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Research Article

A STUDY OF INCIDENCE, RISK FACTORS, PATHOGEN PROFILE AND VENTILATOR ASSOCIATED PNEUMONIA IN NICU AT SMGS HOSPITAL JAMMU

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Abstract

Background: VAP (Ventilator associated pneumonia) is one of the most common healthcare associated infections among ventilated neonates. **Aim:** of the study was to study the incidence, risk factors, pathogen profile and outcome associated with development of Ventilator Associated Pneumonia (VAP) in neonates who require mechanical ventilation for more than 48 hours. **Study design**: Hospital based prospective observational study for 1 year, conducted between Dec 2015 to Nov 2016. **Materials & Methods**: This prospective observational study was conducted in NICU (Neonatal intensive care unit) of SMGS Hospital Jammu. All intubated neonates of age less than 28 days, admitted in NICU who required mechanical ventilation for more than 48 hours, were studied for development of VAP. Neonates who had overt signs and symptoms of pneumonia at the initiation of mechanical ventilation, those with major congenital anomaly, or those with birth weight less than 1000 were excluded from the study. Socio-demographic data, maternal data, Natal and Perinatal data, History of presenting complaints, Anthropometry, General physical examination and systemic examination in detail was recorded. The diagnosis of VAP was made on the basis of criteria given by National Nosocomial Infection Surveillance System (2004) pediatric modification of the original guidelines given by CDC (Center for disease control and Prevention).**Statistical Analysis**: The data was analyzed by "Statistical package For Social Sciences (SPSS) software Version 20.0 and represented as Mean±SD and percentages. **Results:** total neonates included were 105. Out of which 35 developed VAP. Incidence of VAP in our study was 37.9 per 1000 days of mechanical ventilation. Prematurity, birth weight, number of reintubation attempts, duration of mechanical ventilation days and hospital stay in days were significant predictors of VAP on Bivariate analysis. Duration of mechanical ventilation, prematurity and very low birth weight were 3 single independent and statistically significant risk factor for development of VAP on multiple logistic regression analysis. Gram negative organisms predominate as the cause of VAP in our study with klebsiella and E.Coli being the most common. Mortality rates among the neonates developing VAP was 9/35 (25.7%). **Conclusion**: VAP is a potentially lethal and common problem among ventilated patients in NICU. The endotracheal aspirate of intubated patients should be sent routinely. By using aseptic precautions while handling ventilated patients and empirical antibiotics as per the endotracheal aspirate culture sensitivity pattern of NICU in the patients who develop VAP, we may be able to improve the outcome rate of the patients on mechanical ventilation.

Keywords: Neonate, Nosocomial infection, Outcome, Risk factors, Ventilator associated pneumonia (VAP).

INTRODUCTION

VAP is defined as nosocomial pneumonia in mechanically ventilated patients that develops more than 48 hours after initiation of mechanical ventilation with new and persistent infiltrates in chest radiographs. VAP is the second most common nosocomial infection after urinary tract infection in pediatric intensive care units (ICU) patients accounting for 20% of nosocomial infection in this population (Richards *et al.,* 1999). While in developed countries the incidence oscillates between 2.7 to 10.9 episodes per 1000 ventilator days, in developing countries it may reach up to 37.2 cases per 1000 ventilator days (Cernada *et al.,* 2013). Many factors predispose to acquiring VAP. Infants mechanically ventilated in NICU are particularly at a high risk of developing VAP because of poor host factors, severe underlying diseases, prolonged use of mechanical ventilation, inadequate pulmonary toilet & extensive use of invasive devices & procedures. Neonates, especially preterms are highly predisposed to nosocomial infections by virtue of their immature immune system (Apisarnthanarak *et al.,* 2003). VAP occurs when bacteria, fungi, or viruses enter the normally sterile lower respiratory tract. Intubation associated lesions of pharynx and trachea lead to bacterial colonization by decreasing ciliary function and swallowing reflex.

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The presence of ET tube impairs the body's ability to mobilize and expectorate secretions and may increase mucus production. It causes damage to ciliated cells in trachea, inhibits cough reflex and bypasses the body's humidified airways (Garland, 2010). Present study was conducted with the aim to study the Incidence, Risk factors, Pathogen profile and Outcome associated with development of Ventilator Associated Pneumonia (VAP) in neonates who require mechanical ventilation for longer than 48 hours.

