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Original Research Article

Ventilator associated pneumonia: incidence, profile and outcome in pediatric intensive care unit of tertiary care centre

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ABSTRACT

Background: Ventilator-Associated Pneumonia (VAP) refers to nosocomial pneumonia occurring 48 hours or more after initiation of mechanical ventilation (MV), with frequencies ranging from 15-45%. The incidence rates of VAP are higher in developing countries with limited resources. Early and late VAP differ in their pathogenesis, micro-organisms responsible, antibiotic sensitivity, outcome and treatment.
Methods: Retrospective cohort study of all critically ill children between 1 month to 12 years who were admitted and mechanically ventilated in our 8-bedded PICU between January 2015 to June 2016 and developed Ventilator associated pneumonia. PIM3 (Paediatric Index of Mortality 3) was calculated. We compared early and late VAP for risk factors, length of stay on mechanical ventilation (LOS MV) and outcome. The data collected were compiled and tabulated.
Results: The incidence of VAP in this study was 40%. We found significant correlation between early and late VAP with parenteral nutrition ($p = 0.001$), presence of nasogastric tube ($p = 0.012$) and mortality ($p = 0.027$). The LOS MV was Mean 7.25 days in early VAP, while 22.75 days in late VAP; which demonstrated significant correlation ($p = 0.003$). There was no significant correlation of PIM3 with VAP, reintubation and mortality. Most frequent organisms found in Early VAP were *Acinetobacter baumannii* and *MRSA*, whereas in late VAP *Pseudomonas aeruginosa* was commonest isolated organism.
Conclusions: VAP is a major cause of mortality in PICU. Late VAP was associated with longer length of stay on mechanical ventilation (LOS MV), higher mortality. This study thus emphasizes the need for prospective multicentric case-control studies for formulating and applying early preventive strategies in PICU to reduce VAP-related mortality.

Keywords: Outcome, Pneumonia, PICU, PIM3, Ventilator

INTRODUCTION

Ventilator-Associated Pneumonia (VAP) refers to nosocomial pneumonia occurring 48 hours or more after initiation of mechanical ventilation (MV)[1]. VAP is the most common Hospital-Associated Infection (HAI) among adult patients in Intensive Care Units (ICUs), with frequencies ranging from 15-45%. Moreover, it is the second most common HAI after blood stream infection in the paediatric age group, accounting for about 20% of all HAIs in the paediatric intensive care units (PICUs) and has a rate of 2.9-21.6 per 1000 ventilator days.[2] VAP is associated with increased hospital morbidity; mortality; duration of hospitalization by an average of 7-9 days per patient; and health care costs.[3] The incidence rates of VAP are higher in developing countries with limited resources. Two studies from India have shown VAP rates of 32.5% and 20% in children ventilated in Pediatric Intensive Care Units (PICU).[4,5] In a study from north India, the incidence of VAP was reported as 17.5/100 patients.[6] In Egypt, a study of device-associated infection rates in the PICUs in

a number of hospitals has showed that the overall rate of HAIs was 24.5% and that of VAP was 31.8 per 1000 ventilator days.[7]

The onset of VAP can be divided into: Early which occurs 72 hrs after intubation and late which occurs more than 72 hrs after intubation. Early and late VAP differ in their pathogenesis, micro-organisms responsible, antibiotic sensitivity, outcome and treatment. This study aims to determine the incidence, risk factors and outcome of ventilator associated pneumonia in our institution.

METHODS

Present study was a retrospective analytic-descriptive study carried out in Pediatric Intensive Care Unit of a tertiary care hospital. We serve low to middle income population as an economical and tertiary referral unit for pediatric medical and surgical cases, however this excludes pediatric patients who are post-cardiac surgery or those who need extracorporeal membrane oxygenation.

Study population

All critically ill children between 1mth to 12 years of age, who were admitted and mechanically ventilated in our 8bedded PICU between January 2015 to June 2016; and developed Ventilator associated pneumonia were included in the study. We excluded newborns, preterm infants, patients intubated for more than 24 hours prior to PICU admission with us or had incomplete data for PIM3. We followed standard antibiotic policy and management algorithms for clinically or bacteriologically defined pneumonia.

