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ORIGINAL ARTICLE

# Study of Ventilator-Associated Pneumonia in a Pediatric Intensive Care Unit

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**Abstract**
*Objectives* To determine the incidence, etiology, risk factors and outcome of ventilator associated pneumonia (VAP) among mechanically ventilated patients.
*Methods* All PICU patients who were mechanically ventilated for >48 h were consecutively enrolled. The development of VAP was defined by the radiological and clinical criteria described by the Center for Disease Control and Prevention/ National Nosocomial Infection Surveillance (CDC/NNIS) (2003). The risk factors for VAP were determined by univariate and multivariate analysis using appropriate statistical methods.
*Results* The median age of the subjects ($N$=232) was nine mo with a male to female ratio of 1.3:1. Of 232 subjects enrolled, there were 15 episodes of VAP in 14 patients (frequency of 6.03 %) with a mean VAP rate of 6.3/1,000 ventilator days. Eight of the 15 VAP episodes showed positive endotracheal culture with Gram negative organisms as the predominant isolate with *Acinetobacter* being the commonest organism isolated (62.5 %). Neuromuscular disease ($P$=0.005), histamine-2 receptor blockers ($P$=0.0001), tracheostomy ($P$=0.0001), and positive blood culture growth ($P$=0.0008) were found to be significantly associated with VAP (univariate analysis). VAP patients had a significantly longer duration of mechanical ventilation (22.5 *vs.* 5 median days; $P$<0.001), longer PICU stay (23.25 *vs.* 6.5 median days; $P$<0.001) and longer hospital stay (43.75 *vs.* 13.25 median days; $P$<0.001). On multivariate analysis, only positive blood culture growth was a risk factor for VAP. The mortality rate of VAP was 42.8 % (not higher than those without VAP).
*Conclusions* Frequency of VAP was 6.03 % with neuromuscular disease, histamine-2 receptor blockers, tracheostomy and positive blood culture being risk factors for VAP.

**Keywords** Bacterial · Critical · Intensive care unit · Lung · Nosocomial pneumonia · Ventilator

## Introduction

Ventilator associated pneumonia (VAP) is the second most common hospital-acquired infection among Pediatric Intensive Care Unit (PICU) patients [1, 2] and is estimated to occur in 3 to 10 % of ventilated PICU patients [3, 4]. VAP is defined as pneumonia occurring in mechanically ventilated patients that develops later than or at 48 h after the patient has been placed on mechanical ventilation. VAP in adults has been well studied (worldwide) with an incidence ranging from 8 to 28 % [5] as compared to the limited information available regarding Pediatric VAP (especially from India). Adult data of VAP cannot be extrapolated to the PICU population for formulation of diagnostic and management guidelines, as children differ greatly from adults in their anatomy and physiology, nature of their underlying illness, interventions performed and treatment needs. Hence, the present study was conducted in a tertiary care PICU to determine the incidence, etiology, risk factors and outcome of VAP in mechanically ventilated patients.

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## Material and Methods

This was a prospective observational study conducted in the Level III Pediatric (Medical) Intensive Care Unit (PICU) of a multi-speciality teaching and referral tertiary care hospital, over a period of 17 mo (from 1st January 2010 to 4th June 2011). The study was initiated after acquiring the approval of the Ethics committee of the institute. The Pediatric Intensive Care Unit (PICU) has nine beds and admits approximately 500–600 patients annually. All PICU patients who were ventilated for >48 h were consecutively enrolled in the study after obtaining parental consent. Infants<1 mo, post-surgical and post-trauma patients were excluded (as these patients are not admitted to authors' ICU). Demographic data, clinical details, risk factors, laboratory and radiographic reports, treatment details and final outcome of all the enrolled patients were recorded in a specially designed case record form. VAP was diagnosed when the Center for Disease Control and Prevention (CDC/NNIS) criteria (2003) [6, 7] were met (Appendix). Portable chest radiographs, blood culture and qualitative culture analysis of endotracheal aspirate (ETA) was done in patients suspected to have VAP. The endotracheal aspirate (ETA) was collected by nonbronchoscopic method by a resident doctor under aseptic precautions. The ETA was collected with a 8–10 F suction catheter attached to a suction machine. The catheter was introduced into the endotracheal tube and gentle aspiration was performed without instilling saline and the catheter was withdrawn from the endotracheal tube. The secretions were transported in a sterile container to the laboratory and immediately plated for culture analysis.

