ORIGINAL ARTICLE

Ventilator-Associated Pneumonia in Children

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ABSTRACT

Objective: To determine the frequency of Ventilator-Associated Pneumonia (VAP) and to identify the associated factors, causative organisms and outcome of VAP in children admitted to ICU.

Study Design: Cross-sectional, observational study.

Place and Duration of Study: Medical ICU (MICU) of the Children's Hospital and Institute of Child Health, Lahore, from August 2008 to March 2009.

Methodology: All children admitted to MICU and requiring ventilation during the study period were included and monitored for any features suggestive of VAP. Partial septic screen was done in all suspected cases. VAP was labelled when any patient on the ventilator for more than 48 hours had at least 2 of the following features of nosocomial infection - fever > 101°F, TLC < 4000 or > 15000 per mm^3, neutrophils > 85%, CRP > 48 mg/L or new findings on chest examination suggestive of pneumonia; and radiological evidence of new or progressive and persistent infiltrates. Percentages were compared using chi-square test with the significance at p-value less than 0.05.

Results: Of the 93 children requiring mechanical ventilation during the study period, 16 developed VAP (17%). Almost half (46%) were younger than 1 year with male to female ratio of 1.2:1. Children developing VAP required ventilation for 13.5 (± 10.1) days compared to 7.7 (± 5.5) days in those who did not develop VAP. The common organisms isolated were *Pseudomonas, Klebsiella* and *E. coli.* Factors associated with increased frequency of VAP included age less than 1 year, unplanned emergency intubation and use of continuous intravenous sedation. Features that strongly suggested underlying VAP included purulent tracheal secretions compared to increased secretions alone, CRP > 48 mg/L, positive radiological findings and positive tracheal aspirate culture. Overall mortality was 23% among the ventilated cohort. Thirty two percent of them had VAP compared to only 13% among those who survived to discharge (p = 0.03).

Conclusion: The frequency of VAP was 17% in this series. Factors significantly associated with VAP were age less than 1 year, unplanned intubation and continuous sedation. The important predictors of VAP included purulent tracheal secretions, high CRP and persistent new radiological findings.

Key words: *Nosocomial infection. Ventilator associated pneumonia (VAP). Children. Paediatric intensive care.*

INTRODUCTION

Mechanical ventilation is the cornerstone for the management of critically ill children in intensive care setting. This modality has its own complications and hazards. One such complication is the chance of developing pneumonia termed the ventilator-associated pneumonia (VAP).[1]

Ventilator-associated pneumonia is defined as pneumonia occurring after the patient has been on ventilator for more than 48 hours.[1] VAP is different from community acquired pneumonia not only from etiological point of view but also in context of its pathophysiology, risk factors, management strategies and outcome.[2] Diagnosis of VAP has been a subject of on-going debate. High clinical suspicion along with radiological examination and culture of respiratory secretions are required for the diagnosis of VAP.[3]

Amongst the challenges in any intensive care settings, curtailing nosocomial infections like VAP is an important issue.[4,5] The prevalence of VAP in different setups varies.[6-9] It is important to identify the burden of VAP in any setup, so that prevention strategies can be implemented and strengthened. VAP is not only associated with increased mortality but also increases with the length of ICU stay, the cost of treatment and the chances of ventilator dependence.[10] Various risk factors have been identified that may predispose to the development of VAP.[11,12] As with other nosocomial infections, the microbiology of VAP may vary from one centre to the other and certainly the susceptibility pattern to antibiotics do vary not only from unit to unit but may show changing trend within a unit from time to time.[13,14]

More and more centres in Pakistan are now extending mechanical ventilatory services for children. It is hence important to identify the characteristics of VAP in children in local settings. In this context, this study was done to determine the frequency of ventilator associated pneumonia (VAP) and identify the possible risk factors, etiological agents and outcome of VAP in children.

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METHODOLOGY

This observational study was carried out in the Medical Intensive Care Unit (MICU) of the Children's Hospital and the Institute of Child Health, Lahore, from August 2008 to March 2009. MICU caters to admission of critically sick children with various medical conditions. Children requiring elective ventilation postoperatively and cardiac patients are admitted in separate ICUs.

All children on mechanical ventilation during the study period were included in the study. They were closely monitored for any features suggestive of nosocomial infection or VAP especially purulent tracheal secretions, new and persistent chest findings on auscultation and body temperature instability. All such children underwent partial septic screen including complete and differential blood counts, serum CRP (C-reactive protein) level, blood and urine cultures, tracheal aspirate for culture and chest X-ray. Tips of endotracheal tubes were also sent for culture whenever there was need of changing the tube or at the time of extubation.

The criteria for diagnosing VAP was adapted and modified from CDC guidelines.[15] VAP was identified in any patient on ventilator for more than 48 hours with (i) at least two of the features suggestive of nosocomial infection not previously observed (unexplained fever > 101°F, total leukocyte count < 4000 or > 15000 per mm^3, neutrophils > 80%, serum CRP > 48 mg/L or new chest findings on examination suggestive of pneumonia) or purulent tracheal secretions; and (ii) radiological evidence of new or progressive and persistent infiltrates. Empiric antibiotic therapy was modified depending upon the reports of the blood or tracheal aspirate cultures.

