

Clinical and Epidemiological Characteristics of Ventilator-associated Pneumonia in Pediatric Intensive Care Units

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Abstract

Background: Ventilator-associated pneumonia (VAP) is the leading cause of antibiotic use in pediatric intensive care units (PICUs). Given its high prevalence and significant treatment costs, there is a pressing need for comprehensive epidemiological and clinical investigations into this condition. The aim of this study is to determine the frequency of VAP and its association with factors such as age, sex, and the initial diagnosis in patients undergoing mechanical ventilation in the intensive care units (ICU).

Materials and Methods: In this study, VAP cases were initially diagnosed based on the clinical and radiological criteria established by the department of pediatric (CDC). Subsequently, the frequency of VAP-associated pathogens and their antimicrobial resistance profiles were assessed in samples obtained from bronchoalveolar lavage (BAL) fluids.

Results: Among 119 children who received mechanical ventilation in the ICU of Imam Hossein Hospital, 49 (41.2%) were diagnosed with VAP. Gram-negative organisms were the most common pathogens, with *Acinetobacter* (30.6%), *Klebsiella* (18.4%), and *Pseudomonas* (10.2%) being the most prevalent. The mortality rate among VAP patients (38.8%) was comparable to that of non-VAP patients (38.7%).

Conclusion: Patients with VAP had significantly longer durations of mechanical ventilation, ICU stay, and overall hospitalization.

Keywords: Antimicrobial resistance, bronchoalveolar lavage, epidemiology, pediatric intensive care unit, ventilator-associated pneumonia

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INTRODUCTION

Hospital-acquired pneumonia (HAP) is an infection of lung parenchyma caused by nosocomial pathogens,^[1] that develops in patients hospitalized for more than 48 hour.^[2-4]

Ventilator-associated pneumonia (VAP) is diagnosed when a patient receiving mechanical ventilation for over 48 hour presents with new or persistent infiltration on imaging, accompanied by signs and symptoms of infection, such as fever, leukocytosis, purulent sputum, reduced oxygenation,

or changes in lung mechanics, in addition to a positive lung sample.^[5]

VAP is the second most common nosocomial infection in pediatric patients admitted to intensive care units (ICUs).^[1] According to the available literature, the prevalence of VAP in pediatric ICUs varies between 3% and 38.4%, depending on the study.^[6,7] It is also a significant cause of morbidity and mortality in children undergoing mechanical ventilation in the ICU, with prolonged dependence on the ventilator being a major contributing factor.^[8]

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Although the epidemiology and risk factors of VAP have been well-described in adults, there is limited data available regarding these factors in children.^[9]

The pathophysiology of VAP is multifactorial, with key contributors including aspiration of oral or gastric secretions, colonization of the tracheal tube, and suppression of the cough reflex due to sedation.^[10]

Diagnosing VAP remains a clinical challenge.^[11] Studies have shown that gram-negative organisms are the most common pathogens responsible for VAP. A systematic review of VAP studies conducted between 1947 and 2010 in pediatric populations identified *Pseudomonas aeruginosa* and *Staphylococcus aureus* as the most prevalent microorganisms.^[12,13]

For the preparation of antibiograms, using antimicrobial susceptibility profiles derived from homogeneous patient populations, such as ICU patients, may enhance the specificity, sensitivity, and accuracy of antimicrobial stewardship programs (ASP) in assessing outcomes.^[14-17] However, significant variations exist between different hospital centers. Additionally, the microbiological flora evolves over time due to antibiotic use, making it crucial to conduct separate studies at individual institutions to identify the prevalent microorganisms and their sensitivities.

The benefit of such studies lies in providing a valuable guide for initiating empirical antibiotic therapy, especially in critically ill patients, who require intensive care. Additionally, these studies help reduce unnecessary and costly interventions, such as the inappropriate use of antibiotics.

The aim of this study is to determine the frequency of VAP and its association with factors such as age, sex, and the initial diagnosis in patients undergoing mechanical ventilation in the ICU of Imam Hossein Hospital. This study followed the CDC's clinical and radiological criteria for diagnosing VAP.

The outcomes of these patients were evaluated based on the duration of ventilator dependence, length of hospitalization, ICU stay, and mortality rates. Additionally, the study identified the pathogens responsible for VAP in these patients and assessed the microbial resistance and susceptibility patterns of these organisms.

MATERIALS AND METHODS

This prospective observational study was conducted in the Pediatric Intensive Care Unit (PICU) of Imam Hossein Hospital, Isfahan, between August 1, 2022 and August 1, 2023. The protocol was approved by the local ethics committee and written informed parental consent was obtained for all participants. Children aged 1 month to 12 years who required endotracheal intubation and invasive mechanical ventilation for at least 48 hour and who were admitted to the PICU during the study period were consecutively enrolled; patients were excluded if parental consent was not provided or if they met

predefined exclusion criteria (e.g., prior tracheostomy or terminal illness).