There is no gold standard for diagnosis of ventilator associated pneumonia. As per Johansan's criteria, the diagnosis of VAP is defined as the occurrence of a new and persistent radiographic infiltrate not otherwise explained, appearing on chest radiograph along with 2 of the following: body temperature 38.3°C, leukocytosis (≥10.000 WBC/ml), purulent tracheal aspirate.[8] The diagnosis of VAP was established using clinical pulmonary infection score (CPIS) as per standard protocol in our PICU.[9,10] CPIS of greater than six was used as diagnostic criteria for VAP. Endotracheal secretions were sampled under strict universal aseptic precautions.

Early-onset VAP was defined as VAP occurring within the first 72 hours and late-onset VAP was defined as VAP occurring after 72 hours after mechanical ventilation respectively.

PIM -3(Paediatric index of mortality) will be calculated as:

Calculation of PIM3 (and PIM3 risk of death%)

PIM3val= (3.8233 * Pupils) – (0.5378 * Elective) + (0.9763 * MechVent) + (0.0671 * (absolute BaseExcess)) – (0.0431*SBP) + (0.1716*(SBP*SBP/1000)) + (0.4214 *(100*FiO2/PaO2)) –(1.2246*Recov_CardBypPr) – (0.8762*Recov_CardNonBypPr) – (1.5164*Recov_NonCardPr) +(1.6225* VHRdiag) + (1.0725*HRdiag) – (2.1766*LRdiag) – 1.7928. PIM3 risk of death = ePIM3val / (1 + ePIM3val).

Categorization of diagnosis will be done based on PIM3 guidelines. This will be calculated automatically through data entered in Anzics CORE -Severity Score and Risk of Death Calculator-PIM3(Excel version).[11]

PICU LOS (length of stay) is a commonly used clinical endpoint reflecting both severity of illness and resource utilization.[3] However, because LOS is influenced by a variety of clinical and logistic factors that may not be completely apparent in a retrospective chart review, hence we will analyze the data in relation to the duration of mechanical ventilation (LOS MV) and outcome.

Statistical analysis

All the data collected were compiled and tabulated. The statistical analysis was done by chi-square test, fisher test and paired t test. The p value was calculated and <0.05 was considered significant.

RESULTS

Of the 119 mechanically ventilated patients, 48 (40%) developed ventilator associated pneumonia and were included in the study. Our PICU has overall mortality of 10.1%. 48 children with VAP included 31 (64.5%) males and 17 (35.4%) females.

Median age was 1.35 years i.e. 16months (Min.0.16yr-Max5yrs). 19 (39.5%) patients were <1yr age and 29 (60.4%) were between 1-5yrs age. Severe acute Malnutrition was seen in 21 (43.8%) patients, whereas 41.6% had no malnutrition. Median PIM3 Score was 2.35. Early VAP was noted in 36 (75%) patients while 12 (25%) patients had Late VAP.

The chief diseases requiring mechanical ventilation and development of VAP were as follows: respiratory disease (n = 16, 33.3%); neurological disease (n = 13,27%), cardiovascular disease (n = 08,16.7%), Gastroenterology and Hepatic diseases (n = 08, 16.7%) and Hemato-oncological diseases (n = 2, 4.16%). Anemia was present in 62.5% (n = 30) patients. Shock was noted in majority of patients (n = 40, 83.3%). Subsequent leukocytosis was noted in 34 (70.8%) patients with VAP. 23 patients (47.8%) had Hyponatremia. Coagulopathy noted in 20 (41.6%) patients. Hepatic dysfunction and Acute Kidney injury were seen in 18 (37.5%) and 12 (25%) patients respectively. VAP also occurred in 05(10.4%) of patients with Status Epilepticus. The mean length of stay on MV (LOS MV) was 8.16 days (Min 02 days - Max 52 days). In Early VAP, Mean LOS MV was 7.25 days, whereas in Late VAP it was 22.75 days. The correlation of LOS MV and VAP was statistically significant (p = 0.003). 72.9%

(n = 35) patients had a nasogastric tube (NGT) in-situ. All children had head of bed elevated at least 30 degrees and had no clinical evidence of aspiration during study period. 23 children (47.9%) received parenteral nutrition. Reintubation was done in 26 (54%) patients. The Mean LOS MV was 10.77 days (Min 3 days -Max 52 days) in those requiring reintubation, while the Mean LOS MV was 5.09 days (Min 2 - Max 12 days) in the remaining patients. There was no correlation between reintubation and mortality (p = 0.158, OR 0.390).

Table 1: Correlations of early and late VAP.

