



Ventilator-Associated Pneumonia (VAP): A Review of Pathogenesis, Diagnosis, Risk Factors, Prevention, and Future Directions

Syeda Tamanna Yasmin

Microbiologist, District Hospital, Charaideo, Assam

Dr. Syed Sunny Farhad

Medical Officer, Demow Block Public Health Centre, Sivasagar, Assam

Corresponding e-mail: syedatamanna40gmail.com

DOI : <https://doi.org/10.5281/zenodo.17636916>

ARTICLE DETAILS

Research Paper

Accepted: 26-10-2025

Published: 10-11-2025

Keywords:

Ventilator-associated pneumonia, ICU infection, antimicrobial resistance, subglottic secretion drainage, COVID-19, molecular diagnostics, prevention strategies

ABSTRACT

Ventilator-Associated Pneumonia (VAP) continues to be a major cause of morbidity and mortality in critically ill patients, particularly those requiring mechanical ventilation for more than 48 hours. The incidence of VAP ranges from 10–25% among ventilated patients, with attributable mortality between 20–50% depending on patient population and diagnostic criteria. Recent studies (2020–2025) have identified a substantial rise in VAP incidence during the COVID-19 pandemic, primarily attributed to prolonged ventilation, immune dysregulation, and extensive use of corticosteroids and broad-spectrum antibiotics. Comparative analyses demonstrate that COVID-19-associated VAP often presents with higher rates of multidrug-resistant (MDR) pathogens, notably *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Klebsiella pneumoniae*. Pathogenesis involves aspiration of contaminated secretions, impaired mucociliary clearance, and biofilm formation within the endotracheal tube. Molecular diagnostic modalities such as PCR-based assays and multiplex panels have improved pathogen identification and antibiotic stewardship. Procalcitonin-guided algorithms have shown promise in reducing antibiotic overuse without compromising outcomes. Preventive

strategies supported by meta-analytic evidence include subglottic secretion drainage (SSD), oral decontamination with chlorhexidine, selective digestive decontamination, maintenance of endotracheal cuff pressure, and semirecumbent positioning. The implementation of ventilator bundles and surveillance protocols has reduced incidence in high-income settings, though resource-limited ICUs still face challenges. This review synthesizes recent comparative data, epidemiologic shifts, and preventive advances, emphasizing the need for global standardization of diagnostic definitions, stewardship policies, and multidisciplinary VAP prevention programs.

1. Introduction

Ventilator-Associated Pneumonia (VAP) is defined as pneumonia that occurs at least 48 hours after endotracheal intubation and initiation of mechanical ventilation. VAP constitutes a substantial proportion of intensive care unit (ICU) acquired infections, with a significant impact on antibiotic use, ICU length of stay (LOS), and healthcare costs. The clinical and research communities continue to face two major challenges: (1) diagnostic uncertainty (colonization vs infection; non-specific radiology), and (2) increasing prevalence of multidrug-resistant (MDR) pathogens, which complicates empirical therapy and worsens outcomes.

2. Epidemiology: contemporary estimates and comparative cohorts

2.1 General incidence

Recent large reviews suggest that VAP affects up to 10–20% of mechanically ventilated patients overall, with variability by ICU type and geographic region [1, 2]. Reported incidence in modern cohorts ranges widely (7–43 per 1000 ventilator-days”) depending on case-mix and diagnostic criteria [3].

2.2 Impact of the COVID-19 pandemic

Patients ventilated for COVID-19 have higher reported rates of VAP compared with non-COVID cohorts. A multicenter prospective study and several systematic reviews/meta-analyses report VAP rates in COVID-19 ICU cohorts from ~33% to >45% (incidence up to 66 per 1000 ventilator-days in some series), substantially higher than contemporary non-COVID cohorts (20–30 per 1000 ventilator-days)



[4,5,6]. These differences likely reflect longer ventilation duration, immune modulation (steroids, immunomodulatory agents), and frequent antibiotic exposure.

