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Incidence, Clinical and Microbiological Pattern of Ventilator Associated Pneumonia (VAP) In Neonatal Intensive Care Unit in Amritsar, India

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Abstract

Introduction: Ventilator Associated Pneumonia (VAP) is a pneumonia where the patient is on mechanical ventilation for >2 calender days on the date of event, with day of ventilator placement being on day 1 and the ventilator was in place on the date of event or the day before.VAP continues to be major threat to patients admitted in intensive care units and receiving mechanical ventilation. 86% of nosocomial pneumonias are associated with mechanical ventilation. VAP accounts for high mortality, morbidity and health care cost burden.

Material and methods: The study was done on all intubated neonates in neonatal intensive care units (NICU), Bebe Nanki Mother and Child Care Centre attached to Government Medical College, Amritsar for a period of one year from February 2016 to January 2017. All interventions were recorded; Centre for Disease Control & Prevention (CDC) criteria were applied to find the incidence of VAP per 1,000 mechanical ventilation days. Cultures from tracheal aspirates and blood were done and analyzed.

Results: Out of 116 cases analyzed, 22 (18.96%) developed VAP, incidence being 36.9/1000 mechanical ventilation days. The mean duration of ventilation before the onset of VAP was 132.45+78.15 hours. About two-third of the cases (63.64%) developed late onset VAP. Clinically, worsening of gas exchange on pulse oximetry, increases in oxygen and ventilation demand were most common features. X-rays of chest showed that 45.45% patients had new infiltrates and consolidation. Acinetobacter (80%) and Klebsiella (20%) were the most commonly cultured pathogens from tracheal aspirates.

Conclusion: The incidence of VAP was higher as compared to developed countries; it needs interventions at various levels to bring it down. Use of preventive measures, early extubation, prevention of prematurity, empirical antibiotic use as per culture reports and improved nursing care can decrease VAP and hence neonatal mortality in our NICU.

Keywords: neonatal intensive care unit (NICU), ventilator associated pneumonia (VAP), mechanical ventilation, tracheal aspirates, blood stream infection (BSI)

Introduction

The survival rate of preterm infants and lesser than normal birth weight neonates in the last decade has substantially improved.[1] Interventions that have helped to achieve this include improved perinatal care, use of antenatal steroids and postnatal supplementation with surfactant. New modalities of mechanical ventilation, efficient antibiotics, enhanced nutrition options have all contributed towards decreasing mortality among lesser than normal birth weight infants, but VAP is a serious complication in neonates on mechanical ventilation and accounts for 6.8-32.2% of health care associated infections among neonate.[2]

VAP is a pneumonia in mechanically ventilated patients that develop later than or at 48 hrs after the patient has been placed on mechanical ventilation. VAP is the 2nd most common nosocomial infection after Blood Stream Infection (BSI) in Neonatal Intensive Care Units (NICU). It has a large impact on neonatal morbidity, survival, hospital costs and duration of neonatal intensive care unit stay.

The European Multicenter Trial involving eight countries, with a total of 14,675 admissions, found that the VAP infected patients had a longer mean length of stay, and higher mortality rates (p= 0.065) and significantly higher cost of hospitalization.[3]

The lack of gold standard for the diagnosis of VAP in neonates makes an interpretation of the literature complex.VAP as defined by the Centre for Disease Control and prevention (CDC) is a pneumonia where the patient is on mechanical ventilation for >2 calendar days on the day of the event, with the day of ventilator placement being on day 1, and the ventilator was in place on the date of the event or the day before one.[4] CDC permits the diagnosis of "clinically defined pneumonia" based only on clinical and radiological findings, without any isolated pathogen. Isolation of pathogen without clinical and radiological signs is not diagnostic of VAP. Previous studies have reported the incidence of VAP among ventilated neonates to be was 27-30%.[5,6] Variable studies in the past have found that the number of cases with late onset VAP patients exceeds the number of cases with early onset VAP.[5,6,7] Enterobacteriaceae, *H.influenzae*, *Staphylococcus aureus*, *Streptococcus pneumoniae* and Candida species are more common in early onset VAP, while non-fermenters like Pseudomonas and Acinetobacter are significantly associated with late onset VAP. The most common organisms causing VAP in various NICU settings, as reported by authors from India and abroad, were Klebsiella, Acinetobacter and Pseudomonas.[8,9,10] Early and accurate diagnosis is of critical importance for the treatment of VAP as delay is associated with increased morbidity and mortality.