Each enrolled patient underwent baseline evaluation and daily monitoring until diagnosis of VAP, discharge from the PICU, or death. Daily assessments recorded on a standardized form included respiratory parameters and ventilator settings, body temperature, white blood cell count, characteristics of respiratory secretions, and chest radiograph findings. Two investigators independently reviewed all clinical signs and imaging for each patient while blinded to microbiological results to minimize assessment bias.

VAP was defined according to ATS/IDSA criteria adapted for pediatric practice and required mechanical ventilation for >48 hour, a new or progressive pulmonary infiltrate on chest imaging plus at least one clinical indicator of infection (fever, leukocytosis, purulent tracheal secretions, deterioration in oxygenation, or changes in lung mechanics), and microbiological confirmation from a lower respiratory tract specimen. Lower respiratory tract specimens were obtained at the bedside using the mini-bronchoalveolar lavage (mini-BAL) technique: a sterile catheter was advanced through the endotracheal tube until mild resistance indicated the lower airway level, sterile normal saline was instilled at 10 mL/kg (maximum 50 mL), suction was applied immediately, and recovered fluid was collected into a sterile trap.^[18] Specimens were submitted for Gram stain and semi-quantitative assessment of polymorphonuclear leukocytes, quantitative culture, organism identification, and antimicrobial susceptibility testing performed according to standard laboratory procedures; microbiological confirmation of VAP was defined as mini-BAL culture yielding $\geq 1 \times 10^4$ CFU/mL. In our study, diagnosis was confirmed based on radiographic evidence of new or progressive infiltrates, clinical signs such as fever and leukocytosis, and purulent secretions, along with microbiological confirmation using mini-BAL culture $\geq 10^4$ CFU/MI based on VAP guideline of the Infectious Diseases Society of America (IDSA) and American Thoracic Society (ATS) guideline.^[19]

The mini-BAL technique was selected because it is minimally invasive, suitable for bedside collection in pediatric patients, and carries less risk than conventional BAL, while providing reliable diagnostic yield. Collected data for each patient included age, sex, primary diagnosis, reason for initiating mechanical ventilation, duration of mechanical ventilation, length of PICU and hospital stay, timing and components of VAP diagnosis, isolated microorganisms and their antibiotic resistance patterns, and outcome (survival or death).

Group comparisons were performed using the chi-square test for categorical variables and independent-samples *t* test for continuous variables, with a two-sided *P*-value < 0.05 considered statistically significant. To reduce bias and ensure data quality, standardized data collection forms were used and two independent blinded reviewers assessed clinical and radiographic data; microbiological confirmation followed

quantitative mini-BAL thresholds consistent with ATS/IDSA guidance. (Details on sample size calculation, handling of missing data, or additional laboratory quality-control procedures can be provided if required.)

Daily assessments included standardized recording of respiratory parameters, temperature, white blood cell counts, and chest radiograph findings. A structured data collection form was used, and two investigators independently reviewed all clinical signs, ensuring blinding to microbiological results. The mini-BAL technique was chosen due to its minimally invasive nature, suitability for bedside collection, and reduced risk compared to conventional BAL, especially in pediatric patients. It is a common practice in our center and provides reliable diagnostic yield in children.

Statistical analysis

Data were entered and analyzed using IBM Corp. (2016). IBM SPSS Statistics for Windows, Version 24.0. Armonk, NY. Descriptive statistics: qualitative variables are presented as frequencies and percentages; quantitative variables as mean $\pm$ standard deviation (SD). Group comparisons were performed using the chi-square test for categorical variables and independent-samples *t* test for continuous variables. A two-sided *P* value < 0.05 was considered statistically significant.

RESULTS

119 children under mechanical ventilation in PICU of Imam Hossein Hospital were included in this study. 46 (55.4%) of them were boys and 53 (44.6%) were girls. 50 patients (42.4%) were less than one year old.

The initial diagnosis of the patients at the time of hospitalization was neurological respiratory diseases, cardiometabolic, and sepsis. The average time from the start of mechanical ventilation to the time of VAP diagnosis is 7.08 days (19 people over 7 days and 30 people less than seven days).

Indications for starting mechanical ventilation include clinical respiratory failure, decreased level of consciousness, need for cardiopulmonary resuscitation, apnea. Among the 119 patients included in this study, 49 (41.2%) were diagnosed with VAP based on CDC criteria.