Variable	Early VAP (n)	Late VAP (n)	p	OR	95% CI
Mortality	25	12	0.027	0.676	0.540-0.845
NGT in-situ	23	12	0.012	1.522	1.198-1.933
Parenteral nutrition	12	11	0.001	22.00	2.534-190.9
LOS MV mean days	7.25 days (SD 3.36)	22.75 days (SD14.49)	0.003		

We did not find any significant correlation between PIM3 score and Early/Late VAP (p=0.940), Reintubation (p=0.978), Mortality (p=0.536) and Anemia (p=0.283). However, we found significant correlation between occurrence of Early/Late VAP with Mortality, receiving parenteral nutrition and presence of nasogastric tubing (Table 1).

Table 2: Causative organisms, frequency and associated mortality.

Organism	Early VAP	Late VAP	Survived-Yes (%)	Survived-No (%)	Total (%)
Acinetobacter baumannii	5	1	1 (6.7)	5 (83.3)	6 (20.7)
Candida	1	0	0 (0)	1 (100)	1 (3.4)
Citrobacter	0	1	0 (0)	1 (100)	1 (3.4)
Enterococcus spp.	4	0	0 (0)	4 (100)	4 (13.8)
MRCONS	2	0	0 (0)	2 (100)	2 (6.9)
MRSA	5	1	4 (66.6)	2 (33.3)	6 (20.7)
Pseudomonas aeruginosa	1	3	0 (0)	4 (100)	4 (13.8)
Streptococcus	2	0	0 (0)	2 (100)	2 (6.9)
Klebsiella pneumoniae	2	1	0 (0)	3 (100)	3 (10.3)
Total	22	7	5	24	29 (60.4)
No growth	14	5	5	14	19 (39.6)
Total	36	12	11	37	48 (100)

Out of Endotracheal aspirate culture in total 48 VAP patients, most number of isolates were *Acinetobacter baumannii* and Methicillin resistant *Staphylococcus Aureus (MRSA)* (20.7% Each) followed by *Enterococcus* (13.8%) and were noted in those with Early VAP. Whereas, *Pseudomonas aeruginosa* (13.8%) was most commonly noted in Late VAP (Table 2) Blood cultures were positive in 39.6% patients

DISCUSSION

Relevance of studies that define the risk factors for nosocomial infections, especially in critical infants and children cannot be undermined as they significantly help in providing effective preventive measures and formulating relevant policies in the paediatric intensive care setting. The incidence of VAP in present study was 40% and mortality amongst these was 77%. Being a tertiary charitable referral centre for many critical and end stage patients due to mainly economical and other reasons, could have contributed to higher incidence. Incidence of VAP differs greatly based on setting and location in critically ill children in PICU.[12] The incidence rates of VAP are higher in developing countries with limited resources. Patra et al and Sharma et al from India have shown VAP rates of 32.5% and 20% in children ventilated in Pediatric Intensive Care Units (PICU).[4,5] Gupta et al demonstrated an incidence of VAP as 17.5/100 patients.[6] In Egypt, a study of device-associated infection rates in the PICUs in a number of hospitals has showed that the overall rate of HAIs was 24.5% and that of VAP was 31.8 per 1000 ventilator days.[7] El-Kholy et al. reported that VAP was the most commonly identified device-associated nosocomial infection (90%) among 490 pediatric

patients.[13] Awasthi et al demonstrated that VAP developed in 36.2% of children requiring mechanical ventilation in India, which is compatible with present study incidence.[14] Another national multicenter study on nosocomial infections in Spain, reported very low incidence of VAP (1.3%) among children undergoing mechanical ventilation in PICU.[15] Bozorgmehr R et al concluded with prevalence of VAP as 11% among the studied patients and mortality due to it was estimated to be 78.9%.[16] Late referral, younger age, co-morbidities, and lack of appropriate implementation of standard VAP Prevention Guidelines may have contributed to higher VAP-related mortality in the present study.

A variety of cases developed VAP in present study including ependymoma, situs inversus and dextrocardia with transposition of great arteries, meningitis, viral encephalitis, dengue shock syndrome, Guillian Barre syndrome, metabolic encephalopathy, fulminant hepatic failure, secondary hemophagocytic lymphohistiocytosis, cardiogenic shock, etc.

We found that Late VAP was associated with longer length of stay on mechanical ventilation (LOS MV) and higher mortality. LOS MV almost tripled in this study in those with Late VAP as compared to Early VAP, this significantly increased the financial and psychological burden on patient's families.

