DOI: https://doi.org/10.53350/pjmhs02024181960

ORIGINAL ARTICLE

Clinical Outcomes of Ventilator-Associated Pneumonia in Critically Ill Patients Admitted to Intensive Care Unit

MUZAMIL MEHMOOD[1], SHAH ZAMAN GUL[2], FAISAL IQBAL[3], MUHAMMAD SHABEER KHAN[1], ABDUL KABIR[4], SABA GUL[4]
[1]*Medical Officer, Intensive Care Unit, Lady Reading Hospital, Peshawar*
[2]*Medical Officer / Clinical Coordinator, Intensive Care Unit, Lady Reading Hospital, Peshawar*
[3]*Junior Registrar Anesthesia, Lady Reading Hospital, Peshawar*
[4]*Medical Officer Anesthesia, Lady Reading Hospital, Peshawar*
Correspondence to: Shah Zaman Gul, Email: shahzzaman@gmail.com

ABSTRACT

Background: Ventilator-associated pneumonia is a frequent hospital-acquired infection among critically ill patients receiving invasive mechanical ventilation. It is associated with prolonged ICU stay, longer duration of mechanical ventilation, antimicrobial resistance, septic shock and increased mortality. Timely recognition of VAP and evaluation of its outcomes are essential to improve ICU care.

Objective: To determine the clinical outcomes of ventilator-associated pneumonia in critically ill patients admitted to the intensive care unit.

Methods: This prospective observational cohort study was conducted in the Intensive Care Unit of Lady Reading Hospital, Peshawar, from April 2023 to August 2023. A total of 75 mechanically ventilated adult patients were enrolled through non-probability consecutive sampling and followed during ICU admission. Patients admitted with pneumonia, ventilation duration <48 hours and incomplete records were excluded. Demographic data, comorbidities, VAP status, microbiological findings, APACHE II score, duration of mechanical ventilation, ICU stay, septic shock, acute kidney injury, vasopressor requirement and ICU mortality were recorded. Data were analyzed using SPSS version 25. Effect sizes were reported as mean differences or odds ratios with 95% confidence intervals. A p-value <0.05 was considered statistically significant.

Results: Out of 75 mechanically ventilated ICU patients, VAP was diagnosed in 28 (37.3%) patients, while 47 (62.7%) did not develop VAP. Late-onset VAP was more frequent than early-onset VAP [18 (64.3%) vs 10 (35.7%)]. The most common organisms were Acinetobacter baumannii, Klebsiella pneumoniae and Pseudomonas aeruginosa. Patients with VAP had longer duration of mechanical ventilation, prolonged ICU stay, higher septic shock, greater vasopressor requirement and increased ICU mortality compared with non-VAP patients. ICU mortality was 50.0% in the VAP group and 25.5% in the non-VAP group (OR = 2.92, 95% CI: 1.10–7.72, p = 0.031). APACHE II score was independently associated with ICU mortality (AOR = 1.12, 95% CI: 1.02–1.24, p = 0.021). Mortality was also higher among patients with multidrug-resistant organisms.

Conclusion: Ventilator-associated pneumonia was associated with poor clinical outcomes among critically ill ICU patients. VAP patients had longer ventilation duration, prolonged ICU stay, higher septic shock, increased vasopressor support and greater ICU mortality. Baseline severity of illness and multidrug-resistant infection further contributed to mortality risk. Strict infection-control practices, ventilator-care bundles, early diagnosis and culture-guided antibiotic therapy are essential to reduce the burden of VAP in ICU settings.

Keywords: Ventilator-associated pneumonia, ICU, mechanical ventilation, clinical outcomes, mortality, septic shock, multidrug resistance, APACHE II.

INTRODUCTION

Ventilator-associated pneumonia (VAP) is a severe infection that occurs in ventilated patients, those who are breathing with a mechanical ventilator inserted into the windpipe or tracheostomy. It usually occurs after 48 hours of mechanical ventilation and is considered one of the most important hospital-acquired infections in intensive care units. The high-risk patients include critically ill who have had poor cough reflex, have compromised immunity, are on an intubated ventilator, or have had exposure to invasive devices, which increase their risk of developing septicemia. VAP continues to be a significant problem in the ICU setting, impacting patient survival and hospital resource utilization[1-3].

Several factors are associated with the development of VAP, including patient-related and ICU-related factors. They may be more prone to infection if they're older and have other complications, have low consciousness, continue ventilation, reintubated, low oral hygiene scores, or stay in the intensive care unit for more than three days. The endotracheal tube opens the airway away from the protective mechanisms and provides the opportunity for the microaspiration of contaminated secretions into the lower respiratory tract. Biofilm formation within the tube can also serve as a source of re-infection making infection control challenging[4-6].