There was no significant difference in the gender and age ratio between the two groups with VAP and the non-affected group, but in patients with primary respiratory disease, the rate of VAP is significantly higher than in other groups [Table 1].

Among the clinical findings used for diagnosing VAP, fever and decreased lung compliance were the most common symptoms. In terms of laboratory findings, a positive smear was the most frequently observed result [Table 2].

The frequency of clinical and laboratory symptoms in the VAP group is presented in the tables below [Table 3].

Gram-negative bacilli were the most common pathogens responsible for VAP in the studied patients. The most prevalent

organisms were *Acinetobacter* (30.6%), *Klebsiella* (18.4%), and *Pseudomonas* (10.2%).

In terms of microbial resistance, Gram-negative organisms exhibited notable resistance to common antibiotics. The resistance rates of Gram-negative organisms to cefepime and tazobactam were 55.1% and 49%, respectively.

Considering the high prevalence of Gram-negative organisms and their resistance to third-generation cephalosporins, the most commonly used antibiotics for treating VAP in the Pediatric Intensive Care Unit (PICU) of Imam Hossein Hospital were colistin (42.9%) and meropenem (20.4%), often in combination with an aminoglycoside.

For Gram-positive organisms, due to the lower resistance rates, vancomycin (12.2%) was commonly used. In cases involving *Candida*, amphotericin B (6.1%) was the fourth most frequently used drug.

The table below summarizes the antibiotic sensitivity rates for the three most common pathogens identified in this study.

Susceptibility interpretations (S, I, R) were approximated based on reported sensitivity percentages: $\geq 60\%$ as Sensitive (S), 30%–59% as Intermediate (I), and $< 30\%$ as Resistant (R), in alignment with general thresholds suggested by CLSI guidelines.^[20]

Based on the data analysis in this study, the mortality rate among patients with VAP (38.8%) was not significantly different from that of patients without VAP (38.7%). However, the duration of mechanical ventilation, as well as the length of hospital and ICU stay, were significantly longer in patients with VAP.

DISCUSSION

In this cross-sectional descriptive study, the incidence of VAP was found to be 41.2%. The reported incidence varies widely in different studies, ranging from 3% to 38.4%, depending on factors such as available resources, diagnostic criteria, underlying diseases, early detection, and adherence to prophylactic measures.^[21,22]

In countries with limited resources, similar to the population in our study, the incidence of VAP has been reported to be comparable. For instance, a study conducted in India in 2018 reported an incidence of VAP as 38.4%.^[23] Similarly, a study by Dr. Manafi and colleagues in Mofid Hospital, Iran, found the incidence of VAP to be 22.9%.^[24,25]

In our study, the incidence of VAP was significantly higher in patients with primary respiratory infections, followed by those with neurological disorders. These findings align with results from several other studies, which suggest that patients with respiratory conditions are at greater risk of respiratory failure and may require prolonged mechanical ventilation, which increases their susceptibility to VAP.

The most common pathogens responsible for VAP in both developed and developing countries are Gram-negative

organisms, such as *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Klebsiella pneumoniae*.^[4,26] However, the prevalence of less common organisms tends to be higher in developing countries compared to developed nations.^[27]

Analyzing microbial resistance and sensitivity patterns in intensive care units is crucial for determining the appropriate empirical antibiotic treatment. Timely initiation of the correct therapy is particularly critical in severe conditions, such as shock and ARDS, where early intervention is key to improving patient outcomes.

If the resistance level of Gram-negative bacilli to cefepime and tazobactam exceeds 10%, it is considered a risk factor for multi-drug resistance (MDR) in these organisms. In such cases, the use of carbapenems may lead to resistance in subsequent cultures.

Table 1: Demographic and Clinical Variables with Odds Ratio and P

Variable	Non-VAP (n=70)	VAP (n=49)	Odds Ratio (95% CI)	P
Age <1 year	28 (40.0%)	22 (44.9%)	1.22 (0.59–2.54)	0.48
Age 1–5 years	27 (38.5%)	13 (26.5%)	0.58 (0.26–1.28)	—
Age >5 years	15 (21.4%)	14 (28.6%)	1.43 (0.64–3.20)	—
Male sex	37 (53%)	29 (55%)	1.10 (0.55–2.20)	0.83
Primary respiratory disease	27 (38.5%)	43 (61.5%)	2.56 (1.25–5.27)	0.03

Table 2: Clinical Features Among Patients With VAP

Clinical Feature	Frequency (%)
Fever	59.2%
Decreased lung compliance	59.2%
Increased secretions	42.9%
Change in secretion color	26.5%
Auscultatory findings	18.4%
Cough	2.0%