To date, there are no diagnostic criterion that has both a high degree of sensitivity and specificity. So we are following CDC criteria for ≤1 year age patient, as they did not mention any different criteria for neonates.[4]

Materials and Methods

This study aims to find incidence, clinical and microbiological pattern of VAP in Neonatal Intensive Care Unit (NICU) of Government Medical College (GMC) Amritsar.

All neonates who were ventilated in NICU were included in this study. A detailed history taking including birth weight, gestation age at birth, weight for gestation (AGA/SGA status), clinical signs/symptoms, radiological examination, any intervention done on patient, any problem during NICU stay, number of ventilation days and its management were recorded daily, till the day of event or 48 hours after extubation. Patients who were clinically diagnosed as VAP according to CDC criteria, their tracheal aspirate culture and blood culture were done to find the microbiological pattern and sensitivity. Ethical clearance was obtained from the Institutional Ethics Committee and informed consent of the parents/guardian was obtained.

Study design: Prospective study.

Study Period: One year from February 2016 to January 2017.

Inclusion criteria:

1. Age of infant < 28 days,
2. Patients intubated and on mechanical ventilation for MORE THAN 48 hrs
3. Patients extubated and on follow up for 48 hours.

Exclusion criteria:

1. Age of infants more than 28 days,
2. Patients who developed pneumonia within 48 hours of mechanical ventilation and
3. any surgical problem related to respiratory tract/congenital malformation.

The patients were diagnosed with VAP based on CDC criteria for diagnosis of Nosocomial Pneumonia -2016.[4]

All newborns with VAP in the study were investigated for Complete blood count,Chest X ray, Pulse Oximetry, Endotracheal aspirate for culture & sensitivity and Blood for culture & sensitivity.

Procedures:

Tracheal aspirate sample collection[11]: Specimen was collected before the antibiotics were started or changed. Heart rate, blood pressure and. SpO2 were monitored throughout the procedure. Patient was pre-oxygenated for 5-10 minutes with 100% oxygen before disconnection from ventilator. Obtained specimen was processed within 30 minutes; was refrigerated if any further delay was expected. Sterile suction catheters of sizes appropriate for the different sized Endotracheal tubes (ETT) were used. Position of ETT was confirmed in the chest radiograph, before the sampling. The length of both the connector and ETT was added to estimate the length of suction catheter to be inserted. The catheter was then connected to the mucus trap unit and inserted in the ETT and advanced 1 cm beyond the tip of tube. Suctioning was done with wall mounted suctioning device and the aspirates were collected in sterile mucus trap.

Blood Sample collection[11]: An area of approximately 5cm over the venipuncture site was disinfected with 70% alcohol vigorously and allowed to dry. This was followed by application of povidone iodine in concentric circle over the site & allowed to dry for at least 1 minute, thereafter again cleaned with 70% alcohol. About 1ml of blood sample was taken and inoculated aseptically into a blood culture bottle. Sample was sent to Microbiology laboratory for Gram's staining, culture and antibiotic susceptibility testing by standard technique.

Calculation of incidence of Ventilator Associated Pneumonia (VAP) [12]

Calculate the device associated infection rates/1000 device days

$$\frac{\text{Number of VAP episodes}}{\text{Number of ventilator days}} \times 1000$$

Data were analyzed using statistical software package SPSS.

Results

The study was conducted in NICU of Government Medical College, Amritsar from 1st February 2016 to 31st January 2017. Total 125 cases were intubated during this period in NICU. Eight babies died and one left against medical advice (LAMA) within 48 hours of intubation.116 cases were enrolled in this study after obtaining written informed consent from parents and studied till the day of event or 48 hours after extubation.

Among the 116 cases, 22 (18.96%) cases developed VAP. Among these 22 cases 8 (36.37%) developed VAP within 96 hours of intubation (early onset VAP) and 14 cases (63.63%) had late onset VAP.

