30-34	75%
>34	85%

[Table/Fig-2]: Acute Physiology and Chronic Health Evaluation score II (APACHE II) Mortality scoring system.

#### STATISTICAL ANALYSIS

Data were analysed using SPSS version 20. Continuous variables were presented as mean±Standard Deviation (SD) or interquartile ranges. Categorical variables were expressed as frequencies and percentages. The Chi-square test was used to compare categorical variables between the two groups. Receiver Operating Characteristic (ROC) curve analysis was performed to assess the predictive validity of APACHE II and SOFA scores, with significance set at p<0.05.

# **RESULTS**

The baseline demographic and clinical characteristics were largely comparable between the two groups. The mean age was significantly higher in the pulmonary group ( $58\pm16.4$  years) compared to the non pulmonary group ( $49\pm18.0$  years, p=0.0256). Both groups showed a male predominance: 45 (71.4%) in the pulmonary group versus 48 (76.2%) in the non pulmonary group (p=0.5449). There were no significant differences in smoking history (39 (61.9%) vs. 35 (55.6%), p=0.4709) or alcohol use 37 (58.7%) vs. 43 (68.3%), p=0.2688), suggesting similar lifestyle factors across the groups [Table/Fig-4].

Among the 63 cases of pulmonary indications for MV in this study, COPD was the most frequent aetiology at 16 (25.39%), followed by community-acquired pneumonia at 12 (19.04%), and post-Tuberculosis sequelae and pulmonary TB each at 9 (14.28%), as shown in [Table/Fig-5]. In non pulmonary indications, Traumatic Brain Injury (TBI) was the most frequent aetiology at 18 (28.57%), followed by sepsis at 11 (17.46%) and stroke at 8 (12.70%) [Table/Fig-6].

The overall incidence rate of VAP in our study was 37.2% per 1000 ventilator days. VAP occurred in 52.5% (63/120) of patients with non pulmonary indications and 47.0% (63/134) of those with pulmonary indications, as shown in [Table/Fig-7]. Although the difference is not statistically significant, the higher proportion of VAP in the non pulmonary group suggests a potential need for enhanced surveillance in this population.

The Acinetobacter baumannii complex was isolated in n=16 (25.39%) of pulmonary cases and n=15 (23.80%) of non pulmonary cases, while Klebsiella pneumoniae was isolated in n=14 (22.22%) of both groups. A statistically significant difference was observed in the isolation of

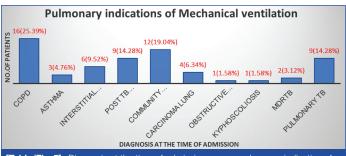
Variables	0	1	2	3	4
Respiratory Pao <sub>2</sub> /Fio <sub>2</sub> mmHg	>400	≤400	≤300	≤200	≤100
Coagulation platelets×1000/mm³	>150	≤150	≤100	≤50	≤20
Liver bilirubin mg/dL	<1.2 (<20)	1.2-1.9 (20-32)	2.0-5.9 (33-101)	6.0-11.9 (102-204)	>12.0 (>204)
Cardiovascular hypotension	No hypotension	MAP <70 mmHg	Dopamine≤5 or dobutamine (any dose) *	Dopamine > 5 or epinephrine ≤ 0.1 or norepinephrine ≤ 0.1*	Dopamine > 15 or epinephrine > 0.1 or norepinephrine > 0.1*
Central nervous system GCS	15	13-14	10-12	6-9	<6
Renal creatinine	<1.2 (<110)	1.2-1.9 (110-170)	2.0-3.4 (171-299)	2.0-3.4 (171-299)	>5.0 (>440)
OR urine output				<500 mL/d	<200 mL/d

[Table/Fig-3]: Sequential organ assessment score (SOFA) scoring system

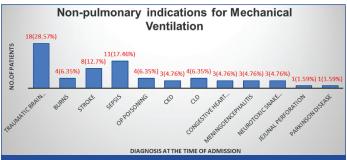
Demographic data	Pulmonary indications for mv (n=63)	p-value	Non pulmonary indications for mv (n=63)	Chi-square test
Mean age±SD	58±16.4 years		49±18.03	
Number of male patients	45	0.5449	48	0.3666
Number of female patients	18	0.5449	15	0.366
Smoking	39	0.4709	35	0.5198
Alcoholism	37	0.2688	43	1.2228

[Table/Fig-4]: Baseline demographic and clinical characteristics.