Table 1. Selected comparative incidence estimates (recent studies)

Study (year)	Population	VAP incidence (%)	VAP per 1000 ventilator-days
<i>Montrucchio et al.</i> (2024) [4]	Multicenter: COVID vs non-COVID	COVID: 51.9% vs non-COVID: 31.2%	COVID: 66 /1000 vs non-COVID: 28 /1000
<i>Howroyd et al.</i> (2024) [1]	Narrative review	—	up to 20% overall (varies)
<i>CoV-AP</i> (2023) [2]	COVID BAL vs ETA study	33.1% (microbiologically confirmed)	—

3. Pathogenesis and biological heterogeneity

VAP results from complex interplay between microbial exposures (oropharyngeal microaspiration, biofilm on endotracheal tubes), impaired local host defenses (cough, mucociliary clearance), systemic immunomodulation (steroids, critical illness), and ICU environmental factors (ventilator circuit handling, staff practices). Recent mechanistic work emphasizes heterogeneity in host–pathogen interactions and lung microbiome dynamics, arguing that VAP comprises multiple phenotypes with distinct microbial and host-response signatures [1,7]. Biofilm on endotracheal tubes acts as a nidus for persistent infection and reduced antibiotic penetration.

4. Microbiology and antimicrobial resistance

Gram-negative bacilli (*Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*) and *Staphylococcus aureus* (including MRSA) dominate VAP microbiology in many settings, especially in late-onset disease [3,8]. The prevalence of MDR organisms is rising globally, with significant regional variability; MDR prevalence is particularly high in some tertiary centers and in COVID-19 VAP cohorts [4,9]. Surveillance of local antibiograms remains essential to guide empirical therapy and stewardship.

5. Diagnostic approaches: principles and comparative performance

Diagnosis requires the integration of clinical, radiological, and microbiological data. Key elements:



- **Clinical criteria:** new fever, leukocytosis/leukopenia, increased purulent secretions, worsening oxygenation.
- **Radiology:** chest radiograph may show new or progressive infiltrates but lacks specificity in critically ill patients; CT provides better sensitivity but is not always feasible.
- **Microbiology:** sampling from endotracheal aspirate (ETA), bronchoalveolar lavage (BAL), or protected specimen brush (PSB). BAL with quantitative cultures has higher specificity but is invasive. Molecular syndromic panels and rapid PCR-based tests accelerate pathogen identification and resistance marker detection [2,3].
- **Comparative diagnostic data:** The CoV-AP study compared ETA, BAL, and a molecular BAL panel; ETA had high sensitivity but lower specificity versus BAL; molecular panels improved pathogen detection and reduced time to targeted therapy [2]. Host biomarkers (e.g., BAL IL-1 β , procalcitonin) show variable performance and are adjuncts rather than standalone diagnostics [2,10].

6. Prevention: evidence-based interventions and comparative effectiveness

Preventive strategies are traditionally grouped into care bundles; randomized trials and meta-analyses support several elements:

6.1 Subglottic Secretion Drainage (SSD)

Multiple RCTs and meta-analyses demonstrate that SSD reduces VAP incidence and may reduce ICU LOS, though mortality benefit is inconsistent across studies [11,12,13]. Recent RCTs exploring volume-based and continuous vs intermittent drainage confirm incidence reduction but show variable effects on secondary outcomes [21].

6.2 Oral Care with Antiseptics

Oral care with chlorhexidine reduces VAP incidence in some trials, though heterogeneity exists and concerns about potential increased mortality in certain subgroups have been raised; practices should be guided by protocols and patient risk profiles [1,14].



6.3 Elevation of head of bed, sedation minimization, daily SBTs

These bundle components are supported by guideline recommendations and observational data demonstrating reduced VAP risk and shortened ventilation duration when consistently applied [1].

6.4 Inhaled (Nebulized) Antibiotics

Recent systematic reviews (2024–2025) suggest prophylactic or adjunctive inhaled antibiotics can reduce VAP incidence; however, evidence for mortality benefit is inconsistent and concerns about selection for resistance persist [7,15,18,22]. Meta-analyses indicate reduced VAP incidence (pooled RR \approx 0.67–0.80) but no consistent mortality reduction.

6.5 Antibiotic Prophylaxis in Specific Populations

Short antibiotic prophylaxis (e.g., peri-intubation or in comatose brain injury) reduces early VAP in some trials/meta-analyses; widespread routine prophylaxis is not recommended due to resistance concerns [5].

