Original Article ISSN (O):2395-2822; ISSN (P):2395-2814

Prospective Observational Study of Ventilator Associated Pneumonia in Pediatric Intensive Care Unit in a tertiary care hospital, New Delhi.

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Received: May 2017
Accepted: June 2017

ABSTRACT

Background: Ventilator associated pneumonia (VAP) is defined as nosocomial pneumonia in mechanically ventilated patients that develops more than 48 hrs after initiation of mechanical ventilation. The study was done to determine the incidence of VAP in pediatric patients undergoing mechanical ventilation and to identify the common microbes incriminated in causing VAP in patients admitted and put on mechanical ventilation. **Methods:** This study is the prospective and observational study done from December 2010 – January 2012. The aim of the study was to find out a) the incidence of ventilator-associated pneumonia in pediatric intensive care unit and b) the bacteria responsible for VAP and their antibiotic sensitivity pattern. Data will be coded and analyzed by using SPSS version 12 or 16. Statistical analysis was done by using Student's paired t-test for quantitative and Chi-square test for qualitative parameters. The p value of <0.05 was considered as statistically significant. **Results:** Incidence of VAP in terms of per 1000 ventilator days was 26.13/1000. Out of the 103 study group patients 43 (41.74%) were culture positive with significant bacterial counts but only 31 (30%) patients were diagnosed as VAP as per the inclusion criteria. Of 31 patients diagnosed as VAP, 22 (70.96%) patients had infection with single organism and 9 (29.03%) had polymicrobial infection. The most common isolate was Acinetobacter (37.5%) followed by Pseudomonas and Klebsiella (27.5%). Among the polymicrobial infection Acinetobacter along with Klebsiella and Pseudomonas was the common combination seen. **Conclusion:** The role of microbiology in VAP is to identify the organisms commonly responsible for causing VAP and to know the antibiotic resistance pattern of these organisms. This will help the clinicians in formulating a proper empirical and therapeutic strategy against the causative organisms of VAP.

Keywords: Micro-organism, Pediatric, Ventilator associated pneumonia.

INTRODUCTION

Intensive care units have come to represent the most frequently identifiable source of nosocomial infections within the hospital, with the infection rates and rate of antimicrobial resistance several fold greater than the general hospital setting.[1]

Ventilator associated pneumonia (VAP) is defined as nosocomial pneumonia in mechanically ventilated patients that develops more than 48 hrs after initiation of mechanical ventilation.[2] ventilator associated pneumonia is divided into early onset pneumonia which occurs in 5 days of mechanical ventilation and late onset pneumonia which develops five or more days after initiation of mechanical ventilation. The importance of segregating VAP in early and late onset is that, the pathogenesis, microorganisms responsible and outcome in these groups are different and so the therapeutic implications also differ.[1] Early onset VAP, which occurs within the first five days of mechanical ventilation, usually is less severe, associated with better prognosis, and is more likely to be caused by antibiotic sensitive bacteria. Late onset VAP, which develops five or more days after initiation of mechanical ventilation, is caused by multidrug resistant (MDR) pathogens and is associated with increased morbidity and mortality.[3]

Diagnosis of VAP is made by clinical criteria by National Nosocomial Infection Surveillance (NNIS) for pediatric patients.[4] Diagnosis of VAP can be made on the basis of radiographic findings, clinical findings, results of microbiological tests. The likelihood of VAP increases if a patient has clinical signs and symptoms such as fever, leukocytosis, and purulent sputum in addition to abnormal findings on chest radiographs.

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The incidence of VAP in neonatal ICU in a study conducted was 37.2 per thousand days of mechanical ventilation. The mean duration of ventilation before the onset of pneumonia was 5 days.46.6% developed VAP within 5 days of mechanical ventilation and were classified as early onset VAP.53.3% cases developed pneumonia ≥5 days of mechanical ventilation and were categorized under late onset VAP.[3] Most common bacterial isolate from endotracheal aspirate (ETA) was Klebsiella spp (32.87%)followed by Eshcherichia coli and Acinetobacter. The mean length of ICU stay was significantly longer in patients with VAP as compared to those without VAP i.e. 232.7 days vs 19.7 days. Mortality rates were higher in patients with VAP (40%) and lower in non-VAP cases (22.06%).[1] The incidence of VAP in this study is comparable to the incidence of VAP in earlier neonatal studies such as Apisarnatharak et al 28.3%, Petdachai et al 50 % and Yuan et al 20.1%.[6-7]

Pathophysiology of VAP involves 2 main processes: colonization of respiratory tract and microaspiration of secretions of the upper and lower parts of airway.[8] Colonization of bacteria refers to presence of bacteria without an active host response. Bacterial colonization of lungs can be due to spread of organisms from many different sources, including the oropharynx, sinus cavities, nares, gastrointestinal tract, patient to patient contact and ventilator circuit.[9] Inhalation of colonized bacteria from any of these sources can cause an active host response and ultimately VAP.