MV: Mechanical Ventilation; \*Statistically significant p-value<0.05; Chi-square test is applied



[Table/Fig-5]: Diagnosis at the time of admission among pulmonary indications for Mechanical Ventilation (MV).



[Table/Fig-6]: Diagnosis at the time of admission among non pulmonary indications for Mechanical Ventilation (MV).

Indications	Patients with VAP	n (%)	Patients without VAP	n (%)	Total (n)
Pulmonary	63	47.00%	71	53.00%	134
Non-pulmonary	63	52.50%	57	47.50%	120
Total	126	49.60%	128	50.40%	254

[Table/Fig-7]: Incidence of VAP among pulmonary and non pulmonary indications of Mechanical Ventilation (MV).

VAP: Ventilator-associated pneumonia

Serratia marcescens, which was found only in the pulmonary group (n=5; 7.93%, p=0.0230). Other organisms such as *Pseudomonas* aeruginosa, *Staphylococcus* aureus, and *Escherichia* coli showed no significant intergroup differences [Table/Fig-8].

Acinetobacter baumannii exhibited significantly higher resistance in the non pulmonary group to Levofloxacin (73.33% vs. 18.75%, p=0.0023), Amoxicillin/Clavulanic acid (66.6% vs. 18.75%, p=0.0020),

Endotracheal tube secretions/tracheostomy tube secretions culture organism	Pulmonary indications for MV	Non pulmonary indications for MV	Chi- square value	p-value using Chi-square test
Acinetobacter baumanni complex	16 (25.39%)	15 (23.80%)	0.0424	p=0.8368
Klebsiella pneumoniae	14 (22.22%)	14 (22.22%)	2.0161	p=1.000
Pseudomonas aeruginosa	8 (12.69%)	4 (6.34%)	0	p=0.2266
Klebsiella spp pneumoniae (MDRO)	3 (4.76%)	6 (9.52%)	1.0684	p=0.3013
Staphylococcus aureus	4 (6.34%)	6 (9.52%)	0.2066	p=0.5115
Serratia marcescens	5 (7.93%)	0	0.1501	p=0.0230*
Klebsiella aerogenes	2 (3.17%)	1 (1.58%)	1.462	p=0.6985
Acinetobacter baumannii (MDR)	0	2 (3.17%)	2.0161	p=0.1556
Pseudomonas aeruginosa (MDR)	0	2 (3.17%)	1	p=0.1556
Enterobacter cloacae complex	1 (1.58%)	0	0.1501	p=0.3173
Escherichia coli	4 (6.34%)	3 (4.76%)	1	p=0.6985
Escherichia coli (CRE)	0	1 (1.58%)	5.1653	p=0.3173
Klebsiella oxytoca	2 (3.17%)	3 (4.76%)	0.431	p=0.6494
Staphylococcus aureus (MRSA)	1 (1.58%)	5 (7.93%)	2.7778	p=0.0956
Streptococcus pneumoniae	3 (4.76%)	0	3.0488	p=0.0808
Citrobacter freundii	0	1 (1.58%)	1	p=0.3173

[Table/Fig-8]: Microorganisms isolated from ET/tracheostomy secretions in Ventilator Associated Pneumonia (VAP) cases.

MDRO: Multidrug-resistant organism; MDR: Multidrug-resistant; CRE: Carbapenem-resistant Enterobacteriaceae; p<0.05 considered statistically significant and marked with asterisks; Chisquare test is applied

and Trimethoprim/Sulfamethoxazole (86.66% vs. 31.25%, p=0.0018). For *Klebsiella pneumoniae*, significantly higher resistance was observed in the pulmonary group to Cefuroxime and Cefuroxime Axetil (both p=0.001), as well as to Piperacillin/Tazobactam (p=0.0002). Resistance to Imipenem was markedly higher in the non pulmonary group (p=0.010), as shown in [Table/Fig-9]. These findings highlight important intergroup differences in antibiotic resistance patterns, which are critical for guiding empirical therapy.