A clinical diagnosis of VAP can typically be made based on a combination of the aforementioned criteria: fever, purulent tracheal secretions, elevated leukocyte count, increasing oxygen requirement and development of new or progressive infiltrates on a chest radiograph. Culture of endotracheal aspirate (or culture of tracheal secretion) is useful for microbiological confirmation of the organism and to direct antibiotic treatment. Sepsis, acute respiratory distress syndrome (ARDS), pulmonary edema, or other lung disease, however, may have overlapping clinical features, making the diagnosis difficult in the critically ill patient[7, 8].

VAP microbiology is different depending on the hospital ward, length of stay on the ventilator, prior antibiotic use and local infection control policies. Acinetobacter baumannii, Klebsiella pneumoniae and Pseudomonas aeruginosa are commonly isolated from patients in the ICU. Late onset VAP is much more likely to be due to the presence of MDR organisms that may reduce antibiotic options and increase morbidity. Thus, the knowledge and utilization of culture-based treatment and periodic review of local antibiograms are crucial to good management[9, 10].

There are several unfavourable clinical outcomes that are associated with VAP. VAP patients may need more mechanical ventilation, longer length of stay in the ICU, increased antibiotic therapy, and more supportive therapy. Additionally, infected patients are at higher risk for complications like septic shock, acute kidney injury, need for vasopressors and mortality. These outcomes lead to a higher clinical and economic burden on health care systems, especially in high workload tertiary care hospitals with limited resource facilities, such as intensive care units (ICUs)[11, 12].

While improved treatment in the ICU has reduced the incidence of VAP, it is still a preventable, but frequent

Received on 12-10-2023
Accepted on 29-12-2023

complication. Its occurrence can be reduced by preventive measures, including hand hygiene, bed elevation at the head end, oral care, subglottic secretion drainage, if available, sedation interruption at least once a day, early mobilization, and timely assessment for extubation. The frequency and the outcomes of VAP in the local ICU setting are important to study due to differences in microbiological patterns and patient outcomes between hospitals[13, 14].

The present study was conducted to assess the clinical outcomes of ventilator-associated pneumonia among critically ill patients admitted to the ICU of Lady Reading Hospital, Peshawar. The study focused on VAP frequency, microbial profile, duration of mechanical ventilation, ICU stay, septic shock, vasopressor requirement, acute kidney injury, and mortality. The findings may help improve local ICU protocols, strengthen infection-control measures, and support early management strategies for patients at risk of VAP.

METHODOLOGY

This study was conducted as a prospective observational cohort study in the Intensive Care Unit of Lady Reading Hospital, Peshawar, from April 2023 to August 2023. Patients were selected by non-probability consecutive sampling. All eligible patients who fulfilled the inclusion criteria during the study period were included until the required sample size was achieved. All eligible mechanically ventilated patients were enrolled and followed during their ICU admission. The sample size was calculated using the WHO sample size calculator for a single population proportion. The expected proportion of ventilator-associated pneumonia among mechanically ventilated ICU patients was taken as 37%, based on a recent systematic review and meta-analysis that reported a pooled VAP incidence of 30% with an upper 95% confidence limit of 37% among ICU patients receiving mechanical ventilation (15). The confidence level was kept at 95%, with an absolute precision of 11%. The calculated sample size was approximately 75 patients. The sample size was calculated for estimating the frequency of ventilator-associated pneumonia among mechanically ventilated ICU patients and not specifically for detecting differences in clinical outcomes or mortality between VAP and non-VAP groups. Therefore, outcome comparisons and regression findings should be interpreted as exploratory. Therefore, 75 eligible mechanically ventilated ICU patients were included in the final analysis. The total number of patients in the study was 75 with severe illness. All patients (both men and women) aged 18 years or older who were still mechanically ventilated after 48 hours were eligible. Ventilator-associated pneumonia (VAP) was defined as pneumonia that occurred after mechanical ventilation for ≥48 hours and endotracheal intubation, which is confirmed by clinical, radiological and laboratory criteria. Patients admitted with pneumonia, patients with ventilation duration of less than 48 hours, those with incomplete clinical data, those that were transferred from other hospitals with a prior diagnosis of LRTI were excluded from the study. Disease severity was assessed within the first 24 hours of ICU admission using the APACHE II score. The score was calculated from routine clinical and laboratory parameters available in the patient record and was used as an adjustment variable during multivariable analysis. APACHE II score was also compared between VAP and non-VAP groups to assess baseline severity differences.