Epidemiology and outcomes of VAP are well described in adults,[10] but few data exist for pediatric patients particularly with respect to risk factors and outcomes such as attributable morbidity, mortality. Also few data exist for bacteriological profile of VAP and semiquantitative method of bacterial isolation of tracheal aspirate.[5,8]

A prospective observational study was done to determine the incidence of VAP in pediatric patients undergoing mechanical ventilation and to identify the common microbes incriminated in causing VAP in patients admitted and put on mechanical ventilation in PICU of Lady Hardinge Medical College & Associated Hospitals, a tertiary care hospital in New Delhi, India.

MATERIALS AND METHODS

This study is the prospective and observational study done from December 2010 – January 2012. The aim of the study was to find out a) the incidence of ventilator-associated pneumonia in pediatric intensive care unit and b) the bacteria responsible for VAP and their antibiotic sensitivity pattern. All pediatric patients admitted in PICU of Lady Hardinge Medical College and Associated Hospitals New Delhi. Who are intubated and put on mechanical ventilation. The patients were selected irrespective of sex, diagnosis at point of admission, length of hospital stay or antimicrobial use. The patients were informed about the study and written consent from the parents was taken.

Inclusion criteria

Subjects classified as the case of VAP which fulfill the simplified version from CDC and American Thoracic Society (2005) criteria:[11]

1) The patient should have been on mechanical ventilation (either through an endotracheal tube or through tracheostomy) in an ICU for more than 48 hours to be qualified to be a case under consideration of VAP.
2) Rales or dullness to percussion on physical examination of chest.

And any of the following:

New onset of purulent sputum or change in character of sputum.

Same organism isolated from blood culture as from respiratory tract with no other source of infection.

Isolation of pathogen from specimen obtained by transtracheal aspirate, bronchial brushing, BAL or biopsy.

OR

3) Chest radiographic examination showing new or progressive infiltrate/ consolidation, Cavitation without carcinoma or tuberculosis or pleural effusion

AND any of the following:

a) New onset of purulent sputum or change in character of sputum.
b) Same organism isolated from blood culture as from respiratory tract with no other obvious source of infection.
c) Isolate of pathogen from specimen obtained by transtracheal aspirate, bronchial brushing, BAL or biopsy.
d) Histopathological evidence of pneumonia.

Exclusion criteria

a) Patients with pneumonia prior to mechanical ventilation.
b) Not giving consent for participation in study.

Four sequential samples of tracheal secretion aspirate will be collected from each patient. First tracheal secretion collection will be performed within 24 hrs of intubation and subsequent samples will be taken at regular intervals of 48, 96 hrs and 144 hrs after the first. The specimen collected will be transported to the microbiology laboratory as soon as possible. Semi-quantitative culture was done on

tracheal aspirate. Measured amount 0.001 ml of aspirate will be used for plating on Blood agar and Mac-Conkey agar .After overnight incubation at 37⁰ C the growth of single type of 100 colonies by this method indicates the presence of 10^5 bacteria/ml of aspirate.[20] Colony characteristics will be observed and identified in accordance with standard recommendations.[21] Bacterial identification will be done to the species level with the help of standard biochemical tests.[21] Sensitivity of the organisms isolated will be done by disc diffusion method.10^5 CFU/ml of endotracheal aspirate will be taken as cut off between organisms causing VAP and colonization.

Data will be coded and analyzed by using SPSS version 12 or 16. Statistical analysis was done by using Student's paired t-test for quantitative and Chi-square test for qualitative parameters. The p value of <0.05 was considered as statistically significant.

RESULTS

The prospective and observational study was done from December 2010 –January 2012. A total of 103 patients were included in the study and analyzed. Out of total 103 patients in the study group 31 (30%) developed VAP [Figure 1]. Demographic details of the subjects are shown in [Table 1].