A total of 35 patients were excluded from our study for various reasons, including Discharge Against Medical Advice (DAMA) due to financial issues, family matters, or referral to higher centers. Of the 91 remaining patients, the overall mortality rate among VAP patients in our study was 32 (25.3%), while improvement was seen in 59 (46.8%) patients. This study showed a high mortality rate in the pulmonary group (19 (30.1%)) compared to the non pulmonary group (13 (20.6%)). Death due to Cardio-Pulmonary Arrest (CPA) was significantly more frequent in pulmonary cases (n=15; 23.8%, p=0.0002\*), suggesting a greater impact of respiratory compromise on mortality. Death due to sepsis was more common in non pulmonary cases (n=11; 17.5%, p=0.05\*), emphasising the increased risk of systemic infections in non pulmonary patients.

		Acinetobacter baumanni complex				Kle	bsiella pneumoni	ae
Antibiotics	Pulmonary n (%)	Non pulmonary n (%)	Chi-square value	p-value using Chi-square test	Pulmonary n%	Non pulmonary n%	Chi-square value	p-value using Chi-square test
Amikacin	11 (68.75%)	13 (86.66%)	1.422	p=0.2331	6 (42.8%)	7 (50%)	0.144	p=0.701
Gentamycin	11 (68.75%)	13 (86.66%)	1.422	p=0.2331	5 (35.7%)	5 (35.7%)	0.000	p=1.001
Cefoperazone/sulbactam	3 (18.75%)	7 (46.66%)	2.761	p=0.0966	8 (57.14%)	4 (28.57%)	2.333	p=0.132
Ceftriaxone	13 (81.25%)	13 (86.66%)	0.168	p=0.6820	13 (92.85%)	13 (92.85%)	0.000	p=1.000
Ciprofloxacin	9 (56.25%)	13 (86.66%)	3.476	p=0.0622	5 (35.7%)	10 (71.42%)	3.590	p=0.061
Levofloxacin	3 (18.75%)	11 (73.33%)	9.314	p=0.0023*	3 (21.4%)	9 (64.28%)	5.250	p=0.231
Cefuroxime	3 (18.75%)	1 (6.66%)	1.006	p=0.3159	8 (57.14%)	0	11.200	p=0.001*
Cefuroxime axetil	3 (18.75%)	1 (6.66%)	1.006	p=0.3159	8 (57.14%)	0	11.200	p=0.001*
Amoxicillin/clavulinic acid	2 (18.75%)	10 (66.6%)	9.574	p=0.0020*	3 (21.4%)	10 (71.42%)	7.036	p=0.009*
Piperacillin/tazobactam	10 (62.5%)	12 (80%)	1.151	p=0.2834	11 (78.5%)	1 (7.14%)	14.583	p=0.0002*
Imipenem	15 (93.75%)	13 (86.66%)	0.444	p=0.5050	1 (7.14%)	7 (50%)	6.300	p=0.01*
Meropenem	16 (100%)	14 (93.3%)	1.102	p=0.2938	12 (85.71%)	11 (78.5%)	0.243	p=0.701
Trimethoprim/ sulfamethoxazole	5 (31.25%)	13 (86.66%)	9.764	p=0.0018*	6 (42.8%)	5 (35.7%)	0.150	p=0.612
Tigecycline	1 (6.25%)	0	0.969	p=0.3250	1 (7.14%)	0	0.969	p=0.213

[Table/Fig-9]: Antibiotic resistance patterns of Acinetobacter baumannii and Klebsiella pneumoniae in pulmonary and non pulmonary indications of MV. p-values<0.05 are statistically significant and marked with asterisks

Improvement rates were significantly higher in pulmonary cases (35 (55.6%)) compared to non pulmonary cases (24 (38.1%)), which is statistically significant with p=0.05\*, possibly reflecting a better treatment response for respiratory infections. An odds ratio of 1.002 indicates that the likelihood of mortality is almost the same for both pulmonary and non pulmonary infections [Table/Fig-10].