Multidrug-resistant organism was defined as non-susceptibility to at least one antimicrobial agent in three or more antimicrobial categories. Acute kidney injury was defined according to KDIGO criteria as an increase in serum creatinine by ≥0.3 mg/dL within 48 hours, an increase in serum creatinine to ≥1.5 times baseline within seven days, or reduced urine output. Septic shock was defined as sepsis with persistent hypotension requiring vasopressor support to maintain mean arterial pressure ≥65 mmHg despite adequate fluid resuscitation, along with evidence of tissue hypoperfusion. Approval was granted from the hospital ethical review committee and data were collected. Most patients were in the ICU and unable to provide informed consent; therefore, the patient's attendant or legal guardian was asked to sign informed consent. All patients were treated confidentially throughout the study and no identifying information was used in the analysis of the data. All data was captured on a structured proforma specially developed for this research.

The demographic variables were age and gender. Baseline clinical parameters were the reason for admission to the intensive care unit, presence of comorbid conditions (diabetes mellitus, hypertension, chronic obstructive pulmonary disease, chronic kidney disease, and ischemic heart disease). ICU-associated complications included mechanical ventilation, length of stay on the ICU, requirement for vasopressor support, septic shock, acute kidney injury, and patient outcome. Patients were categorized into two groups: those who developed VAP and those who did not develop VAP during ICU admission.

Ventilator-associated pneumonia was diagnosed based on the presence of new or progressive infiltrates on chest X-ray, plus clinical signs including fever, purulent tracheal secretions, elevated total leukocyte count, increased need for oxygen, and positive endotracheal aspirate or tracheal secretion culture when available. VAP was then classified as early VAP (onset within the first four days of mechanical ventilation) and late VAP (onset after four days of mechanical ventilation). Cultures were reported as positive or negative, and organism type.

Primary outcome variables were mortality in the ICU, mechanical ventilation, length of stay in the ICU, septic shock, acute kidney injury and use of vasopressors. Mortality was considered to be death during admission to the ICU. Mean duration of ICU stay and mechanical ventilation were used to assess prolonged ICU stay and prolonged mechanical ventilation, respectively, between VAP and non-VAP patients. To assess the impact of VAP on the morbidity and mortality of the patients, the clinical outcomes of patients with VAP were compared with those who did not develop VAP in the same ICU.

The data were entered and analyzed by SPSS version 25. Quantitative data (age, length of mechanical ventilation, length of stay in ICU) were represented as mean and standard deviation. Frequency and percentage were used for qualitative variables like gender, comorbidities, VAP status, type of VAP, isolated organisms, septic shock, requirement of vasopressor, acute kidney injury and mortality. Chi square was used to compare categorical variables between the VAP and non-VAP groups. Continuous variables like ICU stay and MV duration were compared using the independent sample t-test. The study used a p value < 0.05 as the criterion for the statistical significance. Effect sizes were calculated as mean differences for continuous variables and odds ratios for categorical variables. Corresponding 95% confidence intervals were reported to show the magnitude and precision of associations. Binary logistic regression analysis was performed to identify independent predictors of ICU mortality. ICU mortality was taken as the dependent variable. Independent variables entered into the model included VAP status, APACHE II score, septic shock, vasopressor requirement, and multidrug-resistant organism. Adjusted odds ratios with 95% confidence intervals were calculated. Because of the limited number of ICU mortality events, the multivariable logistic regression model was considered exploratory. The adjusted odds ratios were used to assess the direction and possible strength of association rather than to provide definitive prediction estimates. A p-value <0.05 was considered statistically significant.

RESULTS

A total of 75 critically ill patients admitted to the ICU and requiring invasive mechanical ventilation were included in the final analysis. The mean age of the patients was 52.6 ± 15.8 years. Most patients were in the age group of 41–60 years, followed by patients older than 60 years. Out of 75 patients, 46 (61.3%) were males and 29 (38.7%) were females. Respiratory failure, septic peritonitis, postoperative complications and neurological disorders were the most frequent reasons for ICU admission. The mean APACHE II score of the study population was 18.9 ± 5.6, indicating moderate-to-severe baseline illness severity among the included ICU patients.

Table 1 shows the baseline demographic and clinical characteristics of the study participants. The majority of patients were male, and the most frequent age group was 41–60 years. Hypertension and diabetes mellitus were the most common comorbid conditions. APACHE II score was also included to describe baseline severity of illness.