The associated organism was identified and antibiotic susceptibility pattern was obtained. Data of VAP patients were compared with those without VAP with respect to demographic details, presenting illness, procedures, medications, duration of mechanical ventilation, duration of ICU and hospital stay, to identify risk factors for ventilator associated pneumonia (VAP). All the patients were followed till discharge from Pediatric Intensive Care Unit (PICU) or death. Outcome was measured in terms of survival and death.

Categorical variables were compared using Chi-square test and Fischer's Exact test. Continuous variables were compared using Student 't' test and Mann–Whitney test. $P$ value<0.05 was considered to be significant. All tests of significance were two-tailed. Variables found to be significantly associated with ventilator associated pneumonia on univariate analysis were subjected to multiple logistic regression analysis. The results were analyzed using a computerised statistical program (SPSS version 13.0).

## Results

During the study period, 219 patients fulfilled the inclusion criteria and were enrolled in the study. However, 13 out of the 219 patients were readmitted to the PICU and hence a total of 232 admissions were analysed ($N$=232). The median age of the study population at the time of admission was nine mo (mean age-32.6±41.19 mo) with a male to female ratio of 1.3:1. The patient demographics, underlying illness, medications, procedures done and outcome are summarized in Table 1.

The frequency of VAP was 6.03 % (14 of 232 admissions) with one patient developing VAP twice during the course of the study. The pooled mean ventilator associated pneumonia rate was 6.3/1,000 ventilator days. Mean duration of ventilation prior to the first episode of VAP in the index study was 11.48 d (median 8.5 d; range 3–40.8 d). Gram negative organisms were isolated from endotracheal (ET) aspirates in 8 (53.3 %) of the 15 VAP episodes with *Acinetobacter* [5 (62.5 %)] being the predominant isolate followed by *Pseudomonas aeruginosa* [4 (50 %)]. *Escherichia coli*, *Klebsiella pneumoniae* and *Methicillin resistant coagulase negative staphylococcus* were isolated from one patient each (12.5 %). *Candida* species [3 (50 %)], *Acinetobacter* [2 (33.3 %)] and *Streptococcus* [one patient (16.6 %)] were isolated from blood cultures of six ventilator associated pneumonia (VAP) patients. Polymicrobial growth was found in 9 (31 %) out of the 29 positive ET culture samples found in the index study. Concomitant endotracheal and blood culture positivity was seen in 4 (28.5 %) out of 14 VAP patients of which 2 (50 %) had the same organism (*Acinetobacter*) isolated in endotracheal aspirate (ETA) and blood culture. The comparison of microbiology results of ETA of ventilator associated pneumonia and endotracheal colonization are given in Table 2.

The probable risk factors like demographic characteristics, presenting illness, procedures performed, medications used, duration of mechanical ventilation, duration of ICU and hospital stay were compared between the patients who developed ventilator associated pneumonia (VAP) and those who did not develop VAP (No VAP group) to identify the significant risk factors for ventilator associated pneumonia (VAP). Univariate analysis (Table 3) showed the following risk factors to be significantly associated with VAP-presence of neuromuscular disease ($P$=0.005), use of histamine-2 receptor blockers ($P$= 0.0001), tracheostomy ($P$=0.0001) and positive blood culture growth ($P$=0.0008). The patients with VAP had a significantly longer duration of mechanical ventilation (22.5 *vs.* 5 median days; $P$ <0.001), longer PICU stay (23.25 *vs.* 6.5 median days; $P$ <0.001) and longer hospital stay (43.75 *vs.* 13.25 median days; $P$<0.001) as compared to those without VAP (Table 3). There was no statistical difference between the two groups with respect to age, gender, PRISM III score, grade of malnutrition, immunocompromised state (2 were HIV infected and 98 grade IV protein energy malnutrition), endotracheal intubation attempts, other underlying illness and use of steroid/ inotropes and other procedures. On subjecting the significant variables to binomial logistic regression analysis, only

**Table 1** Study population characteristics (*N*=232)

| Patient characteristics | *n* (%) [Total *N*=232] |
|---|---|
| Demographics | |
| Males | 135 (58 %) |
| Age (median) | 9 mo |
| PRISM (mean) ± SD | 6.94±6.83 |
| Grade IV PEM | 98 (42.2 %) |
| Immunocompromised state | 100 (43.1 %) |
| Underlying illness | |
| Respiratory illness | 67 (28.8 %) |
| Heart disease | 49 (21.1 %) |
| CNS disorder | 37 (15.9 %) |
| Neuromuscular disorder | 22 (9.4 %) |
| GI disorder | 7 (3 %) |
| Hematological | 5 (2.1 %) |
| Chronic renal disease | 5 (2.1 %) |
| Others | 40 (17.2 %) |
| Coma | 73 (31.4 %) |
| Procedures | |
| Reintubation | 181 (78 %) |
| Central venous catheterisation | 153 (65.9 %) |
| Tracheostomy | 19 (8.1 %) |
| Thoracostomy/placement of intercostal drain | 9 (3.8 %) |
| Dialysis | 6 (2.5 %) |
| Ventricular tap/shunt | 5 (2.1 %) |
| Bronchoscopy | 1 (0.43 %) |
| Medications | |
| Histamine-2 receptor blockers | 146 (62.9 %) |
| Inotropes | 143 (61.6 %) |
| Steroids | 92 (39.6 %) |
| Outcomes | |
| PICU LOS (mean, d) ± SD | 11.35±14.19 |
| Hospital LOS (mean, d) ± SD | 19.99±21.16 |
| Death | 132 (56.8 %) |