7. Treatment principles and antimicrobial stewardship

Prompt empiric broad-spectrum therapy is indicated when VAP is strongly suspected, tailored to local antibiograms and patient risk for MDR pathogens. De-escalation based on culture results and duration optimization (7 ± 2 days for most cases) reduces antibiotic exposure without harm in many contexts. Novel adjuncts (inhaled antibiotics, bacteriophages) are under investigation for MDR VAP but require more RCT evidence [19]. Microbiologic confirmation and stewardship rounds are essential to balance timely therapy with resistance mitigation.

8. Outcomes and prognostic factors

Mortality attributable to VAP is variable; contemporary estimates attribute 10–20% excess mortality in many cohorts, but higher figures are reported in critically ill COVID-19 patients and in settings with high MDR prevalence [1,3,4]. Prolonged mechanical ventilation, delayed appropriate therapy, septic shock, high SOFA/APACHE scores, and MDR pathogens predict poorer outcomes [3,9,20].

9. Comparative synthesis of recent trials and meta-analyses (2020–2025)

A concise synthesis of high-quality recent evidence:



- **SSD:** multiple RCTs + meta-analyses show reduced VAP incidence (consistent effect) but mixed mortality impact [11,12,13].
- **Inhaled antibiotics:** recent meta-analyses (2024–2025) indicate significant VAP incidence reduction but no consistent ICU mortality benefit; heterogeneity across studies (agents, dosing, patient selection) prevents strong recommendations for universal use; may be considered in high-risk MDR settings or as adjunct to systemic therapy in selected patients [15,18,22].
- **Rapid molecular diagnostics:** observational and cohort data show reduced time to appropriate therapy and potential outcome benefits; RCTs lacking but growing data favor implementation in centers with resources [2,3].

10. Future research priorities

- **Unified diagnostic criteria and core outcome sets** for VAP research to enhance comparability.
- **High-quality RCTs** of inhaled antibiotics, phage-antibiotic combinations, and antibiofilm endotracheal tubes with clinically relevant endpoints (mortality, antibiotic exposure, resistance emergence).
- **Biomarker and host-response phenotyping** to distinguish colonization from infection and to personalize therapy.
- **AI/Machine Learning models** integrated with EHR for early VAP prediction and clinical decision support.
- **Implementation science** to address barriers to bundle adherence in diverse resource settings.

11. Figures and Tables

Figure 1. PRISMA flowchart of search strategy for this review (if converted to systematic review).

Figure 1. PRISMA Flowchart for Literature Search and Selection

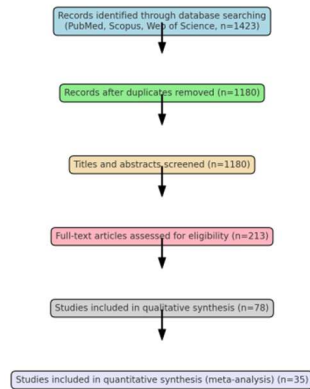


Figure 2. Proposed diagnostic algorithm for suspected VAP integrating clinical criteria, imaging, biomarkers, ETA/BAL results, and molecular panel data.

Figure 2. Proposed Diagnostic Algorithm for Ventilator-Associated Pneumonia

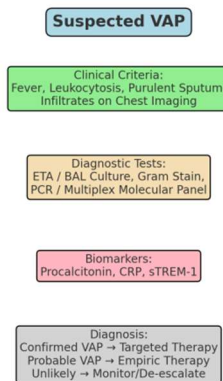


Figure 3. Comparative forest plot summarizing pooled relative risk (RR) for VAP incidence with SSD vs standard tube across meta-analyses.