Ventilator-associated pneumonia was diagnosed in 28 (37.3%) patients, while 47 (62.7%) patients did not develop VAP during ICU admission. Late-onset VAP was more frequent than early-onset VAP [18 (64.3%) vs 10 (35.7%)]. The mean time from initiation of mechanical ventilation to diagnosis of VAP was 5.8 ± 2.1 days.

Table 2 presents the frequency and type of VAP among mechanically ventilated ICU patients. More than one-third of the patients developed VAP. Among VAP cases, late-onset VAP was more common than early-onset VAP.

Of the 28 patients with VAP, microbiological culture was positive in 22 (78.6%) cases, while 6 (21.4%) cases were culture-negative. The most commonly isolated organisms were Acinetobacter baumannii, Klebsiella pneumoniae, Pseudomonas aeruginosa and Staphylococcus aureus. Multidrug-resistant organisms were identified in 15 (53.6%) VAP cases, showing a considerable burden of resistant infection among mechanically ventilated ICU patients.

Table 3 shows the microbiological profile of patients with VAP. Acinetobacter baumannii was the most frequently isolated organism, followed by Klebsiella pneumoniae and Pseudomonas aeruginosa. Culture-negative VAP was reported in 21.4% of cases.

Patients who developed VAP had worse clinical outcomes compared with patients without VAP. The mean APACHE II score was higher in the VAP group than in the non-VAP group (20.3 ± 5.8 vs 18.1 ± 5.3), although this difference was not statistically significant (p = 0.098). The mean duration of mechanical ventilation was significantly longer among VAP patients compared with non-VAP patients (9.6 ± 3.4 vs 5.1 ± 2.2 days, p = 0.001). Similarly, the mean ICU stay was significantly longer in the VAP group than in the non-VAP group (13.8 ± 4.6 vs 8.4 ± 3.1 days, p = 0.001). Septic shock, vasopressor requirement and ICU mortality were also significantly more frequent among patients with VAP. ICU mortality was 14 (50.0%) in the VAP group compared with 12 (25.5%) in the non-VAP group (OR = 2.92, 95% CI: 1.10–7.72, p = 0.031).

Table 4 compares clinical outcomes between patients with and without VAP. Patients with VAP had significantly longer mechanical ventilation duration, longer ICU stay, higher frequency of septic shock, greater vasopressor requirement and higher ICU mortality. Effect sizes and 95% confidence intervals were added to show the magnitude and precision of these associations. Acute kidney injury was more frequent in the VAP group, but the difference was not statistically significant.

Mortality was higher among patients with late-onset VAP and among those infected with multidrug-resistant organisms. Among the 18 patients with late-onset VAP, 11 died, giving a mortality rate of 61.1% within the late-onset VAP subgroup. In Table 5, late-onset VAP was present in 11 of the 14 non-survivors, representing 78.6% of deaths among VAP patients. This difference is due to the use of different denominators. Mortality was also higher among patients infected with multidrug-resistant organisms compared with those without multidrug-resistant organisms [10 (66.7%) vs 4 (30.8%)].

Table 5 shows factors associated with mortality among patients who developed VAP. Multidrug-resistant organism infection, septic shock and vasopressor requirement were significantly associated with ICU mortality. Late-onset VAP was more common among non-survivors, but the association did not reach statistical significance. As Table 5 included only VAP patients, with 14 survivors and 14 non-survivors, these subgroup p-values should be interpreted cautiously because the small cell counts may reduce statistical stability. Therefore, these associations should be considered exploratory.

Multivariable logistic regression was performed among all 75 mechanically ventilated ICU patients, with ICU mortality as the dependent variable. APACHE II score was included in the model to adjust for baseline severity of illness. After adjustment for other clinically important variables, Multivariable logistic regression was performed as an exploratory analysis among all 75 mechanically ventilated ICU patients, with ICU mortality as the dependent variable. APACHE II score was included to adjust for baseline severity of illness. In this exploratory model, VAP, APACHE II score, septic shock, vasopressor requirement, and MDR organism infection showed increased adjusted odds of ICU mortality. However, these findings should be interpreted cautiously because the number of mortality events was limited in relation to the number of predictors entered into the model. Patients who developed VAP had 2.41 times higher odds of death compared with patients who did not develop VAP (AOR = 2.41, 95% CI: 1.01–5.78, p = 0.048). Each one-point increase in APACHE II score increased the odds of ICU mortality by 12% (AOR = 1.12, 95% CI: 1.02–1.24, p = 0.021). Septic shock was the strongest independent predictor, with patients having septic shock showing 3.18 times higher odds of ICU mortality (AOR = 3.18, 95% CI: 1.09–9.27, p = 0.034). Vasopressor requirement and MDR organism infection were also significantly associated with increased ICU mortality, with adjusted odds ratios of 2.76 and 2.89, respectively.