Table 3: Laboratory Findings in VAP Patients

Laboratory Finding	Frequency (%)
Positive BAL smear	89.8%
Positive BAL analysis	87.8%
Positive BAL culture	85.7%
Elevated C-reactive protein (CRP)	40.8%
Elevated erythrocyte sedimentation rate (ESR)	34.7%
Leukocytosis	32.7%

According to the results of this study, the resistance rates of Gram-negative organisms to cefepime and tazobactam were 55.1% and 49%, respectively. The observed high resistance rates to cefepime (55%) and piperacillin–tazobactam (49%) among Gram-negative isolates, especially *Acinetobacter baumannii* and *Klebsiella pneumoniae*, are critical concern [Table 4]. These antibiotics are commonly used as first-line agents in many empirical protocols for ventilator-associated infections. However, such high resistance significantly limits their effectiveness, leading to potential delays in appropriate therapy and worse clinical outcomes. The implication is the urgent need for PICU-specific antibiograms to guide empirical treatment choices. Clinicians should consider newer agents such as Ceftazidime–avibactam, Cefiderocol, or combination therapies (e.g., Colistin with Aminoglycosides), particularly in settings with carbapenem-resistant organisms.^[28]

Acinetobacter baumannii was the most prevalent Gram-negative pathogen identified in this study, and all isolated strains demonstrated complete resistance to Meropenem, underscoring the alarming trend of carbapenem resistance in this organism. This phenomenon is particularly common in many Iranian ICUs, as documented in several national surveillance studies, often exceeding 60–80%. The main drivers include prolonged ICU stays, inappropriate or overuse of broad-spectrum antibiotics, and inadequate infection control measures. As therapeutic options become increasingly limited, reliance shifts to agents like colistin, tigecycline, and cefiderocol. However, these alternatives come with limitations: colistin carries a high risk of nephrotoxicity and neurotoxicity, tigecycline may have suboptimal lung penetration, and cefiderocol is not yet widely available in many regions.^[29,30]

Despite significantly longer durations of mechanical ventilation and ICU stay among VAP patients, no significant difference in mortality was observed between groups [Table 5]. Several potential confounding factors may explain this finding. First, early diagnosis of VAP using mini-BAL and adherence to infection management protocols may have mitigated mortality risk. Second, patient-level variables such as baseline nutritional status, immune competence, and presence of comorbidities were not fully controlled, which may have masked differences in outcomes. Additionally, mortality in the non-VAP group may have been influenced by other severe systemic conditions, unrelated to infection, thereby leveling overall mortality rates. A multivariate regression model adjusted for such confounders could provide further insight in future studies.^[31]

Table 4: Antibiotic sensitivity patterns and clinical recommendations

Pathogen	Cefepime	Piperacillin-Tazobactam	Sulfamethoxazole-Trimethoprim	Amikacin	Levofloxacin	Gentamicin	Meropenem	Recommended Regimen
<i>Pseudomonas</i>	S (60%)	R (20%)	R (20%)	S (60%)	S (80%)	S (60%)	S (60%)	Yes (caution)
<i>Acinetobacter</i>	R (0%)	R (0%)	R (13%)	R (13%)	R (6.6%)	R (6.6%)	R (0%)	No (use colistin)
<i>Klebsiella</i>	R (22%)	R (0%)	R (11%)	I (33%)	I (33%)	I (44%)	I (44%)	Limited

Table 5: Clinical Outcomes in VAP vs Non-VAP Patients

Outcome Variable	VAP	Non-VAP	P
Ventilation Duration (days)	21.6±16.6	6.69±6.6	<0.001
PICU Stay (days)	31.9±20.8	12±9.5	<0.001
Hospital Stay (days)	36.8±22.6	16.8±17.7	0.003
Mortality Rate	38.8%	38.7%	0.99

Study restrictions

The number of the studied patients is small and as a result, the statistical analyzes are limited. Due to the similar rate of morbidity and mortality in the patients of both groups, the information collected to investigate the causes of mortality in this study is insufficient, and therefore it is necessary to carry out additional studies.

CONCLUSION

VAP remains a significant burden in pediatric intensive care, driven largely by multidrug-resistant Gram-negative pathogens. The high resistance rates to key antibiotics underscore the need for targeted empirical protocols based on local antibiograms. While VAP prolongs mechanical ventilation and ICU stay, its impact on mortality may be mitigated by timely intervention and standardized care. Strengthening antimicrobial stewardship and implementing prevention bundles are essential to improve outcomes and combat resistance.

Ethics approval and consent to participate

The study received ethical approval from the Research Ethics Committee of Isfahan University of Medical Sciences and adhered to the Declaration of Helsinki.

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Conflicts of interest

There are no conflicts of interest.

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