Parenteral nutrition and presence of nasogastric tubing were significantly associated with late onset VAP as compared to early VAP. Very few studies provide evidence about the risk factors of VAP in critically ill children in PICU. Reintubation or self-extubation might be a risk factor for VAP. The most likely mechanism of this is aspiration of oropharyngeal secretions or gastrointestinal contents during the procedure. Aspiration appears to be important in the pathogenesis of VAP, as demonstrated in some studies.[3,17]

As per previous studies, Awasthi et al reported that VAP mostly occurred in children who were ventilated for more than 4 days, while Bilan et al reported VAP mostly occurring in those who were re-intubated.[14,18]

Though we did not find significant correlation with reintubation ($p = 0.502$), we did find higher mortality in those developing late VAP ($p = 0.027$). Sharma et al found significant association between use of H2 blockers (Ranitidine) for >2 days with development of VAP in children.[5] Liu et al in a meta-analysis concluded that genetic syndrome, reintubation or self-extubation, steroids, bloodstream infection, prior antibiotic therapy and bronchoscopy were regarded as risk factors for VAP of patients in PICU.[1] Though the Mean LOS MV was double i.e. 10.77 days (Min 3 days to Max 52 days) in those requiring reintubation, while the Mean LOS MV was 5.09 days (Min 2 to Max 12 days) in the remaining patients. We found no correlation between reintubation and mortality ($p = 0.158$, or 0.390).

We did not find any significant correlation between PIM3 (Paediatric index of mortality) score and early/late VAP, reintubation, anemia or mortality. APACHE II score was utilized by Naved et al and Gupta et al to evaluate the condition of patient at admission and they found that patients with VAP had higher scores and hence higher mortality rate.[19,20] A prospective longitudinal study would have provided better information on the role of PIM3 in predicting mortality in VAP.

Acinetobacter baumannii and Methicillin resistant *Staphylococcus aureus* (MRSA) were the most common organisms followed by *Enterococcus spp*. in those with Early VAP, while *Pseudomonas aeruginosa* was mostly noted in late VAP. We found no significant correlation between Culture positivity and mortality in VAP ($p = 0.067$). We noted multidrug resistance in most pathogens. Patra et al demonstrated VAP in 76% of patients with hospital-acquired pneumonia and this represented the most frequent nosocomial infection in intensive care units (80%) with an overall mortality of nosocomial pneumonia reaching 60%; all of these were secondary to Gram-negative infections with Pseudomonas contributing to 57.1% of deaths followed by *Klebsiella*, *Escherichia coli* and *Acinetobacter*.[4] Rising incidence of antibiotic resistant pathogens contributes significantly to the mortality and prognosis of these patients.

The major drawback of this study was it being a secondary analysis of existing database, hence dynamic monitoring and assessment of patients with serial CPIS was not possible. Also sample size and usage of data from single PICU setting is a limitation, thus restricting generalized applicability of the results. Late referral, younger age, co-morbidities, and lack of implementation of standard VAP Prevention Guidelines may have contributed to higher VAP-related mortality in the present study. A prospective, multi-centric study in developing country PICU setting for determining risk factors would be desirable for devicing further clinically applicable management and early prevention strategies.

CONCLUSION

VAP is a major cause of mortality in PICU. Late VAP was associated with longer length of stay on mechanical ventilation (LOS MV) and higher mortality. This significantly increased the financial and psychological burden on patient's families. Parenteral nutrition and presence of nasogastric tubing were significantly associated with late onset VAP as compared to early VAP. Though Reintubation lead to longer LOS MV, it was not a significant risk factor in this study. PIM3 score did not affect the outcome of early and late VAP. Most frequent organisms found in Early VAP were *Acinetobacter baumannii* and MRSA, whereas in Late VAP it was *Pseudomonas aeruginosa*. This study thus emphasizes the need for applying early preventive strategies in PICU to reduce VAP-related mortality. Further larger, prospective

and multicentric case-control studies are required to evaluate the risk factors and outcome of VAP.