Table 6 presents the multivariable logistic regression analysis for predictors of ICU mortality. VAP, higher APACHE II score, septic shock, vasopressor requirement and MDR organism infection remained independently associated with increased odds of ICU mortality.

Overall, the results showed that VAP occurred in more than one-third of mechanically ventilated ICU patients. Patients with VAP had significantly longer duration of mechanical ventilation, prolonged ICU stay, higher septic shock, greater vasopressor requirement and increased ICU mortality compared with patients without VAP. Baseline severity of illness, as assessed by APACHE II score, was also associated with ICU mortality. Multidrug-resistant organisms further contributed to poor outcomes among VAP patients.

Table 1: Demographic and baseline clinical characteristics of study participants

Variable	Frequency / Mean	Percentage
Total patients	75	100%
Mean age	52.6 ± 15.8 years	—
APACHE II score	18.9 ± 5.6	—
Age ≤40 years	18	24.0%
Age 41–60 years	34	45.3%
Age >60 years	23	30.7%
Male	46	61.3%
Female	29	38.7%
Diabetes mellitus	24	32.0%
Hypertension	29	38.7%
COPD	16	21.3%
Chronic kidney disease	9	12.0%

Table 2: Frequency and type of ventilator-associated pneumonia

VAP status	Frequency	Percentage
VAP present	28	37.3%
VAP absent	47	62.7%
Early-onset VAP	10	35.7% of VAP cases
Late-onset VAP	18	64.3% of VAP cases

Table 3: Microbiological profile among VAP patients

Organism isolated	Frequency	Percentage
Acinetobacter baumannii	8	28.6%
Klebsiella pneumoniae	6	21.4%
Pseudomonas aeruginosa	5	17.9%
Staphylococcus aureus	3	10.7%
Culture negative	6	21.4%
Total VAP cases	28	100%

Table 4: Comparison of clinical outcomes between VAP and non-VAP patients

Clinical outcome	VAP present n=28	VAP absent n=47	Effect size	95% CI	p-value
APACHE II score	20.3 ± 5.8	18.1 ± 5.3	Mean difference = 2.20	−0.40 to 4.80	0.098
Duration of mechanical ventilation, days	9.6 ± 3.4	5.1 ± 2.2	Mean difference = 4.50	3.10 to 5.90	0.001
ICU stay, days	13.8 ± 4.6	8.4 ± 3.1	Mean difference = 5.40	3.60 to 7.20	0.001
Septic shock	12 (42.9%)	9 (19.1%)	OR = 3.17	1.11 to 9.04	0.026
Acute kidney injury	9 (32.1%)	8 (17.0%)	OR = 2.31	0.76 to 7.04	0.128
Need for vasopressors	15 (53.6%)	14 (29.8%)	OR = 2.72	1.04 to 7.11	0.039
ICU mortality	14 (50.0%)	12 (25.5%)	OR = 2.92	1.10 to 7.72	0.031
Discharged/improved	14 (50.0%)	35 (74.5%)	OR = 0.34	0.13 to 0.91	0.031

Table 5: Factors associated with mortality among patients with VAP

Factor	Survived n=14	Died n=14	p-value
Age >60 years	4 (28.6%)	8 (57.1%)	0.127
Late-onset VAP	7 (50.0%)	11 (78.6%)	0.115
Multidrug-resistant organism	5 (35.7%)	10 (71.4%)	0.048
Septic shock	3 (21.4%)	9 (64.3%)	0.023
Vasopressor requirement	5 (35.7%)	10 (71.4%)	0.048
ICU stay >10 days	9 (64.3%)	12 (85.7%)	0.190

Table 6: Multivariable logistic regression analysis for predictors of ICU mortality

Variable	Adjusted OR	95% CI	p-value
VAP present	2.41	1.01–5.78	0.048
APACHE II score	1.12	1.02–1.24	0.021
Septic shock	3.18	1.09–9.27	0.034
Vasopressor requirement	2.76	1.01–7.54	0.047
MDR organism	2.89	1.03–8.14	0.044

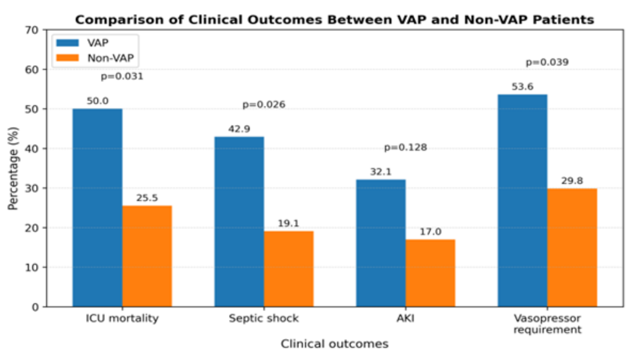

Figure 1. Comparison of clinical outcomes between VAP and non-VAP patients admitted to the ICU. Patients with VAP showed higher ICU mortality, septic shock, acute kidney injury, and vasopressor requirement compared with non-VAP patients. P-values show the statistical comparison between both groups.