*SD* Standard deviation; *CNS* Central nervous system; *PRISM* Pediatric risk of mortality; *GI* Gastrointestinal; *PEM* Protein energy malnutrition; *LOS* Length of stay

positive blood culture was found to be an independent risk factor for the development of ventilator associated pneumonia (VAP) (Table 4). The overall morality was 56.8 % in the study group and there was no significant difference in mortality (42.8 % *vs.* 57.7 %) between the two groups (VAP *vs.* No VAP) and no significant predictors of mortality were found on analysis.

## Discussion

The frequency of ventilator associated pneumonia (VAP) in the index study was found to be 6.03 % which is lower than that reported till date by many previous researchers [8–10]. Most studies on VAP have been conducted in developed countries with use of quantitative culture analysis by protected specimen brush (PSB)/bronchoalveolar lavage (BAL) method [11–13]. The index subjects were diagnosed on the basis of clinical criteria (with low specificity) along with qualitative endotracheal aspirate culture analysis (isolation of micro-organism) unlike other studies where positive microbiological results (isolation and colony count of micro-organism) were used as an inclusion criteria and hence a lower incidence of VAP has been probably reported in the present study.

A predominance of gram negative organisms in association with VAP was observed, similar to the finding in other studies [8, 9]. Organisms associated with VAP reflect the common organisms present in the gut, oropharynx and environment [14], and hence the high incidence of gram negative VAP in the present study reflects the pattern of colonization among ventilated patients in authors' PICU. Knowledge about the common/resident flora and the antibiotic resistance pattern guides the choice of antibiotics for empirical therapy of VAP, thereby decreasing the emergence of drug resistant strains.

Neuromuscular disease and tracheostomy were found to be significant risk factors (on univariate analysis) for VAP which is probably due to the increased risk of aspiration and prolonged ventilation in these candidates. However, both these factors were not independent predictors of VAP on

**Table 2** Comparison of microbiology results of ETA of VAP *vs.* endotracheal colonization

| Organism | ETA (*N*=8) *n* (%) | Endotracheal colonization (*N*=21) *n* (%) |
|---|---|---|
| *Acinetobacter spp* | 5 (62.5) | 10 (47.6) |
| *Pseudomonas aeruginosa* | 4 (50) | 10 (47.6) |
| *Escherichia coli* | 1 (12.5) | 0 |
| *Klebsiella pneumoniae* | 1 (12.5) | 6 (28.5) |
| *Methicillin resistant coagulase negative staphylococcus* | 1 (12.5) | 0 |
| *Acid Fast bacilli* | 0 | 1 (4.7) |
| *Staphylococcus aureus* | 0 | 1 (4.7) |

**Table 3** Significant risk factors on univariate analysis

| Significant risk factors | VAP [*N*=14] *n* (%) | No VAP [*N*=218] *n* (%) | *P* value |
|---|---|---|---|
| Neuromuscular disease | 5 (35.7 %) | 17 (7.8 %) | 0.005* |
| Tracheostomy | 6 (42.8 %) | 13 (5.9 %) | 0.0001 |
| Histamine-2 receptor blockers | 10 (71.4 %) | 136 (62.3 %) | 0.0001 |
| Blood culture growth | 6 (42.8 %) | 17 (7.7 %) | 0.0008* |
| Duration of ventilation (median, days) | 22.50 (IQR-39) | 5.00 (IQR-5) | <0.001# |
| PICU LOS (median, days) | 23.25 (IQR-44) | 6.50 (IQR-7) | <0.001# |
| Hospital LOS (median, days) | 43.75 (IQR-40) | 13.25 (IQR-17) | <0.001# |

*VAP* Ventilator associated pneumonia; *LOS* Length of stay; *IQR* Interquartile range

* *P* value of Fischer's Exact test

# Mann–Whitney test applied

multivariate analysis. Positive blood culture growth was independently associated with VAP on multivariate analysis in the index study, as also seen by Elward et al. [3]; an observation which has not been frequently reported in other previous studies [8–10]. Majority of the blood culture isolates showed fungal growth, which probably reflects the relative immunodeficient state of these patients due to primary illness or following prolonged use of broad spectrum antibiotics. The concomitant positivity of endotracheal and blood culture analysis (which was present in 28.5 % of the index VAP patients) signifies the probability of increased risk of VAP due to the same organism as that of the primary bloodstream infection or organism present in the gut/oropharynx in critically ill children with decreased local host defences (in the presence of risk factors for VAP).

