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VENTILATOR-ASSOCIATED PNEUMONIA IN THE INTENSIVE CARE UNIT: A RETROSPECTIVE COHORT STUDY OF INCIDENCE, RISK FACTORS, AND CLINICAL CHARACTERISTICS

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ABSTRACT

Background: Ventilator-associated pneumonia (VAP) is a major nosocomial infection in intensive care units (ICUs) and is associated with prolonged mechanical ventilation, increased healthcare burden, and adverse clinical outcomes. Aim was to assess the incidence of pneumonia in ICU patients and to examine its association with mechanical ventilation, with a particular focus on ventilator-associated pneumonia.

Methods: A retrospective cohort study was conducted in the ICU of a tertiary hospital. All patients hospitalized during 2023 and 2024 were included. Data on demographics, mechanical ventilation, duration of ventilation, laboratory parameters, microbiological findings, and pneumonia occurrence were collected. Statistical analyses included χ^2 tests and independent t-tests, with significance set at $p < 0.05$.

Results: 1,511 patients were analysed in total. The overall incidence of pneumonia decreased significantly from 8.1% in 2023 to 5.7% in 2024 ($p = 0.045$). VAP represented 29.0% of pneumonias in 2023 and 27.9% in 2024. Pneumonia occurred more frequently among mechanically ventilated patients than among non-ventilated patients, although this difference was not statistically significant. Patients with VAP had a significantly longer duration of mechanical ventilation compared with those without VAP ($p < 0.001$). VAP developed earlier during ICU stay than other pneumonias. Gram-negative bacteria predominated, particularly Klebsiella pneumoniae, Acinetobacter baumannii, and Pseudomonas aeruginosa. C-reactive protein levels were significantly higher in patients with VAP.

Conclusion: Prolonged mechanical ventilation is a key risk factor for ventilator-associated pneumonia. The observed reduction in pneumonia incidence suggests improved preventive practices. Ongoing surveillance and strategies aimed at minimizing the duration of invasive mechanical ventilation are essential for reducing the burden of ventilator-associated pneumonia in ICU patients.

Keywords: *Ventilator-associated pneumonia, intensive care unit, mechanical ventilation, nosocomial infections, risk factors.*

INTRODUCTION

Hospital-acquired infections remain a major patient-safety concern in intensive care settings. Ventilator-associated pneumonia (VAP) is one of the most frequent and clinically relevant infections in the intensive care unit (ICU), occurring in patients who require invasive mechanical ventilation for more than 48 hours. Historically, VAP has been recognized as a complication of mechanical ventilation since the mid-20th century, with subsequent evidence highlighting airway colonization and biofilm formation on the endotracheal tube as key mechanisms

facilitating lower respiratory tract infection (1).

Mechanical ventilation is a life-saving intervention in acute respiratory failure; however, prolonged ventilation increases the risk of VAP and is associated with adverse outcomes such as longer ICU stay, higher morbidity, and increased mortality (2). Surveillance data indicate that VAP incidence varies substantially depending on diagnostic criteria and local practices, with reported ranges from very low rates per 1,000 ventilator-days to much higher proportions of ventilated patients (2). Clinically, VAP is suspected in the presence of a new or progressive pulmonary infiltrate accompanied by systemic and respiratory signs of infection, such as fever, leukocytosis or leukopenia, respiratory deterioration, and purulent tracheobronchial secretions (3). Mortality attributable to VAP is considerable and is particularly high when multidrug-resistant pathogens are involved (4).

VAP pathogenesis is multifactorial. In addition to impaired host defences during intubation, microaspiration around the endotracheal tube cuff, biofilm-related bacterial persistence, and gastric colonization in the context of stress-ulcer prophylaxis have all been described as contributing factors (5,6,7). Diagnosis remains challenging and requires integration of clinical, radiographic, and microbiological data. Prevention and timely management are essential to reduce complications and resource utilization (5-10).

Therefore, present study aimed to assess the association between mechanical ventilation and pneumonia in ICU patients, with particular emphasis on VAP occurrence and its timing in relation to ventilation duration.

STUDY AIMS

PRIMARY AIM

- To evaluate the association between the duration of invasive mechanical ventilation and the occurrence of VAP in ICU patients.

SECONDARY AIMS

- To describe the overall number of ICU admissions during the retrospective study period.
- To determine the proportion of ICU patients who developed pneumonia and the time from ICU admission to pneumonia onset.
- To determine the proportion of mechanically ventilated patients and the proportion who developed pneumonia/VAP.
- To compare pneumonia incidence between mechanically ventilated and non-ventilated ICU patients.
- To describe the timing of VAP occurrence in relation to ICU admission and ventilation exposure.