DISCUSSION

In the present study, VAP was diagnosed in 28 out of 75 mechanically ventilated ICU patients, giving a frequency of 37.3%. This finding shows that more than one-third of critically ill ventilated patients developed pneumonia after mechanical ventilation. The observed frequency is within the broad range reported in previous literature, where VAP incidence has varied considerably depending on patient population, diagnostic methods, and ICU infection-control practices. Papazian et al. reported that the incidence of VAP may range from 5% to 40% among mechanically ventilated adults, while systematic evidence from Asia has shown that VAP remains a common ICU-acquired infection, particularly in low- and middle-income countries[1, 11].

The current study found that patients with VAP had significantly longer duration of mechanical ventilation and longer ICU stay compared with patients without VAP. This is clinically expected because pneumonia delays respiratory recovery, worsens oxygenation, increases airway secretions, and makes ventilator weaning more difficult. The effect size also supported this finding, as VAP patients had a mean mechanical ventilation duration that was 4.5 days longer than non-VAP patients, and the mean ICU stay was 5.4 days longer. Similar findings were reported by He et al., who observed that ventilator-associated events were associated with longer ICU and hospital stay and increased mortality risk among mechanically ventilated ICU patients[7]. Luo et al. also reported poorer short-term and long-term prognosis among ICU patients with VAP compared with those without VAP[8].

ICU mortality was higher among patients with VAP than among non-VAP patients in the present study. This finding supports the concept that VAP is not only a pulmonary infection but also a marker of severe systemic illness. VAP may increase inflammatory burden, worsen sepsis, contribute to hemodynamic instability, and promote multiorgan dysfunction. In the present study, patients with VAP had almost three times higher odds of ICU mortality compared with patients without VAP, as shown by the odds ratio and 95% confidence interval in the outcome analysis Although mortality in ICU patients is influenced by several factors, including underlying disease severity, comorbidities, shock, and organ failure, VAP has been repeatedly linked with poor clinical outcomes in critically ill populations[1, 7, 8].

Baseline severity of illness was assessed using the APACHE II score. The mean APACHE II score was higher among patients who developed VAP than among non-VAP patients, although this difference was not statistically significant. However, APACHE II score was significantly associated with ICU mortality in the multivariable regression model. This indicates that baseline illness severity contributed to mortality risk and supports the inclusion of APACHE II as an adjustment variable in the analysis.

Septic shock and vasopressor requirement were also more frequent among patients with VAP. This suggests that VAP may contribute to systemic infection and hemodynamic compromise in critically ill patients. The association between VAP, sepsis, and multiorgan dysfunction is clinically important because early recognition and timely antimicrobial treatment may reduce progression to shock. In the present study, septic shock remained an important predictor of mortality among VAP patients, which is consistent with previous evidence showing that critically ill patients with infection-related complications have worse outcomes and higher mortality[12, 13]. The odds of septic shock and vasopressor requirement were higher among VAP patients, further supporting the clinical importance of these complications.

The microbiological profile in the current study showed that gram-negative organisms were the most common isolates among VAP patients. Acinetobacter baumannii was the most frequently isolated organism, followed by Klebsiella pneumoniae and Pseudomonas aeruginosa. This pattern is similar to many ICU-based studies in which gram-negative bacteria predominate, especially in late-onset VAP and in patients exposed to broad-spectrum antibiotics. Multidrug-resistant organisms were also common in the present study and were associated with higher mortality. This finding highlights the need for local antibiogram-based empirical therapy, culture-guided de-escalation, and antimicrobial stewardship[5, 6, 11].

Late-onset VAP was more common than early-onset VAP in this study. Late-onset cases also showed higher mortality than early-onset cases. Among late-onset VAP patients, 11 out of 18 died, giving a mortality rate of 61.1% within that subgroup. In the survivor and non-survivor comparison, 11 of the 14 deaths among VAP patients occurred in late-onset VAP cases, representing 78.6% of non-survivors. This clarification explains the difference in percentages because the denominators are different. This may be related to prolonged ICU stay, greater baseline severity of illness, repeated antibiotic exposure, colonization with resistant organisms, and longer duration of mechanical ventilation. Similar observations have been reported in previous studies, where late-onset VAP has been more frequently linked with multidrug-resistant pathogens and adverse clinical outcomes[16-18].