	Pulmonary indications n (%)	indications Non pulmonary Total		Odds Ratio (OR)
Death	19 (30.1%)	13 (20.6%)	32 (25.3%)	1.002
Improved	35 (55.5%)	24 (38%)	59 (46.8%)	1.002

[Table/Fig-10]: Clinical outcomes in pulmonary and non pulmonary Ventilator Associated Pneumonia (VAP) cases.

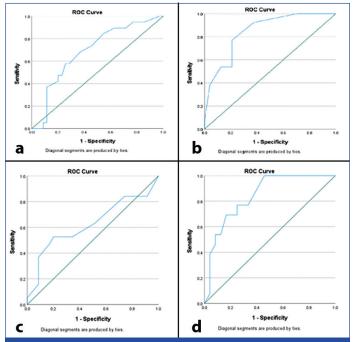
Patients who took Discharge Against Medical Advice (DAMA) or were lost to follow-up were excluded. OR: 1.002; 95% CI: 0.4173 to 2.4068 and p=0.9961 which indicates there is no significant difference between mortality and improvement between two groups

These findings suggest that while the incidence and resistance patterns may differ, the ultimate clinical outcomes of VAP were not significantly influenced by the indication for MV. Both APACHE II and SOFA scores demonstrated stronger predictive accuracy for mortality in the non pulmonary group. The APACHE II score had an Area Under the Curve (AUC) of 0.841 (95% CI: 0.715–0.965), with a sensitivity of 100% and specificity of 54%. The SOFA score had an AUC of 0.846 (95% CI: 0.721–0.971), with a sensitivity of 53% and specificity of 80%, indicating excellent discriminative power (p=0.001 for both). In contrast, the pulmonary group showed moderate predictive value, with an APACHE II AUC of 0.688 (p=0.024), sensitivity of 58%, and specificity of 74%. The SOFA AUC was 0.626 (p=0.130), with a sensitivity of 77% and specificity of 79% [Table/Fig-11,12]. These findings suggest that both scoring systems are more reliable for mortality prediction in non pulmonary VAP patients.

# **DISCUSSION**

The VAP continues to be a critical concern among ICU patients receiving MV, with considerable implications for patient outcomes and healthcare burdens. In this study, we compared VAP incidence, microbial patterns, antibiotic resistance, clinical outcomes, and the predictive value of APACHE II and SOFA scores between pulmonary and non pulmonary indications for MV-a comparison that many studies on VAP lack.

In our study, the mean age of VAP patients with pulmonary indications for MV was 58±16.4 years, with 71.4% being males



**[Table/Fig-11]:** ROC curve of: a) APACHE 2 score in pulmonary indications; b) APACHE 2 score in non pulmonary indications; c) SOFA score in pulmonary indications; d) SOFA score in non pulmonary indications. Larger values of the test variables indicate stronger evidence for a positive actual state.

Scoring system	Group	Cut-off Score	AUC (95% CI)	p- value	Sensitivity (%)	Specificity (%)
APACHE	Pulmonary	>23	0.688 (0.541–0.834)	0.024	58%	74%
II	Non- pulmonary	>18	0.841 (0.715-0.965)	0.001	100%	54%
SOFA	Pulmonary	≥8	0.626 (0.456-0.795)	0.13	53%	80%
	Non- pulmonary	≥7	0.846 (0.721-0.971)	0.001	77%	79%

[Table/Fig-12]: APACHE II and SOFA Score comparison with ROC analysis in pulmonary and non pulmonary Ventilator Associated Pneumonia (VAP) cases. AUC: Area Under the ROC Curve; CI: Confidence interval. AUC > 0.8 indicates strong predictive ability; APACHE II: Acute physiology and chronic health evaluation score; SOFA: Sequential organ functional assessment score

and 28.5% females. In comparison, a study conducted in 2023 by Mumtaz H et al., reported a mean age of 53.5 years for VAP patients with pulmonary indications, with 64.8% being males [16]. In another study by Khilnan GC et al., the mean age of VAP patients

with COPD was  $62.45\pm8.32$  years, with 58.8% being males [17]. The mean age for non pulmonary indications in our study was  $49\pm18.03$  years, which is nearly similar to a study by Battaglini D et al., reported that a mean age of 54 years for non pulmonary VAP patients, with 45.6% being males and 37.6% being females [18].