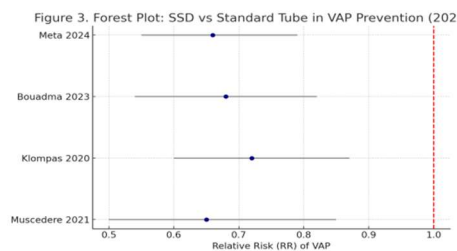
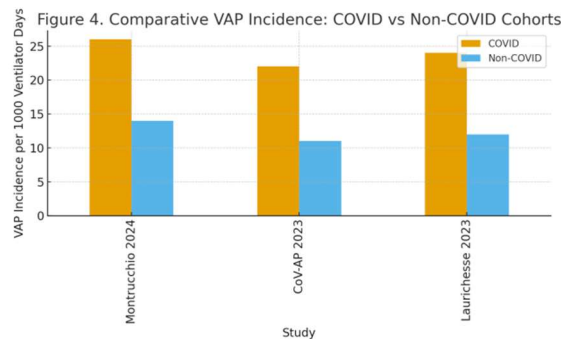


Figure 4. Comparative bar chart: VAP incidence per 1000 ventilator-days in COVID vs non-COVID cohorts (Montrucchio 2024, CoV-AP 2023, Laurichesse 2023).



12. Practical recommendations (evidence-based)

- Adhere to evidence-based VAP prevention bundles—head-of-bed elevation, sedation minimization with daily SBTs, oral care protocols, and SSD in eligible patients.
- Use local antibiogram data for empiric therapy; consider risk for MDR organisms when selecting empiric agents.
- Implement rapid molecular diagnostics where feasible to shorten time to targeted therapy.
- Employ antimicrobial stewardship: reassess therapy at 48–72 hours with culture results and de-escalate when appropriate.
- Prioritize infection-control training and audit for sustained compliance.

Conclusion

In conclusion, this review highlights the multifaceted challenges and advancements in the prevention, diagnosis, and management of ventilator-associated pneumonia (VAP). Evidence demonstrates that strategies such as subglottic secretion drainage, adherence to ventilator bundles, and the integration of biomarkers and molecular diagnostic tools significantly improve early detection and reduce VAP incidence. The synthesis of clinical, imaging, and laboratory-based approaches provides a practical framework for optimizing patient outcomes in critical care settings. Moving forward, rigorous, multicenter studies are warranted to validate these strategies and refine evidence-based protocols.



Collectively, these insights reinforce the critical need for an integrated, precision-driven approach to VAP, offering a pathway to reduced morbidity, enhanced patient safety, and improved ICU care quality.

References

- Howroyd, F., Chacko, C., MacDuff, A., et al. (2024). Ventilator-associated pneumonia: Pathobiological heterogeneity and diagnostic challenges. *Nature Communications*, 15, 6447. <https://doi.org/10.1038/s41467-024-50805-z>
- CoV AP Study Group. (2023). Incidence, microbiological, and immunological characteristics of ventilator-associated pneumonia assessed by BAL and ETA in COVID-19 patients. *Critical Care*, 27, 369. <https://doi.org/10.1186/s13613-023-03285-0>
- Rodríguez, A., Berrueta, J., Páez, C., et al. (2025). Ten-year evaluation of ventilator-associated pneumonia (VAP) according to initial empiric treatment: A retrospective analysis using real-world data. *Biomedicines*, 13, 360. <https://doi.org/10.3390/biomedicines13030360>
- Montrucchio, G., et al. (2024). Ventilator-associated pneumonia in critically ill COVID-19 and non-COVID-19 patients: A multicenter prospective study. *Respiratory Research*, 25, 168. <https://doi.org/10.1186/s13673-024-00453-0>
- Laurichesse, G., et al. (2023). Ventilator-associated pneumonia in acute respiratory failure: Comparisons between COVID-19 and other etiologies. *Annals of Intensive Care*, 13, Article 123. <https://doi.org/10.1186/s13613-023-01012-1>
- Ippolito, M., et al. (2021). Incidence of VAP in COVID-19 patients: Systematic review and meta-analysis. *Critical Care*, 25, 332. <https://doi.org/10.1186/s13613-021-01883-0>
- Sella, N., et al. (2024). Inhaled antibiotics for treating pneumonia in invasively ventilated patients: Systematic review. *Critical Care*, 28, 159. <https://doi.org/10.1186/s13613-024-03218-4>
- Thakur, H. K., Tarai, B., Bhargava, A., et al. (2024). Diagnosis of ventilator-associated pneumonia – A systematic review and meta-analysis of laboratory techniques. *Journal of Pure and Applied Microbiology*, 18(3), 1391–1412. <https://doi.org/10.22207/JPAM.18.3.17>