The overall mortality of VAP in the index study was 42.8 % which is similar to the trend seen in several other studies [3, 8, 9, 12, 13]. No significant predictors of mortality were found on multivariate analysis. Duration of ventilation, PICU stay and hospital stay were found to be significantly longer in patients with VAP in the index study, a fact which has been reported in most previous studies [3, 8–10]. This prolonged hospital stay increases the economic burden of medical care in resource limited developing countries [10]. There is a possibility that a higher mortality in the index patients may be a reason for the relatively low incidence of VAP in the study but authors' do not feel this is the main reason for the lower incidence of VAP. Similar to the index study, previous pediatric and adult studies have also shown that the common associated risk factors for VAP include—reintubation, use of $H_2$ blockers, tracheostomy, comatose state, prolonged ventilation and prolonged PICU stay [15–19].

The major limitation of the present study is the inability to use newer techniques (such as bronchoalveolar lavage/ protected specimen brush technique) due to resource constraints and use of less specific clinical criteria for diagnosis of VAP [20–22]. Formulating standard criteria for the uniform definition of Pediatric VAP and case–control studies to determine attributable morbidity and mortality of VAP and thus measure the impact of various preventive strategies on the development of VAP need to be conducted.

**Table 4** Logistic regression analysis of risk factors associated with ventilator associated pneumonia

| Variables-risk factors for VAP | Significance |
|---|---|
| Neuromuscular disease | 0.626 |
| Reintubation | 0.559 |
| Tracheostomy | 0.340 |
| $H_2$ blockers | 0.129 |
| Inotropes | 0.784 |
| Steroids | 0.525 |
| Growth on blood culture | 0.037* |
| Total duration of mechanical ventilation (days) | 0.079 |
| Total duration of PICU stay (days) | 0.898 |
| Total duration of hospital stay (days) | 0.340 |

Cox & Snell $R^2$—0.159

Nagelkerke $R^2$—0.434

* Statistically significant

## Conclusions

In the present study VAP frequency was found to be 6.03 %. VAP did not contribute significantly to mortality. The common pathogens associated with VAP were predominantly gram negative, with the commonest organism being *Acinetobacter*. Positive blood culture was found to be an independent risk factor for development of VAP. Patients with VAP had a significantly prolonged duration of mechanical ventilation, PICU stay and hospital stay.

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**Conflict of Interest** None.

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## Appendix

Center for Disease Control and Prevention/National Nosocomial Infection Surveillance (CDC/NNIS) definition for clinical diagnosis of nosocomial pneumonia [6, 7]:

*Radiologic signs*

Two or more serial chest radiographs with at least one of the following*:

1. New or progressive *and* persistent infiltrate
2. Consolidation
3. Cavitation

* In patients without underlying pulmonary or cardiac disease (*e.g.,* respiratory distress syndrome, bronchopulmonary dysplasia, pulmonary edema, or chronic obstructive pulmonary disease), one definitive chest radiograph is acceptable.

*Clinical signs*

At least one of the following:

1. Fever (temperature>38 °C) with no other recognized cause
2. Leukopenia (leukocyte count<4,000 cells/$mm^3$) or leukocytosis (leukocyte count≥12,000 cells/$mm^3$)

*And at least two of the following*

1. New onset of purulent sputum, or change in character of sputum, or increased respiratory secretions, or increased suctioning requirements
2. New onset or worsening cough, or dyspnea, or tachypnea
3. Rales or bronchial breath sounds
4. Worsening gas exchange [*e.g.*, $O_2$ desaturations (e.g., $PaO_2$–$FiO_2$≤240), increased oxygen requirements, or increased ventilation demand].