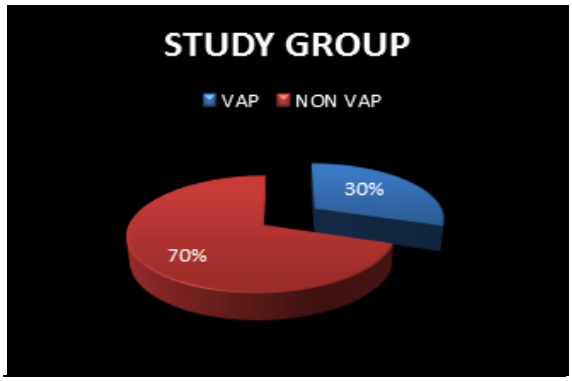

Figure 1: Distribution of study group.

Table 1: Demographic details of the study group (n=103).

Mean age	**2.95 years (4days-14 years)**
Gender (Male:Female)	1.7:1
Mean length of stay in hospital before referral to ICU	4 days (1-15days)
Patient referred from medical disciplines	95 (92.2%)
Patient referred from surgical disciplines	8 (7.77%)
Diagnosed of having infection(other than VAP)before referral to ICU	33 (32.03%)
Mean length of ICU stay	13.05 days (2-120 days)
Mean length of intubation	11.97 days (2-59 days)
Overall mortality in ICU	45 (43.68%)

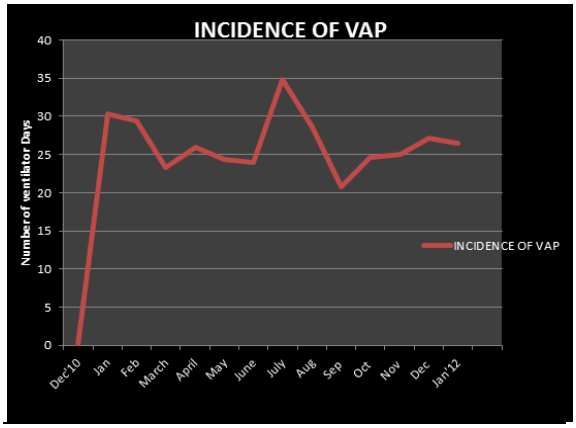

Figure 2: Monthly incidence of VAP cases.

Monthly distribution of VAP cases and incidence of VAP in terms of VAP/1000 ventilator days is shown in [Figure 2]. Mean ventilators day for study group was 11.5 days (range 33-151). Incidence of VAP in terms of per 1000 ventilator days was 26.13/1000 ventilator days (range 20.8-34.9) from Dec 2010-Jan 2012.

Out of the 103 study group patients 43 (41.74%) were culture positive with significant bacterial counts but only 31 (30%) patients were diagnosed as VAP as per the inclusion criteria (clinical + microbiological) [Figure 3].

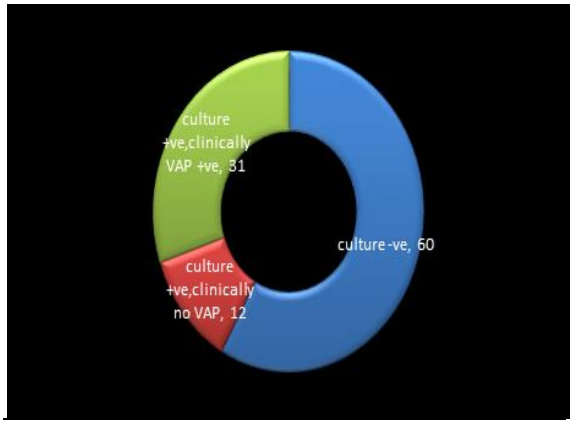

Figure 3: Distribution of patients on basis of culture.

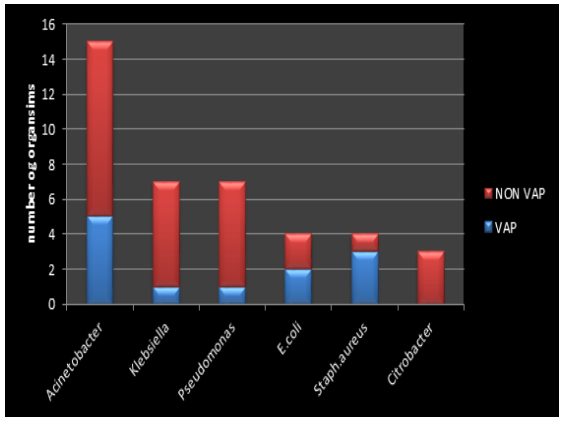

Figure 4: Microbiological profile of VAP cases.

Of 31 patients diagnosed as VAP based on the inclusion criteria, 22 (70.96%) patients had infection with single organism and 9 (29.03%) had polymicrobial infection. The most common isolate was Acinetobacter (37.5%) followed by Pseudomonas and Klebsiella (27.5%). Among the polymicrobial infection Acinetobacter along with Klebsiella and Pseudomonas was the common combination seen [Figure 4].