Table 1 Showing Base Line Characteristics of Vap Vs No Vap Patients

Characteristics of patients	VAP (n=22)	No VAP (n=94)	p-value	OR	95% CI
Sex					
Male [79]	17 (77.3%) [21.51%]	62 (66%) [78.48%]	0.305	0.570	0.193-1.686
Female [37]	5 (22.7%) [13.51%]	32 (34.0%) [86.48%]			
Place of birth					
Inborn [71]	11 (50%) [15.49%]	60 (63.8%) [84.50%]	0.231	1.765	0.692-4.498
Outborn [45]	11 (50%) [24.44%]	34 (36.2%) [75.55%]			
Mode of delivery					
Normal Vaginal Delivery [69]	14 (63.6%) [20.28%]	55 (58.5%) [79.78%]	0.65	0.806	0.308-2.106
Caesarean Section [47]	8 (36.4%) [17.02%]	39 (41.5%) [82.97%]			
Birth weight					
<1.5 kg	15 (20%)	60 (80%)	0.701	1.1214	0.451-3.271
>1.5 kg	7 (17.1%)	34 (82.9%)			
Gestation age					
<34 weeks	10 (18.9%)	43 (81.1%)	0.980	0.988	0.389-2.5
>34 weeks	12 (19.0%)	51(81%)			
Mean Gestational age (weeks)	34.02±3.55	33.69±3.67	0.707		
Mean Birth weight (kg)	2.03±0.63	1.93±0.76	0.576		

In our study 37 (31.9%) were females and 79 (68.1%) males. Sixty nine (59.5%) babies were born by normal vaginal delivery and 47(40.5%) by cesarean section. Out of 116, 71 (61.2%) were inborn and 45 (38.79%) outborn.

Eleven (9.48%) babies had birth weight <1 kg (ELBW); 27 (23.28%) were between 1.0-1.49 kg (VLBW); 44 (37.93%) were between 1.5-2.49 kg (LBW) and 34 (29.31%) were of >2.5 kg. Mean birth weight of the study group was 1.95± 0.73 kg.

The mean gestational age of the study group was 33.76 ± 3.62 weeks. Out of 116, 53 (45.69%) babies were of gestational age <34 weeks (preterms), 47(40.52%) were of gestational age 34-37 weeks (near term), 16 (13.79%) were of >37 weeks (term). The mean duration of mechanical ventilation before developing VAP was 132.45±78.15 hour.

No statistical significance was found on comparison of the VAP group with no VAP group, with respect to sex, birth weight, mode and place of delivery.

Table 2 Showing Clinical, Pathological and Radiological Signs As Observed For Diagnosis of VAP (n=22)

Symptoms and Signs	No.	% age
New infiltrate on x-ray chest	10	45.45
Progressive Infiltrate on x-ray chest	9	40.91
Persistent infiltrate on x-ray chest	5	22.73
Consolidation on x-ray chest	10	45.45
Pneumatocele on x-ray chest	1	4.55
Worsening of gas exchange pulse oximeter	20	90.91
Increase in ventilation demand	19	86.36
Increase in oxygen requirement	19	86.36
Apnoea	7	31.82
Tachypnea	16	72.73
Nasal flaring	12	54.55
Retraction of chest wall	14	63.64
Grunting	3	13.64
Wheezing	2	9.09
Rales	13	59.09
Cough	3	13.64
Tachycardia	18	81.82
Temp instability	4	18.18
Leukocytosis	13	59.09
Left shift on peripheral blood film	5	22.73
New onset of purulent sputum	15	68.18
Change in character of sputum	15	68.18
Increase in respiratory secretions	16	72.73
Increase in suctioning requirements	14	63.64

Following CDC criteria, out of 22 patients 20(90.91%) had worsening of gas exchange and 19(86.36%) had both increase in ventilation demand and increased oxygen requirement were most common clinical features. In X-rays findings new infiltrates and consolidation patch were most common in 10 (45.45%) patients. Forty percent had progressive infiltrates, 22% had persistent infiltrates and 4% had pneumatocele in X-rays. In clinical features, tachypnea, tachycardia, retraction of chest walls, increased respiratory secretions, increased requirement of suctioning and new onset of purulent sputum were the most common signs and symptoms. More than half of the patients showed increased leukocyte count, and a shift to left on peripheral blood film was observed in one –fifth of the patients.

Table 3 Showing incidence Of VAP Per 1000 Ventilation Days

Weight of the neonate	No. of cases	Mechanical Ventilation (days)	Incidence per 1000
<1.0 kg	0	43	
1.0 – 1.49 kg	5	182	27.47
1.5 – 2.49 kg	10	167	59.88
>2.5 kg	7	204	34.31
All weights	22	596	36.9

Out of 116 patients, 22 (18.96%) developed VAP. Incidence was 36.9/1,000 mechanical ventilation days. Weight wise distribution of incidence was 27.47/1,000 mechanical ventilation days in 1.0-1.49 kg group, 59.88/1,000 mechanical ventilation days in 1.5 -2.49 kg group and 34.31 /1,000 mechanical ventilation days in >2.5 kg babies.