The overall VAP incidence in our study was 37.2% per 1000 ventilator days. Our results demonstrated a higher incidence of VAP in non pulmonary cases (52.5%) compared to pulmonary cases (47%), which corresponds to similar findings in previous literature involving trauma, surgical, and neurocritical care patients [18]. The incidence of VAP in the pulmonary group in our study was 47%, resembling a study conducted by Reyes LF et al., where 50.5% of 100 patients developed VAP [19]. A growing body of research indicates that sexspecific reactions to traumatic damage, which reflect variations in immune function, may contribute to the gender gap in VAP incidence. This impact seems to be connected to the negative effects of testosterone and the positive benefits of estrogen.

The two most frequently isolated pathogens were the Gramnegative organisms, namely *Acinetobacter baumannii* Complex and *Klebsiella pneumoniae*, in both groups. Khelagi A et al., in 2017, conducted a study in southern India examining the role that Gramnegative bacteria play in VAP [20]. This aligns well with the current study, which found that 2% of the bacteria were Gram-positive cocci and 98% were Gram-negative bacilli. *Serratia marcescens* was more prevalent in the pulmonary group, with 5 cases (p=0.0230), which correlates with findings by Vetter L et al., who reported that the majority of Serratia marcescens strains in the ICU were isolated from respiratory samples [21].

Antibiotic resistance patterns revealed significantly higher resistance in non pulmonary VAP cases, particularly for Levofloxacin and Amoxicillin/Clavulanic acid among Acinetobacter, and for Piperacillin/Tazobactam and Cefuroxime among Klebsiella pneumoniae in pulmonary cases. Both Imipenem and Meropenem showed high resistance rates in both groups, which correlates with findings by Li Y et al., in 2024 [22]. These findings emphasise the growing need for localised antibiograms and stewardship policies to combat multidrug-resistant (MDR) organisms [23]. Tigecycline sensitivity was observed in 62.5% of pulmonary cases and 100% of non pulmonary cases (p=0.0018\*). Patil P et al., reported that Gram-negative bacteria, especially Acinetobacter baumannii, were highly resistant to most antibiotics except tigecycline and colistin [24]. Tigecycline was particularly effective in non pulmonary VAP caused by Klebsiella pneumoniae. Similarly, Unver E et al., identified tigecycline and amikacin as the most effective treatments for K. pneumoniae infections [25].

This study showed a high mortality rate in the pulmonary group (19 cases, 30.1%) compared to the non pulmonary group (13 cases, 20.6%). In a similar study conducted by Rinaudo M et al., it was demonstrated that the highest mortality is linked to COPD, with rates ranging from 38% to 60% in patients with VAP [26]. Death due to cardiopulmonary arrest was significantly more frequent in pulmonary cases, suggesting a greater impact of respiratory compromise on mortality, whereas death due to sepsis was more common in non pulmonary cases, emphasising the increased risk of systemic infections.

In patients with pulmonary conditions, prevention should focus on optimising bronchial hygiene, utilising non-invasive ventilation where appropriate, and implementing strict antibiotic stewardship due to the higher risk of resistant colonisation. Conversely, non pulmonary patients-particularly those with neurological impairments, trauma, or postoperative status-may benefit more from interventions aimed at reducing aspiration risk, such as head-of-bed elevation and rigorous oral care with chlorhexidine. Early mobilisation, minimisation of sedation, and careful avoidance of re-intubation are especially critical in this group to shorten ventilation duration and reduce VAP incidence. These distinct approaches underscore the importance

of individualised prevention protocols based on the underlying indication for MV.

A key strength of our study was the evaluation of the APACHE II and SOFA scoring systems. Among non pulmonary cases, APACHE II had a better predictive value for mortality with an AUC of 0.841, while the SOFA score similarly showed strong performance with an AUC of 0.846. Likewise, Zhou XY et al., found APACHE II to be stronger compared to CPIS in predicting 30-day mortality in VAP patients [13]. These findings are consistent with those of Naved SA et al., who demonstrated that higher APACHE II scores were associated with increased ICU mortality [27]. Gupta A et al., and Sutiono AB et al., also reinforced the role of these scores in early mortality prediction and triaging ICU care, particularly in resource-limited settings [28,29].