Comparing the resistance pattern of organisms isolated from early onset and late onset cases it was seen that the organisms isolated from late onset VAP cases were more resistant to the common antibiotics used [Table 2,3].

Among the Gram positive organisms 3 isolates of Staphylococcus aureus were obtained from early onset VAP cases while only single isolate was obtained from late onset VAP cases. One of the three isolates from early onset VAP cases was found to be methicillin resistant. Two of the three isolates were resistant to augmentin, ciprofloxacin, erythromycin and gentamicin. The isolate obtained from late onset VAP case was methicillin resistant along with augmentin, ciprofloxacin, erythromycin and gentamicin resistance.

Among Gram negative organisms Acinetobacter was the most common. Out of five isolates of Acinetobacter from early onset cases 1 was resistant to all the first line drugs used, while it was sensitive to colistin and tigecyclin. One isolate was found to be resistant to netilmicin and piperacillin + tazobactem along with the first line drugs used. Ten isolates of Acinetobacter were obtained from late onset VAP cases out of which 3 were resistant to all the antibiotics tested including colistin and tigecyclin. Resistance against ceftriaxone was also seen in 9 out of ten isolates. Five of ten isolates were resistant to imipenem and meropenem. This suggests a higher rate of antibiotic resistance among the isolates of Acinetobacter obtained from late onset VAP cases.

Four of the six isolates of Pseudomonas obtained from late onset VAP cases were resistant to ceftazedime, ceftriaxone, cefepime, suggesting a high prevelance of extended spectrum beta-lactamase (ESBL) producing organism as cause of late onset VAP. These isolates were also found to be resistant to imipenem, meropenem and piperacillin + tazobactem.

Out of the 6 issolates of Klebsiella obtained from late onset VAP cases 2 were found to be resistant to the first line drugs along with colistin and tigecyclin. Four out of six isolates were resistant to ceftriaxone and ceftazedime suggesting a high prevelance of ESBL producing Klebsiella in late onset VAP cases. Two isolates were resistant to both imipenem and meropenem.

Table 2: Antibiotic resistance pattern of the organisms isolated from early onset VAP.

	Acinetobacter	Klebsiella	Pseudomonas	E.coli	Staph.aureus
AC	80%	100%	-	0%	66.67%
AK	60%	0%	100%	0%	-
A	40%	0%	100%	0%	-
CA	-	-	0%	-	-
CF	60%	0%	100%	0%	66.67%
CPM	20%	0%	0%	-	-
CTR	20%	0%	100%	0%	-
CL	0%	0%	0%	0%	-
CX	-	-	-	-	33.33%
E	-	-	-	-	66.67%
G	40%	-	-	-	66.67%
I	40%	-	100%	0%	-
LZ	-	-	-	-	0%
MRP	20%	-	0%	0%	-
NT	20%	0%	-	-	-
PIT	20%	0%	0%	0%	-
TE	-	-	-	-	0%
TIG	0%	0%	0%	-	-
VA	-	-	-	-	0%

DISCUSSION

VAP is the second most common hospital-acquired infection among pediatric and neonatal intensive care unit (NICU) patients. VAP occurs in 3 to 10% of ventilated pediatric ICU patients.[12] Surveillance studies of nosocomial infections in neonatal ICU patients indicate that pneumonia compromises 6.8 to 32.3% of nosocomial infections in pediatric setting. The incidence of VAP is higher in adult ICU patients, ranging from 15 to 30%.[13]

The incidence of VAP in western countries is low as compared to India, this is because of the demographic difference in Indian and western population, the quality of health care services available and the underlying disease state requiring ventilator support.

National Nosocomial Infection Surveillance (NNIS) US, data from 2002 to 2004 shows NICU VAP rates ranging from 1.4 to 3.5 per 1,000 ventilator days.[14] From 2006-2007, within National Healthcare Safety Network (NHSN) facilities almost 5,400 VAPs were

reported and incidence for various types of hospital units ranged from 2.1-11.0 per ventilator days.[15]

A study of 20 PICUs in 8 countries performed by the European Multicenter Study Group found that the incidence of nosocomial infection was 23.6% and the most frequent nosocomial infection was pneumonia (53%).[1] The incidence of VAP in other paediatric studies was 50% and 20.1% respectively.[4] The incidence of VAP in a study conducted by Tripathi et al (Lucknow, India) in 2009 was 30.6% (37.2/1000 ventilator days).[1] Various studies found the incidence of VAP as 30.5% in their study.[6,9,12] These findings of Indian studies were comparable to our study. The variation can be due to difference in diagnostic criteria used, aseptic precautions in intensive care unit and variable sensitivity and specificity of diagnostic tests. The incidence of VAP varied from developed to developing countries and even in different regions of the same country. This can be due to the following reasons: 1. Quality of health-care services available in different countries, 2. Type of surveillance method used to identify VAP cases, 3. Case definition of VAP, 4. Diagnostic method used to detect VAP.[10]