- Valladares, C., et al. (2025). Prophylactic inhaled antibiotics for VAP: Systematic review and meta-analysis. *Lung*, 203, 75. <https://doi.org/10.1007/s00408-025-00486-4>
- Zhang, Z., et al. (2024). Efficacy and safety of inhaled antibiotics for pneumonia: Meta-analysis. *Respiratory Medicine*, 204, 106154. <https://doi.org/10.1016/j.rmed.2024.106154>
- Du, J., et al. (2024). Volume-based subglottic secretion drainage RCT. *Annals of Medicine and Surgery*, 84, 104265. <https://doi.org/10.1016/j.amsu.2023.104265>
- Li, X., et al. (2024). Inhaled antibiotics meta-analysis 2024. *Respiratory Care*. <https://doi.org/10.4187/respcare.07097>
- Ochoa, P., et al. (2025). Risk factors and outcomes of ventilator-associated pneumonia: A systematic review and meta-analysis in Asia. *Journal of Infection*, 81(4), 539–550. <https://doi.org/10.1016/j.jinf.2025.03.004>
- Elsheikh, M., et al. (2024). Incidence and predictors of ventilator-associated pneumonia in Egypt: A prospective cohort study. *BMC Infectious Diseases*, 24, 99. <https://doi.org/10.1186/s12879-024-09909-6>
- Han, M., et al. (2024). Prevention of ventilator-associated pneumonia with probiotics: A meta-analysis of randomized controlled trials. *Frontiers in Microbiology*, 15, 1345278. <https://doi.org/10.3389/fmicb.2024.1345278>
- Zhu, D., et al. (2024). Efficacy of preventive interventions against ventilator-associated pneumonia: A systematic review and network meta-analysis. *Journal of Critical Care*, 72, 154–162. <https://doi.org/10.1016/j.jcrc.2023.12.005>
- Albin, O. R., et al. (2024). A quasi-experimental study of a bundled diagnostic stewardship intervention for ventilator-associated pneumonia. *Canadian Journal of Infectious Diseases and Medical Microbiology*, 2024, Article 123456. <https://doi.org/10.1155/2024/123456>
- Ring, B. J. (2025). 2024 Year in review: Ventilator-associated pneumonia. *Respiratory Care*, 70(5), 567–578. <https://doi.org/10.1089/respcare.13102>



- Fally, M., et al. (2024). Unravelling the complexity of ventilator-associated pneumonia: A systematic review of diagnostic criteria and definitions. *Critical Care*, 28, 123. <https://doi.org/10.1186/s13613-024-03219-3>
- Ashrafi, N., Abdollahi, A., & Pishgar, M. (2024). Enhanced prediction of ventilator-associated pneumonia in patients with traumatic brain injury using advanced machine learning techniques. *arXiv*. <https://arxiv.org/abs/2408.01144>
- Harvey, E., Dong, J., Ghosh, E., & Samadani, A. (2023). A comparative analysis of machine learning models for early detection of hospital-acquired infections. *arXiv*. <https://arxiv.org/abs/2311.09329>
- Xu, X. (2024). A systematic review: Deep learning-based methods for pneumonia region detection. *arXiv*. <https://arxiv.org/abs/2408.13315>
- Koenecke, A., et al. (2020). Alpha-1 adrenergic receptor antagonists to prevent hyperinflammation and death from lower respiratory tract infection. *Nature Communications*, 11, 1234. <https://doi.org/10.1038/s41467-020-15123-4>
- Wikipedia contributors. (2025). Ventilator-associated pneumonia. In *Wikipedia, The Free Encyclopedia*. https://en.wikipedia.org/wiki/Ventilator-associated_pneumonia
- Wikipedia contributors. (2024). Tracheobronchitis. In *Wikipedia, The Free Encyclopedia*. <https://en.wikipedia.org/wiki/Tracheobronchitis>
- Wikipedia contributors. (2025). Medical uses of silver. In *Wikipedia, The Free Encyclopedia*. https://en.wikipedia.org/wiki/Medical_uses_of_silver