### Limitation(s)

The single-center nature of the study restricts the generalisability of the findings to other settings with different patient populations and ICU practices. Variations in clinical judgment and documentation could have affected the accuracy of VAP diagnosis, particularly given the subjective nature of radiological and clinical criteria. Differences in baseline characteristics between patients intubated for pulmonary versus non pulmonary reasons may have further influenced the observed outcomes.

# **CONCLUSION(S)**

The VAP was more common in patients with non pulmonary indications for MV. This study highlights the need for close monitoring of VAP in patients ventilated for non pulmonary indications, as they exhibited a higher incidence despite lacking primary lung pathology. The presence of multidrug-resistant pathogens reinforces the importance of targeted antibiotic stewardship. Although mortality was similar across groups, scoring systems like APACHE II and SOFA were more predictive in non pulmonary cases, suggesting their value for early risk assessment and guiding timely clinical interventions.

#### REFERENCES

- [1] Papazian L, Klompas M, Luyt CE. Ventilator-associated pneumonia in adults: A narrative review. Intensive Care Med. 2020;46(5):888-906. Doi: 10.1007/s00134-020-05980-0.
- [2] Jeannet R, Daix T, Chollet S, Vaidie J, Galinat T, Vignon P, et al. CD16^dim^CD64^+^ granulocytes are of interest in the diagnosis of ventilator associated pneumonia in neurological intensive care unit patients. J Transl Crit Care Med. 2025;7(1):e24-00035.
- [3] Kalanuria AA, Ziai W, Mirski M. Ventilator-associated pneumonia in the ICU. Crit Care. 2014;18(2):208. Erratum in: Crit Care. 2016;20:29.
- [4] Li W, Cai J, Ding L, Chen Y, Wang X, Xu H. Incidence and risk factors of ventilator-associated pneumonia in the intensive care unit: A systematic review and meta-analysis. J Thorac Dis. 2024;16(9):5518-28. Doi: 10.21037/jtd-24-150.
- [5] Ibrahim EH, Tracy L, Hill C, Fraser VJ, Kollef MH. The occurrence of ventilatorassociated pneumonia in a community hospital: Risk factors and clinical outcomes. Chest. 2001;120(2):555-61.
- [6] Safdar N, Crnich CJ, Maki DG. The pathogenesis of ventilator-associated pneumonia: Its relevance to developing effective strategies for prevention. Respir Care. 2005;50(6):725-39; discussion 739-41.
- [7] Erbay RH, Yalcin AN, Zencir M, Serin S, Atalay H. Costs and risk factors for ventilator-associated pneumonia in a Turkish university hospital's intensive care unit: A case-control study. BMC Pulm Med. 2004;4:3.
- [8] Sano M, Shindo Y, Takahashi K, Okumura J, Sakakibara T, Murakami Y, et al. Risk factors for antibiotic resistance in hospital-acquired and ventilator-associated pneumonia. J Infect Chemother. 2022;28(7):985-92.
- [9] Mergulhão P, Pereira JG, Fernandes AV, Krystopchuk A, Ribeiro JM, Miranda D, et al. Epidemiology and burden of ventilator-associated pneumonia among adult intensive care unit patients: A Portuguese, multicenter, retrospective study (eVAP-PT study). Antibiotics (Basel). 2024;13(4):290.
- [10] Vincent JL. Ventilator-associated pneumonia. J Hosp Infect. 2004;57(4):272-80.
- [11] Gursel G, Demirtas S. Value of APACHE II, SOFA and CPIS scores in predicting prognosis in patients with ventilator-associated pneumonia. Respiration. 2006;73(4):503-08.
- [12] Hosseini M, Ramazani J. Evaluation of acute physiology and chronic health evaluation II and sequential organ failure assessment scoring systems for prognostication of outcomes among Intensive Care Unit's patients. Saudi J Anaesth. 2016;10(2):168-73.