Keeping in view the reported frequency of 12% in other studies, worst acceptable frequency of 18% and admission rate of about 500 per annum (population), a sample size of 92 was calculated for a confidence level of 95%, using statistical programme Epi info (version 6.0).

All the demographic, clinical, radiological and micro-biological details were entered in the Statistical Package for Social Sciences (SPSS) version 14.0. Descriptive statistics were used to calculate the frequencies of categorical data, and to compute means and standard deviations of continuous variables. Chi-square test and Fisher exact tests were used for the analysis of categorical variables (like mode of ventilation, gender, use of sedation etc.). Student t-test was applied to find the difference between the means (SD) of continuous variables (length of stay, duration of ventilation etc.). A p-value of less than 0.05 was considered statistically significant.

All children admitted during the study period were divided into two groups - those with VAP and those without VAP. For each of the categorical variable, a 2 x 2 table was generated to compare the occurrence of that variable in each of the two groups. Chi-square test was applied for each of these 2 x 2 table to compute the p-value and risk estimate was done by calculating the odds ratio and 95% CI.

RESULTS

During the study period, 93 children admitted to PICU required mechanical ventilation. Age ranged from 1 month to 15 years and male to female ratio was 1.2: 1. Almost half (43, 46%) of them were one year of age or younger. Sixteen of these children (17%) developed VAP at some point during ventilation.

Majority of them (67, 72%) required ventilation because of respiratory failure (p-value < 0.01), while 24% (23) were ventilated for neuromuscular blockade and paralysis and 3 (3%) were ventilated because of apnoea. Just over half (47, 53%) were ventilated on pressure control mode (p-value < 0.01), while 29 (31%) were put on volume control mode, 11 (12%) on synchronized intermittent mandatory ventilation (SIMV) and 4 (4.3%) on continuous positive airway pressure (CPAP).

The average length of stay in ICU among all admitted cases was 8.77 (± 6.85) days. In children who developed VAP (n=16), mean duration of ventilation was 13.5 (± 10.1) days compared to 7.7 (± 5.5) days in patients who did not develop VAP (n=77) [p =0.04].

Cultures of endotracheal tip were positive in almost all cases irrespective of them having VAP or not. Tracheal aspirates were also sent for culture sensitivity and these were positive in 23 cases (24.7%). Fourteen of these (60%) developed VAP. Blood cultures were positive in 18 children (19.4%) and 6 of them had VAP (33%). Fifteen patients had purulent tracheal secretions and cultures were positive in 7 cases (47%), compared to 21% (16/78) positive cultures in children with no visibly purulent tracheal secretions (p = 0.032).

Analyzing the different variables to find out the possible associated factors, it was seen that age less than 1 year (p =0.04), unplanned emergency intubations (p = 0.02) and use of continuous sedation (p = 0.003) were associated with increased risk of developing VAP. Factors like gender, indication and mode of ventilation, and duration of ventilation were not found to be significantly associated with the development of VAP (p > 0.05, Table I).

Purulent tracheal secretions (p =0.001), CRP more than 48 (p < 0.001), positive tracheal aspirate culture (p < 0.0001) and a suggestive chest radiograph (p < 0.001) were strong predictors of development of VAP. Factors that were poor predictors of VAP included fever > 102°F, increased tracheal secretions that were

not purulent, positive endotracheal tube tip culture, raised TLC and high polymorphonuclear cell count (Table II).

Of this overall cohort of 93 children requiring ventilation, 20 patients died and 2 left against advice in critical condition with overall mortality of 23% (poor outcome group). Amongst the poor outcome group 32% (n=7) children had VAP compared to 13% (n=9) in children who were discharged (p-value=0.038). This gives a 2.24 times higher risk of poor outcome (95% CI 1.09-4.6) in children who acquired VAP.

Table I: Possible risk factors associated with VAP (n = 16/93).

Risk Factor	Frequency of VAP	Chi-square (p-value)	Odds ratio (95% CI)
Age < 1 year	11/43 (25.6%)	3.94 (0.04) *	3.094 (0.97-9.77)
Male gender	10/50 (20%)	0.59 (0.44)	1.54 (0.51-4.66)
Unplanned emergency intubation	2/3 (66.6%)	5.32 (0.02) *	10.85 (0.921-128)
Duration of ventilation > 15 days	13/74 (17.5%)	0.034 (0.85)	1.137 (0.28-4.47)
Continuous sedation	12/39 (30.7%)	8.67 (0.003) *	5.556 (1.63-18.90)
Indication of ventilation	-	NS	-
Mode of Ventilation	-	NS	-
Duration of ventilation Overall	-	3.55 (0.169)	-

** Statistically significant (p-value < 0.05)*

Table II: Features suggestive of VAP (predictors of VAP) n = 16/93.