Table 4 Showing Classification Of VAP According To Time Of Onset Of Pneumonia

Onset	No.	%	Mean±SD(hours)	p-value
Early ≤96 hours	8	36.36	53.00±28.28	0.001
Late >96 hours	14	63.64	177.85±6.66	
Total	22	100.0	132.45±78.15	

A statistically significant difference between durations of ventilation in developing VAP was observed. Fourteen (63.64%) had late onset VAP vs 8 (36.36%) who had early onset VAP (p= 0.001). Mean duration of ventilation in early onset VAP was 53.00±28.28 and mean duration of ventilation in late onset VAP was 177.85±6.66. Total mean duration of ventilation before VAP was 132.45±78.15 hours. As the duration of ventilation increased, chances of developing VAP increased.

Table 5 Showing Microbiology And Sensitivity Pattern Of Endotracheal Aspirates Of Patients with VAP

Organisms	No. of isolates grown	Percentage
Acinetobacter	8	80%
Klebsiella	2	20%
Total isolates	10	100%
Antibiotics	Acinetobacter(8)	Klebsiella(2)
Amoxiclavulanate	0	0
Amikacin	0	0
Ampicillin	0	0
Imipenem	1(12.5%)	1(50%)
Polymyxin –B	2(25%)	1(50%)
Piperacillin+tazobactam	5(62.5%)	1(50%)
Ceftriaxone – S	8(100%)	1(50%)
Colistin	4(50%)	0
Cefoperazone -S	1(12.5%)	0
Minocycline	1(12.5%)	0
Ciprofloxacin	0	1(50%)

Endotracheal aspirates from 22 patients, who developed VAP, were sent for culture sensitivity. 10 patients had positive tracheal aspirates; out of these 8 (80%) had Acinetobacter growth and 2 (20%) had Klebsiella. Acinetobacter was 100% sensitive to ceftriaxone- S and Klebsiella had 50% sensitivity to imipenem, polymyxin-B, piperacillin plus tazobactam, ceftriaxone-S (sulbactam) and ciprofloxacin. The microbiological isolates showed resistance to first line antibiotics.

Table 5 Showing Microbiological and Sensitivity Pattern From Blood Culture In Patients With VAP

Organisms	No. of isolates		Percentage	
Candida	5		33.33%	
Staphylococcus aureus	2		13.34%	
Klebsiella	5		33.33%	
Pseudomonas	2		13.34%	
CONS	1		6.66%	
Total	15		100%	
Antibiotics	*Klebsiella* (5)	*S.aureus* (2)	*Pseudomonas*(2)	CONS (1)
Amikacin	0	1(50%)	2(100%)	0
Gentamycin	0	2(100%)	0	0
Amoxiclav	0	1(50%)	0	0
Linezolid	0	2(100%)	0	0
Imipenem	4(80%)	0	1(50%)	0
Piperacillin+tazobactam	4(80%)	0	0	0
Azithromycin	0	0	0	1(100%)
Oxacillin	0	2(100%)	0	1(100%)
Cefazolin	0	1(50%)	0	0
Cephalexin	0	1(50%)	0	0
Cefoxitin	0	2(100%)	0	0
Ceftriaxone-S	2(40%)	0	2(100%)	0
Cefazoline	0	0	1(50%)	0
Polymyxin-B	1(20%)	0	0	0
Cefoperazone	0	0	1(50%)	0
Ciprofloxacin	3(60%)	1(50%)	2(100%)	1(100%)

Table 6 Showing Correlation Of microbiological Pattern Of Blood Vs Tracheal Aspirates In VAP

Tracheal Aspirate Culture positive	Blood Culture positive		p value
	Yes (15)	No (7)	
Yes (10)	6	4	X^2: 0.566;df: 1; p=0.452
No (12)	9	3	

In our study, tracheal aspirates of 10 (45.45%) were found to be positive. Out of 22, 6 (27.27%) babies were those who had both tracheal and blood culture positive, 4 (18.18%) had only tracheal aspirate positive, 9 (40.9%) had only blood culture positive and 3 (13.63%) had neither blood culture nor tracheal aspirate culture positive. These results had no statistical significance. (p=0.452)

Discussion

In our study, we analyzed 116 patients who were intubated for > 48 hours or who were extubated earlier but were on follow up for next 48 hours. 22 (18.96%) patients developed VAP.