Oslon et al. illustrated the influence of surveillance intensity on the reported prevalence of nosocomial infections by 41-month surveillance study in a children's hospital. Infection control surveillance was conducted twice a week for the first 2 years of the study and then daily for the second 2 years of the study through nursing sentinel sheet. A 50% increase in the incidence of reported nosocomial infections following the introduction of daily surveillance was seen.[10]

Table 3: Antibiotic resistance pattern of the organisms isolated from late onset VAP.

	Acinetobacter	Klebsiella	Citrobacter	Pseudomonas	E.coli	Staph.aureus
AC	70%	66.67%	66.67%	-	100%	100%
AK	70%	50%	33.33%	66.67%	100%	-
A	70%	33.33%	50%	83.33%	100%	-
CA	70%	-	-	66.67%	-	-
CF	80%	66.67%	66.67%	83.33%	100%	100%
CPM	60%	33.33%	33.33%	66.67%	-	-
CTR	90%	66.67%	66.67%	66.67%	100%	-
CL	30%	33.33%	33.33%	33.33%	50%	-
CX	-	-	-	-	-	100%
E	-	-	-	-	-	100%
G	90%	-	-	-	-	100%
I	60%	50%	33.33%	66.67%	50%	-
LZ	-	-	-	-	-	0%
MRP	50%	33.33%	33.33%	50%	50%	-
NT	70%	33.33%	33.33%	-	50%	0%
PIT	60%	33.33%	33.33%	66.67%	50%	0%
TE	-	-	-	-	-	0%
TIG	30%	33.33%	33.33%	-	50%	-
VA	-	-	-	-	-	0%

AC- Augmentin, AK- Amikacin, A- Ampicillin, CA- Ceftazedime, CF- Ciprofloxacin, CPM- Cefepime, CTR- Ceftriaxone, CL- Colistin, CX- Cefoxitin, E- Erythromycin, G- Gentamicin, I- Imipenem, LZ- Lenezolid, MRP- Meropenem, NT- Netilmicin, PIT- Piperacillin+Tazobactem, TE- Tecoplanin, TIG- Tigecyclin, VA- Vancomycin.

Patra P.K. et al observed gram negative predominance, with Acinetobacter spp (54.5%) being the most predominant isolate followed by Pseudomonas aeruginosa (22.7%) and Klebsiella (13.6%). In this study the microbial flora associated with nosocomial pneumonia reflects the common organisms present in the gut, oropharynx and environment. Colonization of ICU patients has been recognized as an important source for Gram-negative infections. Frequent use of broad spectrum empiric antimicrobials in an ICU setting further enhances the risk of colonization with resistant organisms.[14]

Tripathi et al. reported that the most common bacterial isolate from ETA of VAP patients in their study was Klebsiella spp (32.87%), E.coli and Acinetobacter were the other two common organisms. On comparing the organism causing early VAP and late onset VAP, it was found that early onset VAP was most commonly caused by Klebsiella whereas equal number of Klebsiella and Acinetobacter (33.3% each) were the causative agent of late onset VAP.[1]

Alvarez et al demonstrated that patients with VAP due to high risk pathogens (Pseudomonas aeruginosa, Acinetobacter spp., and Stenotrophomonas) had a significantly higher mortality rate (65%) than patients with late onset VAP due to other microbes (31%).[15]

CONCLUSION

VAP is a common nosocomial infection in paediatric setting. Early identification and proper diagnosis of VAP will help us to reduce the morbidity and mortality in paediatric population. The role of microbiology in VAP is to identify the organisms commonly responsible for causing VAP and to know the antibiotic resistance pattern of these organisms. This will help the clinicians in formulating a proper

empirical and therapeutic strategy against the causative organisms of VAP.

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How to cite this article: Sharma M, Jais M, Ranjan R, Kumar V, Singh M, Marwah A. Prospective Observational Study of Ventilator Associated Pneumonia in Pediatric Intensive Care Unit in a tertiary care hospital, New Delhi. Ann. Int. Med. Den. Res. 2017; 3(4): MB06-MB11.

Source of Support: Nil, **Conflict of Interest:** None declared