## References


1. Garner JS, Jarvis WR, Emori TG, Horan TC, Hughes JM. CDC definitions for nosocomial infections. Am J Infect Control. 1988;16:128–40.
2. Gaynes RP, Edwards JR, Jarvis WR, Culver DH, Tolson JS, Martone WJ. Nosocomial infections among neonates in high-risk nurseries in the United States. National Nosocomial Infection Surveillance System. Pediatrics. 1996;98:357–61.
3. Elward A, Warren D, Fraser V. Ventilator-associated pneumonia in Pediatric Intensive Care Unit patients: risk factors and outcomes. Pediatrics. 2002;109:758–64.
4. Almuneef M, Memish ZA, Balkhy HH, Alalem H, Abutaleb A. Ventilator-associated pneumonia in a Pediatric intensive care unit in Saudi Arabia: a 30-month prospective surveillance. Infect Control Hosp Epidemiol. 2004;25:753–8.
5. Chastre J, Fagon JY. Ventilator-associated pneumonia. Am J Respir Crit Care Med. 2002;165:867–903.
6. Miller PR, Johnson JC 3rd, Karchmer T, Hoth JJ, Meredith JW, Chang MC. National nosocomial infection surveillance system: from benchmark to bedside in trauma patients. J Trauma. 2006;60:98–103.
7. Centers for Disease Control and Prevention. Patient safety component protocol : ventilator associated pneumonia (VAP) event. The National Healthcare Safety Network (NHSN) manual. Available at: http://www.cdc.gov/nhsn/PDFs/pscManual/6pscVAPcurrent.pdf. Accessed 23 Nov 2009.
8. Tullu MS, Deshmukh CT, Baveja SM. Bacterial nosocomial pneumonia in paediatric intensive care unit. J Postgrad Med. 2000;46:18–22.
9. Patra PK, Jayashree M, Singhi S, Ray P, Saxena AK. Nosocomial pneumonia in a Pediatric Intensive Care Unit. Indian Pediatr. 2007;44:511–8.
10. Srinivasan R, Asselin J, Gildengorin G, Wiener-Kronish J, Flori HR. A prospective study of ventilator-associated pneumonia in children. Pediatrics. 2009;123:1108–15.
11. Cook DJ, Walter SD, Cook RJ, Griffith LE, Guyatt GH, Leasa D, et al. Incidence of and risk factors for ventilator-associated pneumonia in critically ill patients. Ann Intern Med. 1998;129:433–40.
12. Joshi N, Localio AR, Hamory BH. A predictive risk index for nosocomial pneumonia in the intensive care unit. Am J Med. 1992;93:135–42.
13. Craven DE, Kunches LM, Killinsky V, Litchenberg DA, Make BJ, Mecabe WR. Risk factor for pneumonia and fatality in patients receiving continuous mechanical ventilation. Am Rev Respir Dis. 1986;133:792–6.
14. Toltzis P, Yamashita T, Vilt L, Blumere JL. Colonization with antibiotic resistant gram-negative organism in pediatric intensive care unit. Crit Care Med. 1997;25:538–44.
15. Morrow BM, Argent AC. Ventilator-associated pneumonia in a paediatric intensive care unit in a developing country with high HIV prevalence. J Paediatr Child Health. 2009;45:104–11.
16. Ibrahim EH, Tracy L, Hill C, Fraser VJ, Kollef MH. The occurrence of ventilator-associated pneumonia in a community hospital: risk factors and clinical outcomes. Chest. 2001;120:555–61.
17. Erbay RH, Yalcin AN, Zencir M, Serin S, Atalay H. Costs and risk factors for ventilator-associated pneumonia in a Turkish University Hospital's Intensive Care Unit: a case–control study. BMC Pulm Med. 2004;4:3.
18. Rodrigues PM, Carmo Neto Ed, Santos LR, Knibel MF. Ventilator-associated pneumonia: epidemiology and impact on the clinical evolution of ICU patients. J Bras Pneumol. 2009;35:1084–91.
19. Gadani H, Vyas A, Kar A. A study of ventilator-associated pneumonia: incidence, outcome, risk factors and measures to be taken for prevention. Indian J Anaesth. 2010;54:535–40.
20. Deshmukh CT, Tullu MS, Parmar RC. Nosocomial pneumonia. In: Gupte S, editor. Recent advances in pediatrics. Special Volume 8—'Emergency Pediatrics'. New Delhi: Jaypee Brothers; 2001. p. 151–65.
21. Deshmukh CT, Tullu MS, Parmar RC. Nosocomial pneumonia. In: Lahiri K, Gupte S, editors. Recent advances in pediatrics. Special Volume 10—'Pulmonology'. New Delhi: Jaypee Brothers; 2002. p. 314–28.
22. Foglia E, Meier MD, Elward A. Ventilator-associated pneumonia in neonatal and pediatric intensive care unit patients. Clin Microbiol Rev. 2007;20:409–25.