The incidence of VAP was 36.9/1000 ventilation days. Weight wise distribution of incidence was 27.47, 59.88, 34.31/1000 mechanical ventilation days in groups 1.0-1.49kg, 1.5-2.49kg, and ≥2.5kg respectively. Tripathi et al{2010}, in their study found 30 patients with VAP out of 98 (30.6%); incidence was 37.2/1000 ventilation days.[9] Other studies worldwide have reported incidence of VAP ranging from low of 13.2%,[13] to a high of 50%.[14] It needs to be mentioned that in one study conducted in Germany, the incidence was reported as low as 2.2%.[15] In our study overall incidence was comparable to that other developing countries.

Various reasons contributing to higher rate of nosocomial infections are limited resources including shortage of NICU beds and increased waiting period for few hours to days before shifting to NICU. These babies often acquire infections due to overcrowding and other logistic problems like nurse- patient ratio and non-availability of optimum environment of the NICU.

Secondly, our institute being a tertiary care centre, mostly high risk obstetrical cases of the region is referred, increasing morbidity. Incidence was higher in the 1.5-2.49 kg groups (59.88/1000 ventilation days) compared to 1.0-1.49 kg (27.47/1000 ventilation days). The explanation for this apparent higher incidence in term and higher birth weight babies is that approximately half the no. of VLBW babies were diagnosed with HMD and were given surfactant by INSURE technique, were fit for extubation early and kept on non-invasive mode of ventilation in our NICU.

Comparison of baseline characteristics of two groups with or without VAP showed, no significant difference as regards sex distribution, place of birth and mode of delivery. Mean gestational age of VAP group was 34.02 $\pm$ 3.55 weeks and of without VAP group was 33.69 $\pm$ 3.67 weeks, which was statistically insignificant. Mean birth weight was 2.03 $\pm$ 0.63 kg in VAP group and 1.93 $\pm$ 0.76 kg in without VAP group which was also statistically insignificant.

It is observed in the past that multiple re-intubation, endotracheal suctioning and sepsis or other morbidities increase the duration of mechanical ventilation. In our study mean duration of ventilation before onset of VAP was 132.45$\pm$78.12 hours i.e. 5.5 days. Late onset VAP was also more common than early onset VAP 63.63% vs. 36.36% which however, is statistically significant (p= 0.001).similar results were observed in a study by Tripathi et al (2010) in which the mean duration of ventilation before developing VAP was 5 days. Late onset VAP was more common than early onset VAP 53.3% vs. 46.7% which was statistically not significant.[9] Previous authors concluded that an isolated positive tracheal aspirate does not distinguish between airway colonization and VAP and that routine radiology reports without definitive clinical and laboratory evidence may be misleading.[11]

In our study out of 22 cases with VAP, none of the cases of VAP were caused by the same organism that caused BSI. Our study had almost the same type of isolates as other studies had in the past, conducted in variable NICU settings.[16,17] some studies reported Klebsiella to be the most common organisms isolate from patients of VAP.[9,18]

On study of sensitivity patterns, it was found 100% of Acinetobacter isolates from tracheal aspirates were sensitive to ceftriaxone-Sulbactum combination and none showed sensitivity to first line antimicrobials, like ampicillin and Amikacin. 50% of Klebsiella isolates were sensitive to a number of extended spectrum antibiotics including imipenem, polymyxin-B, piperacillin plus tazobactam, ceftriaxone-Sulbatum combination, but all strains were resistant to first line antibiotics. In blood culture isolates, Klebsiella was 80% sensitive to imipenem and piperacillin plus tazobactam. Staphylococcus was 100% sensitive to gentamycin, linezolid, oxacillin, cefoxitin. Pseudomonas was 100% sensitive to amikacin, ciprofloxacin and ceftriaxone-S. Different studies by other authors, for obvious reasons, had different sensitivity patterns, but all of them showed emerging resistance patterns to first line antimicrobials and also that Frequent use of broad spectrum empiric antimicrobials in an ICU setting further enhances the risk of colonization with resistant organisms.[19,20]

Conclusion

The incidence of VAP was higher as compared to developed countries, and of greater concern is increase in antimicrobial resistance. Use of preventive measures, early extubation, prevention of prematurity, empirical antibiotic use as per culture reports and improved nursing care can decrease the incidence of VAP and hence neonatal mortality in our NICU. The results can be used for ensuring better NICU environment

and in policy making for antimicrobial use in VAP. Good management strategies, early and accurate diagnosis and more specific antimicrobial use may significantly improve patient's outcome. The endotracheal aspirate of the patients on ventilator should be sent routinely for culture sensitivity. If patient develops VAP, antibiotic should be changed according to sensitivity.

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