Features	Frequency of VAP	Chi-square (p-value)	Odds ratio (95% CI)
Purulent tracheal secretions	7/15 (46%)	10.89 (0.001) *	6.70 (1.96-22.93)
CRP > 48	8/17 (47%)	13.01 (< 0.001) *	7.55 (2.27-25.12)
Positive tracheal aspirate culture	14/23 (60%)	40.9 (< 0.0001) *	52.88 (10.29-271.7)
Positive ETT tip culture	14/83 (16%)	0.06 (0.8)	0.812 (0.155-4.23)
Raised TLC	9/39 (23%)	1.62 (0.20)	2.01 (0.67-5.98)
High poly count	10/43 (23%)	2.05 (0.15)	2.22 (0.73-6.73)
Positive blood culture	6/18 (33%)	4.07 (0.04)	3.25 (0.99-10.62)
Suggestive CXR	16/28 (57%)	44.86 (< 0.001) *	-

** Statistically significant*

Table III: Microbial isolates from blood and tracheal aspirate.

Isolate	Blood (n= 18/93)	Tracheal aspirate (n=23/93)
Pseudomonas	06	15
E coli	03	02
Klebsiella	04	05
Streptococcus	01	00
Staphylococcus aureus	03	00
Acinetobacter	01	01

DISCUSSION

Nosocomial infections are one of the most difficult challenges faced in modern ICUs especially in our resource limited setup.[16] The frequency of VAP in children admitted to MICU was 17% in this series. Surveillance studies from PICUs show that VAP occur in 3 - 32% of ventilated patients.[2,6] The prevalence quoted from NICU and adult ICU reports is much higher 15-32%.[1,8]

VAP has been associated with increased morbidity, increased length of stay and duration of ventilation, as was also observed in this series.[6,9,17] Not only that but the mere suspicion of VAP would necessitates the use of antibiotics which may or may not be actually needed.[1] This highlights the importance of adhering to the CDC clinical criteria for diagnosing VAP, so that inappropriate antibiotic therapy can be avoided.[15]

Microbiology of VAP is extremely important to characterize and plan appropriate management. However, the subjects of microbiology based diagnosis and methods of obtaining specimens have been a subject of on-going debate.[3] With regards to the spectrum of isolates, overwhelming majority was of gram negative bacteria - *Pseudomonas*, *Klebsiella* and *E. coli*. Other studies have also reported the gram negative bacteria as the most frequent isolates (42-65%).[1,2,6,10] However, some have also reported organisms like *Staphylococcus aureus*, *Streptococcus pneumoniae* and *Haemophilus influenzae*.[8,17] A study from Malaysia has reported isolation of organisms like *Acinetobacter*.[8] One of isolates in this series was also *Acinetobacter*. Previously, reported local studies have shown similar pattern of more gram negative isolates compared to gram positive organisms in children with nosocomial infections.[16]

One of the most important aspects of nosocomial infections is prevention. Identification of risk factors and predictors is imperative for the appropriate steps in this direction. Table I and II show the possible risk factors and predictors of VAP in this series. Tang *et al.* have also reported age less than one year to be associated with increased chances of VAP.[10] Underlying conditions like genetic syndromes and burns were found to be a risk factor in one study, but no such association was noted in this series.[2]

Of the 3 children who required unplanned emergency intubation because of apnoea, 2 developed VAP (66%). This may point to increased risk of VAP if intubation is not carried in a planned way. Other studies have reported re-intubation as a risk factor for developing

VAP.[2] Various other procedures have also been associated with increased risk of VAP like tracheostomy, central venous catheterization, bronchoscopy, thoracocentesis and transfusions.[2,10]

There was an increased frequency of VAP in children on continuous sedation compared to intermittent boluses. Variable results have been reported from other authors.[8,10] Moreover, use of a number of other medications have also been reported as possible risk factor for VAP. These include total parenteral nutrition (TPN), steroids, H_2 blockers and neuromuscular blocking agents.[2]

In a prospective study, Srinivasan *et al.* found that a rise in TLC was not associated with VAP, but factors like presence of new radiological changes, fever, re-intubation, blood transfusion, use of narcotics and enteral feeding were associated with VAP.[6] Data from Malaysia has, however, shown leucocytosis as an important predictor of VAP, as has the use of heavy sedation and steroids.[8] There has been conflicting reports of the role of stress ulcer prophylaxis in the development of VAP.[2,6,12]

Ventilator associated pneumonia was associated with longer period of ventilation, increase length of ICU stay and increased mortality - the facts have also been observed by a number of other studies.[1,6,9,10,14,18]

CONCLUSION

The frequency of VAP was 17% in this series, highlighting the importance of having high index of suspicion for VAP in ventilated children. Factors significantly associated with VAP were age less than 1 year, unplanned intubation and continuous sedation. The important predictors of VAP included purulent tracheal secretions, high CRP and persistent new radiological findings.

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