METHODS

STUDY DESIGN AND SETTING

This retrospective cohort study included all patients admitted to the intensive care unit (ICU) of University Hospital Sveti Duh, Zagreb, Croatia, during 2023 and 2024. The study assessed the temporal relationship between exposure to invasive mechanical ventilation (including ventilation duration) and the development of pneumonia, with a particular focus on ventilator-associated pneumonia (VAP). Ventilation duration was recorded in hours.

PARTICIPANTS

All patients admitted to the ICU during 2023 and 2024 were eligible. A total of 1,511 ICU admissions were included (763 in 2023; 748 in 2024). Patients of both sexes and all age groups were included if their medical records were complete. Exclusion criteria were: (1) pneumonia diagnosed before ICU admission and (2) incomplete medical documentation.

DATA SOURCES AND VARIABLES

Data were extracted from medical records and the hospital information system. Collected variables included demographic characteristics (age, sex) and relevant clinical data (primary diagnosis, comorbidities, and treatment course). The main outcomes were pneumonia and VAP occurrence, including time from ICU admission to onset. Exposure variables included the use of invasive mechanical ventilation and ventilation duration.

Ventilator-associated pneumonia (VAP) was defined as pneumonia occurring ≥48 hours after initiation of invasive mechanical ventilation, based on clinical and radiological criteria documented in the medical records, in accordance with the Centers for Disease Control and Prevention (CDC) surveillance definitions for ventilator-associated pneumonia (11). Only cases fulfilling these criteria were classified as VAP for analysis.

STATISTICAL ANALYSIS

Descriptive statistics were used to summarize patient characteristics and clinical variables. Categorical variables were presented as frequencies and percentages, and continuous variables as means with standard deviations or medians with interquartile ranges, as appropriate. Group comparisons were performed using the χ^2 test or Fisher's exact test for categorical variables and the independent samples t-test or Mann–Whitney U test for continuous variables, depending on data distribution. A two-sided p-value < 0.05 was considered statistically significant. Statistical analyses were performed using IBM SPSS Statistics version 27 (IBM Corp., Armonk, NY, U.S.A.).

ETHICS

The study was approved by the Ethics Committee of University Hospital Sveti Duh, Zagreb, Croatia (approval no. 03-9370; 3 December 2024). Due to the retrospective design and the use of anonymized clinical data collected routinely, the requirement for informed consent was waived.

RESULTS

PATIENT CHARACTERISTICS

During the two-year study period, a total of 1,511 patients were admitted to the ICU (763 in 2023 and 748 in 2024). The overall number of ICU admissions was comparable between the two years, with only minor monthly fluctuations.

A total of 30 patients developed ventilator-associated pneumonia (VAP), including 18 cases in 2023 and 12 cases in 2024. The sociodemographic characteristics of patients with VAP are presented in Table 1. In both years, patients with VAP were predominantly older adults, with a mean age of 70.8 ± 15.1 years in 2023 and 72.6 ± 17.5 years in 2024. Most patients belonged to the 65–79 and ≥80 age groups. Cardiovascular and metabolic comorbidities, particularly arterial hypertension and diabetes mellitus, were frequently observed.

The distribution of age, sex, and comorbidities among patients with VAP was broadly comparable between the two study years, allowing meaningful comparison of clinical outcomes and ventilation-related variables.

Patients who developed pneumonia (overall, including non-VAP cases) were also predominantly older, with the highest proportion observed in the 65–79 age group in both years. A difference in sex distribution was noted, with a higher proportion of male patients in 2023 and female patients in 2024.

Table 1. Sociodemographic characteristics of patients with ventilator-associated pneumonia (VAP).

Variable	2023 (n = 18)	2024 (n = 12)
Sex (male/female) (n (%)	12 / 6 (66.7% / 33.3%)	5 / 7 (41.7% / 58.3%)
Mean age, years (SD)	70.8 ± 15.1	72.6 ± 17.5
Age range, years	32–87	37–97
Age groups		
< 50 years	11.1%	16.7%
50–64 years	16.7%	8.3%
65–79 years	38.9%	33.3%
≥ 80 years	33.3%	41.7%
Most frequent comorbidities		
Arterial hypertension	44.0%	58.3%
Atrial fibrillation	33.0%	25.0%
Diabetes mellitus	22.0%	25.0%
Neurological diseases	6.0%	25.0%

Note: Data are presented as numbers (%) unless otherwise stated. SD – standard deviation.