The present study also included multivariable logistic regression analysis to identify predictors of ICU mortality. After adjustment for clinically important variables, VAP remained independently associated with ICU mortality. APACHE II score was also included to adjust for baseline severity of illness, which strengthens the analysis because critically ill patients may have different mortality risks even before developing VAP. Septic shock, vasopressor requirement, and MDR organism infection were also associated with increased odds of death. These findings suggest that mortality in mechanically ventilated ICU patients is influenced by both infection-related factors and baseline severity of illness[19, 20]. However, the regression findings should be interpreted with caution because the number of deaths was relatively small compared with the number of predictors included in the model. The regression model should therefore be considered exploratory rather than confirmatory. Larger multicenter studies with adequate outcome events are required to validate these associations and generate more stable adjusted estimates.

The findings of this study have important clinical implications for ICU practice. Strict implementation of ventilator-care bundles, early identification of suspected VAP, timely microbiological sampling, and culture-guided antimicrobial treatment may reduce VAP-related morbidity and mortality. The use of local antibiogram data is particularly important in settings where MDR gram-negative organisms are common. Regular surveillance of VAP frequency, organism profile, and resistance pattern should be part of ICU quality-improvement programs[21].

This study has some limitations. It was conducted at a single tertiary-care hospital with a relatively small sample size; therefore, the findings may not be generalizable to all ICU populations. Some microbiological sensitivity details were incomplete, and SOFA score was not included. However, APACHE II score was used for severity adjustment, and VAP and non-VAP groups were compared for clinically relevant outcomes. The sample size was calculated on the basis of expected VAP frequency/prevalence rather than for outcome comparison or mortality prediction. Similarly, the subgroup analysis in Table 5 was based on only 28 VAP patients, divided into 14 survivors and 14 non-survivors. Therefore, the p-values in this table may be unstable and should be interpreted as exploratory rather than definitive.

Therefore, the study was adequately powered to estimate VAP occurrence, but not specifically powered to compare all clinical outcomes or develop a robust mortality prediction model.

There was also a possibility of regression overfitting, as the number of mortality events was small in relation to the number of variables entered into the multivariable logistic regression model. Therefore, the regression model should be considered exploratory, and adjusted odds ratios should be interpreted cautiously. Further multicenter studies with larger sample sizes, detailed antimicrobial sensitivity patterns, standardized VAP diagnostic criteria, and robust severity-adjusted models are recommended.

CONCLUSION

Ventilator-associated pneumonia was frequent among mechanically ventilated ICU patients and was associated with poor clinical outcomes, including prolonged duration of mechanical ventilation, longer ICU stay, higher septic shock, increased vasopressor requirement, and greater ICU mortality. Late-onset VAP and multidrug-resistant organisms were associated with higher mortality among VAP patients. Baseline severity of illness, reflected by APACHE II score, also contributed to mortality risk. However, because the sample size was calculated for estimating VAP frequency rather than outcome comparison, and because the regression model was exploratory due to limited mortality events, the adjusted associations should be interpreted cautiously. Strict implementation of ventilator-care bundles, early diagnosis, microbiological surveillance, culture-guided antibiotic therapy, and antimicrobial stewardship are recommended to reduce VAP-related morbidity and mortality in ICU settings.