- [13] Zhou XY, Ben SQ, Chen HL, Ni SS. A comparison of APACHE II and CPIS scores for the prediction of 30-day mortality in patients with ventilator-associated pneumonia. Int J Infect Dis. 2015;30:144-47.
- Kalil AC, Metersky ML, Klompas M, Muscedere J, Sweeney DA, Palmer LB, et al. Management of adults with hospital-acquired and ventilator-associated pneumonia: 2016 clinical practice guidelines by the Infectious Diseases Society of America and the American Thoracic Society. Clinical Infectious Diseases. 2016;63(5):e61-e111.
- Baselski V, Klutts JS. Quantitative cultures of bronchoscopically obtained specimens should be performed for optimal management of ventilator-associated pneumonia. J Clin Microbiol. 2013;51(3):740-44. Doi: 10.1128/JCM.03383-12.
- Mumtaz H, Saqib M, Khan W, Ismail SM, Sohail H, Muneeb M, et al. Ventilator associated pneumonia in intensive care unit patients: A systematic review. Ann Med Surg (Lond). 2023;85(6):2932-39.
- Khilnani GC, Dubey D, Hadda V, Sahu SR, Sood S, Madan K, et al. Predictors and microbiology of ventilator-associated pneumonia among patients with exacerbation of chronic obstructive pulmonary disease. Lung India. 2019;36(6):506-11.
- [18] Battaglini D. Parodi L. Cinotti R. Asehnoune K. Taccone FS. Orengo G. et al. Ventilator-associated pneumonia in neurocritically ill patients: Insights from the ENIO international prospective observational study. Respir Res. 2023;24(1):146.
- Reyes LF, Rodriguez A, Fuentes YV, Duque S, García-Gallo E, Bastidas A, et al.; LIVEN-Covid-19; SEMICYUC Study Group. Risk factors for developing ventilator-associated lower respiratory tract infection in patients with severe COVID-19: A multinational, multicentre, prospective, observational study. Sci Rep. 2023;13(1):6553.
- Khelgi A, Prathab B. Bacteriological profile of ventilator associated pneumonia in a tertiary care hospital of South India with special reference to multi drug resistant pathogens. Int J Curr Microbiol Appl Sci. 2017;6(11):5418.
- Vetter L, Schuepfer G, Kuster SP, Rossi M. A hospital-wide outbreak of Serratia marcescens, and Ishikawa's "fishbone" analysis to support outbreak control. Qual Manag Health Care. 2016;25(1):01-07.

- [22] Li Y, Jiang Y, Liu H, Fu Y, Lu J, Li H, et al. Targeted next-generation sequencing for antimicrobial resistance detection in ventilator-associated pneumonia. Front Cell Infect Microbiol. 2025;15:1526087.
- Prieto-Alvarado DE, Parada-Gereda HM, Molano D, Martinez YL, Tafurt GPR, Masclans JR. Risk factors and outcomes of ventilator-associated pneumonia in patients with traumatic brain injury: A systematic review and meta-analysis. J Crit Care. 2025;85:154922.
- [24] Patil P, Muthal A, Shah J, Raut A. Determinants of nosocomial infections and emerging antibiotic resistance in the Intensive Care Unit: A prospective evidencebased study. Asian Pac J Trop Med. 2025;18(1):33-43.
- [25] Unver E, Cikman A, Karakecili F, Koc A, Karavas E. Microorganisms causing ventilator-associated pneumonia and their antibiotic susceptibility. Eurasian J Med Investig. 2019;3(4):376-80.
- Rinaudo M, Ferrer M, Terraneo S, De Rosa F, Peralta R, Fernández-Barat L, et al. Impact of COPD in the outcome of ICU-acquired pneumonia with and without previous intubation. Chest. 2015;147(6):1530-38.
- [27] Naved SA, Siddiqui S, Khan FH. APACHE-II score correlation with mortality and length of stay in an intensive care unit. J Coll Physicians Surg Pak. 2011;21(1):04-08.
- Gupta A, Agrawal A, Mehrotra S, Singh A, Malik S, Khanna A. Incidence, risk stratification, antibiogram of pathogens isolated and clinical outcome of ventilator associated pneumonia, Indian J Crit Care Med. 2011;15(2):96-101
- Sutiono AB, Arifin MZ, Adhipratama H, Hermanto Y. The utilization of APACHE Il score to predict the incidence of ventilator-associated pneumonia in patients with severe traumatic brain injury: A single-center study. Interdiscip Neurosurg. 2022;28:101453.

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