In 2023, 185 ICU patients (24.2%) required invasive mechanical ventilation, compared with 161 patients (21.5%) in 2024. Total ventilation exposure was lower in 2024, reflecting a reduction in both the number of ventilated patients and the overall duration of ventilation (Table 2).

A total of 18 VAP cases were identified in 2023 and 12 in 2024. The incidence of VAP among ventilated patients decreased from 9.7% to 7.5%, while the incidence among all ICU admissions declined from 2.4% to 1.6% (Table 3).

Table 2. Mechanical ventilation exposure among ICU patients.

Variable	2023	2024
Total ICU admissions	763	748
Patients requiring mechanical ventilation, n (%)	185 (24.2%)	161 (21.5%)
Total ventilation time, hours	6,841.7	5,440.3
Mean ventilation time per ventilated patient, hours	37.0	33.8

Note: Percentages are calculated based on the total number of ICU admissions per year.

Table 3. Incidence of ventilator-associated pneumonia (VAP) in ICU patients.

Variable	2023	2024
Total ICU admissions	763	748
Ventilated patients	185	161
VAP cases, n	18	12
VAP incidence among ventilated patients, %	9.7%	7.5%
VAP incidence among all ICU patients, %	2.4%	1.6%

A total of 62 pneumonia cases were recorded in 2023 and 43 in 2024, corresponding to a decrease in overall pneumonia incidence from 8.1% to 5.7% among ICU patients (Table 4).

The incidence of ventilator-associated pneumonia among mechanically ventilated patients declined from 9.7% in 2023 to 7.5% in 2024, while the proportion of VAP among all pneumonia

cases remained relatively stable (Table 4).

Inflammatory markers were elevated in all patient groups. Mean leukocyte counts and CRP values were comparable between patients with VAP and those with pneumonia without mechanical ventilation (Table 5).

Table 4. Incidence of pneumonia and ventilator-associated pneumonia (VAP) among ICU patients.

Variable	2023	2024
Total ICU admissions (n)	763	748
Total pneumonia cases (n)	62	43
Pneumonia incidence among ICU patients, %	8.1	5.7
VAP cases (n)	18	12
Proportion of VAP among all pneumonias, %	29.0	27.9
VAP incidence among all ICU patients, %	2.4	1.6
Mechanically ventilated patients (n)	185	161
VAP incidence among ventilated patients, %	9.7	7.5

Note: Percentages are calculated based on the total number of ICU admissions or mechanically ventilated patients, as appropriate.

Table 5. Inflammatory markers in patients with pneumonia and VAP.

Parameter (mean ± SD)	Pneumonia 2023 (n = 62)	Pneumonia 2024 (n = 43)	VAP 2023 (n = 18)	VAP 2024 (n = 12)
Leukocytes ($\times 10^9$/L)	14.6 ± 9.1	13.5 ± 10.6	14.0 ± 5.1	13.8 ± 6.8
CRP (mg/L)	148.1 ± 97.3	181.7 ± 84.0	179.5 ± 76.0	189.5 ± 106.8

Note: CRP – C-reactive protein; SD – standard deviation.

Patients who developed VAP required significantly longer mechanical ventilation compared with patients without VAP in both study years (Table 6).

Pneumonia generally occurred within the first week of ICU admission. VAP developed earlier than pneumonia overall, with a mean onset of approximately five days after ICU admission (Table 7).

The incidence of pneumonia was higher among mechanically ventilated patients compared with non-ventilated patients in both years; however, the difference did not reach statistical significance (χ^2 test, $p > 0.05$).

Gram-negative bacteria were the predominant pathogens isolated in patients with VAP, with Klebsiella pneumoniae and Acinetobacter baumannii being the most frequently identified organisms (Table 8).

Table 6. Duration of mechanical ventilation (hours) in patients with and without VAP.

Group	2023 (hours, mean ± SD)	2024 (hours, mean ± SD)
Patients with VAP	191.6 ± 96.4	182.3 ± 90.7
Patients without VAP	28.4 ± 19.5	25.6 ± 17.1

Note: VAP – ventilator-associated pneumonia; SD – standard deviation.

Table 7. Time from ICU admission to onset of pneumonia and VAP.

Group	2023 (days, mean ± SD)	2024 (days, mean ± SD)
Pneumonia (overall)	6.1 ± 3.4	5.8 ± 3.1
VAP	4.9 ± 2.7	4.6 ± 2.5

Note: ICU – intensive care unit; VAP – ventilator-associated pneumonia; SD – standard deviation

Table 8. Microbiological pathogens isolated in patients with ventilator-associated pneumonia (VAP).