REFERENCES

1. Papazian L, Klompas M, Luyt CE. Ventilator-associated pneumonia in adults: a narrative review. Intensive care medicine. 2020;46(5):888-906.
2. 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.
3. Kalanuria AA, Zai W, Mirski M. Ventilator-associated pneumonia in the ICU. Critical Care. 2014;18(2):208.
4. Fernando SM, Tran A, Cheng W, Klompas M, Kyeremanteng K, Mehta S, et al. Diagnosis of ventilator-associated pneumonia in critically ill adult patients-a systematic review and meta-analysis. Intensive care medicine. 2020;46(6):1170-9.
5. Ko RE, Min KH, Hong SB, Baek AR, Lee HK, Cho WH, et al. Characteristics, Management, and Clinical Outcomes of Patients with Hospital-Acquired and Ventilator-Associated Pneumonia: A Multicenter Cohort Study in Korea. Tuberculosis and respiratory diseases. 2021;84(4):317-25.
6. Wang H-C, Tsai M-H, Chu S-M, Liao C-C, Lai M-Y, Huang H-R, et al. Clinical characteristics and outcomes of neonates with polymicrobial ventilator-associated pneumonia in the intensive care unit. BMC Infectious Diseases. 2021;21(1):965.
7. He Q, Wang W, Zhu S, Wang M, Kang Y, Zhang R, et al. The epidemiology and clinical outcomes of ventilator-associated events among 20,769 mechanically ventilated patients at intensive care units: an observational study. Critical care (London, England). 2021;25(1):44.
8. Luo W, Xing R, Wang C. The effect of ventilator-associated pneumonia on the prognosis of intensive care unit patients within 90 days and 180 days. BMC Infectious Diseases. 2021;21(1):684.
9. Kharel S, Bist A, Mishra SK. Ventilator-associated pneumonia among ICU patients in WHO Southeast Asian region: A systematic review. PLOS ONE. 2021;16(3):e0247832 DOI: 10.1371/journal.pone.0247832.
10. High J, Enne V, Barber J, Brealey D, Turner D, Horne R, et al. INHALE: the impact of using FilmArray Pneumonia Panel molecular diagnostics for hospital-acquired and ventilator-associated pneumonia on antimicrobial stewardship and patient outcomes in UK Critical Care—study protocol for a multicentre randomised controlled trial. Trials. 2021;22.
11. Bonell A, Azarrafiy R, Huong VTL, Viet TL, Phu VD, Dat VQ, et al. A Systematic Review and Meta-analysis of Ventilator-associated Pneumonia in Adults in Asia: An Analysis of National Income Level on Incidence and Etiology. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2019;68(3):511-8.
12. Tesema HG, Lema GF, Mesfin N, Fentie DY, Arefayne NR. Patterns of Admission and Clinical Outcomes Among Patients Admitted to Medical Intensive Care Unit of a Teaching and Referral Hospital, Northwest Ethiopia. Global advances in health and medicine. 2021;10:2164956121989258.
13. Dickson RP, Schultz MJ, van der Poll T, Schouten LR, Falkowski NR, Luth JE, et al. Lung Microbiota Predict Clinical Outcomes in Critically Ill Patients. American journal of respiratory and critical care medicine. 2020;201(5):555-63.
14. Johnstone J, Meade M, Lauzier F, Marshall J, Duan E, Dionne J, et al. Effect of Probiotics on Incident Ventilator-Associated Pneumonia in Critically Ill Patients: A Randomized Clinical Trial. Jama. 2021;326(11):1024-33.
15. 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. Journal of thoracic disease. 2022;16(9).
16. Zhao J, Li LQ, Chen CY, Zhang GS, Cui W, Tian BP. Do probiotics help prevent ventilator-associated pneumonia in critically ill patients? A systematic review with meta-analysis. ERJ open research. 2021;7(1).
17. Faramarzi E, Mahmoodpoor A, Hamishehkar H, Shadvar K, Iranpour A, Sabzevari T, et al. Effect of gastric residual volume monitoring on incidence of ventilator-associated pneumonia in mechanically

ventilated patients admitted to intensive care unit. Pakistan journal of medical sciences. 2020;36(2):48-53.
18. Wu VKS, Fong C, Walters AM, Lele AV. Prevalence, Clinical Characteristics, and Outcomes Related to Ventilator-Associated Events in Neurocritically Ill Patients. Neurocritical care. 2020;33(2):499-507.
19. Younan D, Delozier SJ, Adamski J, Loudon A, Violette A, Ustin J, et al. Factors Predictive of Ventilator-associated Pneumonia in Critically Ill Trauma Patients. World J Surg. 2020;44(4):1121-5.
20. Tang R, Luo R, Wu B, Wang F, Song H, Chen X. Effectiveness and safety of adjunctive inhaled antibiotics for ventilator-associated pneumonia: A systematic review and meta-analysis of randomized controlled trials. Journal of Critical Care. 2021 Oct 1;65:133-9.
21. Stoclin A, Rotolo F, Hicheri Y, Mons M, Chachaty E, Gachot B, et al. Ventilator-associated pneumonia and bloodstream infections in intensive care unit cancer patients: a retrospective 12-year study on 3388 prospectively monitored patients. Supportive Care in Cancer. 2020;28(1):193-200.

This article may be cited as: Mehmood M., Gul S. Z., Iqbal F., Khan M. S., Kabir A., Gul S., Clinical Outcomes of Ventilator-Associated Pneumonia in Critically Ill Patients Admitted to Intensive Care Unit**.** Pak J Med Health Sci, 2023; 18(1): 960-965.