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REFERENCES

1. Liu B, Li SQ, Zhang SM, Xu P, Zhang X, Zhang YH, et al. Risk factors of ventilator-associated pneumonia in a paediatric intensive care unit: a systematic review and meta-analysis. J Thorac Dis. 2013;5(4):525-31.
2. Tang CW, Liu PY, Huang YF, Pan JY, Lee SS, Hsieh KS, et al. Ventilator-associated pneumonia after paediatric cardiac surgery in southern Taiwan. J Microbiol Immunol Infect. 2009;42(5):413-9.
3. Elward AM, Warren DK, Fraser VJ. Ventilator-associated pneumonia in paediatric intensive care unit patients: risk factors and outcome. Paediatr. 2002;109:758-64.
4. Patra PK, Jayashree M, Singhi S, Ray, Saxena AK. Nosocomial pneumonia in a pediatric intensive care unit. Indian Pediatr. 2007;44:511-8.
5. Sharma H, Singh D, Pooni P, Mohan U. A study profile of ventilator associated pneumonia in children in Punjab. J Trop Pediatr. 2009;55:393-5.
6. Gupta A, Kapil A, Lodha R, Sood S, Dhawan B, Das BK, et al. Burden of healthcare-associated infections in a paediatric intensive care unit of a developing country: a single centre experience using active surveillance. J Hosp Infect. 2011;78:323-6.
7. Rasslan O, Seliem ZS, Ghazi IA, Abd El Sabour M, El Kholy AA, Sadeq FM. Device-associated infection rates in adult and paediatric intensive care units of hospitals in Egypt. International Nosocomial Infection Control Consortium (INICC) findings. J Infect Public Health. 2012;5(6):394-402.
8. Papazian I, Bregeon I, Thirion X. Effects of ventilator-associated pneumonia on mortality and morbidity. AM J Respir Crit Care Med. 1996;154:91-7.
9. Luyt CE, Chastre J, Fagon JY, The VAP Trial Group. Value of the clinical pulmonary infection score for the identification and management of ventilator-associated pneumonia. Intensive Care Med. 2004;30:844-52.
10. Croce MA, Swanson JM, Magnotti LJ, Claridge JA, Weinberg JA, Wood GC, et al. The futility of the clinical pılmonary infection scores in trauma patients. J Trauma. 2006;60:523-8
11. Australian and New Zealand Intensive Care Society (ANZICS). Information Booklet: PIM2 and PIM3 for the ANZPIC Registry; March 2016. Available at http://www.anzics.com.au/www.anzics.com.au/Downloads/PIM2%20%26%20PIM3%20Information%20Booklet%20Mar16.pdf
12. Aelami MH, Lotfi M, Zingg W. Ventilator-associated pneumonia in neonates, infants and children. Antimicrob. Resist Infect Control. 2014;3:30.
13. El-Kholy A, Saied T, Gaber M, Younan MA, Haleim MM, El-Sayed H, et al. Device-associated nosocomial infection rates in intensive care units at Cairo University hospitals: First step toward initiating surveillance programs in a resource-limited country. Am J Infect Control. 2012;40:e216-20.
14. Awasthi S, Tahazzul M, Ambast A, Govil YC, Jain A. Longer duration of mechanical ventilation was found to be associated with ventilator-associated pneumonia in children aged 1 month to 12 years in India. J Clin Epidemiol. 2013;66:62-6.
15. García J, Arriourtúa AB, Torre JA, Antón JG, Vicente JC, González CT. A national multicentre study on nosocomial infections in PICU. An Pediatr. Barc. 2014;80:28-33.
16. Bozorgmehr R, Bahrani V, Fatemi A. Ventilator-associated pneumonia and its responsible germs; an epidemiological study. Emerg. 2017;5(1):e26.
17. Memish ZA, Oni GA, Djazmati W. A randomized clinical trial to compare the effects of a heat and moisture exchanger with a heated humidifying system on the occurrence rate of ventilator-associated pneumonia. Am J Infect Control 2001;29:301-5.
18. Bilan N, Habibi, P. Does Re-intubation Increased Risk of Ventilator-Associated Pneumonia (VAP) in Paediatric Intensive Care Unit Patients? Int J Pediatr. 2015;3:411-5.
19. Naved SA, Siddique S, Khan FH. APACHE II score correlation with mortality and length of stay in an intensive care unit. J College Physicians Surg Pak. 2011;21:4-8.
20. Gupta A, Agrawal A, Mehrotra S, Singh A, Malik S, Khanna A. Incidence, risk stratification, antibiogram of pathogens isolated and clinical outcome of ventilator associated pneumonia. Indian J Crit Care Med. 2011;15:96-101.

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