Pathogen	2023 (n)	2024 (n)
Klebsiella pneumoniae	6	3
Acinetobacter baumannii	6	4
Pseudomonas aeruginosa	3	1
Staphylococcus aureus (MRSA)	2	2
Candida spp.	5	6
Other pathogens*	4	3

Note: Other pathogens include Corynebacterium spp., Enterobacter cloacae, Proteus mirabilis, Aspergillus spp., and Providencia stuartii.

Candida spp. isolates were interpreted primarily as colonization findings in mechanically ventilated patients and were not considered independent causative pathogens of VAP in the absence of supporting clinical and microbiological evidence.

STATISTICAL ANALYSIS OF STUDY OUTCOMES

The overall incidence of pneumonia was significantly higher in 2023 compared with 2024 (8.1% vs. 5.7%; $\chi^2 = 4.02$, $P = 0.045$), indicating a reduction in pneumonia cases during the second study year.

Pneumonia occurred more frequently among mechanically ventilated patients than among non-ventilated patients in both years (2023: 9.7% vs. 7.6%; 2024: 7.5% vs. 4.7%); however, these differences did not reach statistical significance (χ^2 test, $P > 0.05$).

Patients who developed ventilator-associated pneumonia required significantly longer mechanical ventilation compared with patients without VAP in both study years ($t = 8.12$, $P < 0.001$), confirming ventilation duration as a major risk factor for VAP.

The onset of infection occurred earlier in patients with VAP compared with pneumonia overall. VAP developed approximately five days after ICU admission, whereas pneumonia overall occurred after approximately six days; this difference was statistically significant ($t = 2.05$, $P = 0.042$).

Inflammatory markers were elevated in all patient groups. Leukocyte counts did not differ significantly between patients with VAP and those with pneumonia without mechanical ventilation ($P > 0.05$). In contrast, CRP levels were significantly higher in patients with VAP compared with other pneumonia cases ($t = 2.21$, $P = 0.031$).

DISCUSSION

During the two-year study period, a total of 1,511 patients were admitted to the ICU, and a clear reduction in pneumonia incidence was observed, decreasing from 8.1% in 2023 to 5.7% in 2024. Pneumonia occurred more frequently among mechanically ventilated patients, with a particularly strong association observed between ventilator-associated pneumonia (VAP) and prolonged of mechanical ventilation. Most patients who developed VAP required invasive ventilation for more than 96 hours, which is consistent with previous studies showing an increased risk of VAP after 48 hours, especially between the fifth and the ninth day of ventilation.

Microbiological findings confirmed the predominance of multidrug-resistant gram-negative bacteria, particularly Klebsiella pneumoniae, Acinetobacter baumannii, and Pseudomonas aeruginosa. Similar microbiological patterns have been reported in previous national and international studies. Elevated leukocyte counts and C-reactive protein (CRP) levels were observed in most patients, supporting their role as markers of infection. However, these laboratory parameters alone were insufficient to distinguish VAP from other pneumonias, emphasizing the need for combined clinical, radiological, and microbiological assessment.

Patients of advanced age with significant cardiovascular and metabolic comorbidities were particularly susceptible to pneumonia and VAP. These results are in line with previous evidence showing that older, multimorbid ICU patients represent a high-risk population for nosocomial respiratory infections. Similar results have been reported in a Croatian study conducted at University Hospital Dubrava, which identified A. baumannii and K. pneumoniae as the most frequent VAP pathogens and demonstrated higher mortality among patients with prolonged mechanical ventilation (12). Our findings are consistent with these observations, aligning with global data highlighting multidrug-resistant gram-negative bacteria as leading causes of VAP (13,14).

Emerging research on diagnostic biomarkers for bacterial VAP suggests that additional biomarkers may improve diagnostic accuracy compared with conventional inflammatory markers (15). In the present study, CRP and leukocyte counts were used as routine inflammatory markers; however, future studies could benefit from incorporating additional diagnostic biomarkers.

Multicenter Croatian studies have reported VAP incidence rates of 15–20% among patients ventilated for more than 48 hours and identified prolonged ventilation, sedation, and comorbidities as important risk factors, which is in line with our findings (16,17).

Several factors may have contributed to the observed reduction in pneumonia incidence between 2023 and 2024. These may include improved adherence to infection-prevention protocols, greater awareness among healthcare professionals, reinforcement of hand hygiene measures, optimization of oral care and ventilator bundle practices, and ongoing staff education related to ICU infection control. Improved interdisciplinary collaboration and closer monitoring of mechanically ventilated patients may also have played a role. However, due to the retrospective design of the study, these factors could not be analysed individually.

International guidelines and meta-analyses have shown that interventions such as strict hand hygiene, head-of-bed elevation, regular oral care, and staff education can significantly reduce VAP incidence (18,19). Reported VAP incidence rates vary widely in literature, ranging from 4% to 29% or from 1.4 to 16.5 cases per 1,000 ventilator-days (17–20). The incidence observed in our study (7.5–9.7%) was within the lower range of reported values, possibly reflecting relatively effective local prevention practices.

European studies report considerable variability in VAP incidence, with gram-negative pathogens consistently predominating (14). Papazian et al. also emphasized the prognostic importance of distinguishing early-onset from late-onset VAP, with earlier onset generally associated with better clinical outcomes (2). In the present study, most VAP cases developed around the fifth day of ICU admission, corresponding to early-onset VAP. Current guidelines indicate that although CRP and leukocyte levels may support clinical assessment, microbiological confirmation remains necessary

for a definitive diagnosis (17,18).

Overall, our findings are consistent with both national and international data and confirm that prolonged mechanical ventilation remains an important risk factor for VAP development. These results further emphasize the importance of minimizing the duration of invasive ventilation whenever possible, promoting early transition to non-invasive respiratory support, and maintaining continuous microbiological surveillance in ICU patients. Although the retrospective single-center design limits the generalizability of the findings, the study provides useful insight into local ICU practice and VAP prevention. Future studies should include larger multicenter patient populations and evaluate additional outcomes such as mortality and healthcare costs (19,20).

The findings of this study also have important implications for nursing practice and multidisciplinary ICU care. Nurses play a key role in the prevention of ventilator-associated pneumonia through continuous patient monitoring, implementation of oral care measures, maintenance of hand hygiene, appropriate patient positioning, and early recognition of clinical deterioration. Effective VAP prevention also depends on close collaboration between nurses, physicians, infection-control teams, and respiratory therapists to ensure consistent implementation of evidence-based preventive measures and ventilator bundle strategies.

LIMITATIONS OF THE STUDY

This study has several limitations. First, the retrospective single-center design limits the generalizability of the findings to other ICU settings with different patient populations, case-mix, and preventive protocols. Second, the use of routinely collected medical record data carries a risk of incomplete documentation and possible misclassification, particularly regarding the timing and diagnostic certainty of pneumonia and VAP. Third, potential confounding factors such as severity of illness, prior antibiotic exposure, and differences in ventilatory management could not be fully accounted for.

In addition, the lack of statistical significance in the comparison between ventilated and non-ventilated patients may partly be related to the relatively small number of VAP cases and limited statistical power. Finally, microbiological data were based on routine clinical sampling, which may underestimate the true burden of polymicrobial infections. Despite these limitations, the study provides valuable real-world insight into VAP occurrence and its association with the duration of invasive mechanical ventilation.

CONCLUSION

Pneumonia remains a frequent complication in intensive care units, particularly among mechanically ventilated patients. The findings of this study confirm a strong association between prolonged invasive mechanical ventilation and the development of VAP.

A reduction in the incidence of pneumonia and VAP was observed in 2024 compared with 2023, possibly reflecting improvements in preventive measures and clinical practice. Nevertheless, VAP continues to be associated with prolonged hospitalization and increased healthcare burden. These findings emphasize the importance of minimizing the duration of invasive ventilation whenever possible, ensuring consistent implementation of preventive protocols, and supporting continuous education of healthcare professionals in ICU settings.

ETHICS STATEMENT

The study was approved by the Ethics Committee of Clinical Hospital Sveti Duh, Zagreb, Croatia (approval no. 03-9370; 3 December 2024). Due to the retrospective design and the use of anonymized routinely collected clinical data, the requirement for informed consent was waived.

AUTHORS CONTRIBUTION

NS contributed to study conception, data collection, statistical analysis, and manuscript drafting. VK contributed to data interpretation and manuscript revision. SOV, BI, and MS contributed to data interpretation, critical revision of the manuscript, and approved the final version. IK supervised the study, contributed to the study design, methodology, interpretation of the results, critical revision of the manuscript, and mentored the first author throughout the research process. All authors approved the submitted version of the manuscript.

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CONFLICT OF INTEREST

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

GENERATIVE AI STATEMENT

The authors used a generative AI tool to assist with language editing, formatting, and journal-specific manuscript preparation. All AI-assisted output was critically reviewed, revised, and verified by the authors, who take full responsibility for the final content. No AI tools were used for data collection, analysis, or interpretation.

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