METHODS

This prospective observational study was conducted in NICU (Neonatal intensive care unit) of SMGS Hospital Jammu, after taking approval from Institutional Ethical Committee. All intubated neonates less than 28 days, admitted in NICU during the study period (Dec 2015 to Nov 2016) who require mechanical ventilation for more than 48 hours were included in the study. Neonates with overt symptoms & signs of sepsis or pneumonia at the time of initiation of mechanical ventilation, with major congenital anomalies or with birth weight babies (<1000 grams) were excluded from the study. Socio-demographic data, maternal data, Natal and Perinatal data, History of presenting complaints, Anthropometry, General physical examination and systemic examination in detail was recorded. The findings were recorded in a predesigned Performa. Following protocol was followed in our NICU:

- All neonates were ventilated by oro-tracheal tubes of appropriate size, which were changed if blocked or displaced.
- Neonates were ventilated in SIMV mode using Inspiration ventilation system servo-*i* ventilator with heated humidification system.
- One set of disposable ventilation circuits was used in each patient. Open method of suction was used for suctioning of secretions.
- Patients were ventilated in supine position with frequent changing to right/left lateral position and nasogastric tube was used in the patients for decompression.
- Patients were placed on servo controlled warmer with skin temperature set on 36.5°c with an audio-visual alarm system on board.
- Any hyperthermia (>38^0c) or hypothermia (<36^0c) was rechecked by a clinical thermometer by axillary method.
- No prophylactic topical oro-pharyngeal antibiotics and selective gut decontamination was done in any of the patients.
- Baseline TLC(Total Leucocytes Count), DLC(Differential Leucocytes Count) and chest radiographs were done in all patients at the time of initiation of mechanical ventilation.
- Subsequent blood counts were done on day 3rd on which pneumonia was suspected by the onset of fever, new chest signs, increasing ventilation requirements.
- After baseline chest radiograph, it was repeated after 48 hours of mechanical ventilation if patient developed signs and symptoms of pneumonia, and subsequently, as and when required by treating physician.
- Follow up included clinical examination for pneumonia and chest radiographs after one week of extubation.

The diagnosis of VAP was made on the basis of criteria given by National Nosocomial Infection Surveillance System (2004) pediatric modification of the original guidelines given by Centre Of Disease Control & Prevention (CDC) (5). Neonates who fulfilled all of the following three criteria were diagnosed to have VAP.

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

   New or progressive and persistent infiltrates Consolidation, Cavitations or Pneumatoceles.

2. **Signs/Symptoms/Laboratory:** Worsening gas exchange (e.g. O2 desaturation, increased oxygen requirement, or increased ventilator demand). **And** at least three of the following:
3.

- Temperature instability with no other recognizable cause.
- Leucopenia (<4000 WBC/mm3) or Leucocytosis (>15000 WBC/mm3) and left shift (>10% band forms).
- New onset of purulent secretions or change in character of secretions, or increased respiratory secretions or increased suctioning requirements.
- Apnea, tachypnea, nasal flaring with retraction of chest wall and grunting.
- Wheezing, rales, or rhonchi.
- Cough.
- Bradycardia (<100 beats/minute) or Tachycardia (>170 beats/minute).

MICROBIOLOGICAL CRITERIA

Positive blood culture or Positive Endotracheal aspirate >10^5CFU/ml. Collection of endotracheal aspirate for culture- After proper hand washing and wearing sterile gloves before suctioning, hyper-oxygenation with Fio_2 >20% of baseline for two minutes was done, then endotracheal secretions were collected by instilling 1-2 ml of sterile normal saline into the endotracheal tube and then collecting it back with the help of polyethylene tubes with a suctioning pressure of 60 mmHg for 8 seconds. The specimen collected was immediately transported to the laboratory within two hours. Semi-quantitative culture was done using blood agar, chocolate agar and Mc Conkey's agar as plating media.

Collection of blood for culture- 1-2 ml blood withdrawn from a peripheral vein after proper

Data was analyzed using SPSS software version 20.0 and expressed as Mean±SD and percentages. Student's independent t-test was employed for continuous variables. Chi-square test or Fischer's exact test, whichever appropriate, was used for comparison of categorical variables. Multivariate Logistic Regression Analysis was performed to determine independent risk factor for VAP. A p-value of less than 0.05 was considered statistically significant.

RESULTS

1. A total of 5345 neonates were admitted in NICU during the study period. Neonates who needed mechanical ventilation were 238.Out of these 105 neonates fulfilled the inclusion criteria and were included in the study. VAP developed in 35 of 105 ventilated neonates (33.33% VAP rate), incidence of VAP was 37.9 cases per 1000 days of mechanical ventilation.

2. Out of 35 VAP cases 21(60%) were males, while in the Non-VAP group 39(55.7%) were males out of 70. Sex (Male/Female) is not statistically significant for development of VAP (OR 1.19;95% CI 0.53-2.72;p-0.676).

3. Out of 35 VAP cases 32 (91.25%) were <37 weeks of gestation in comparison to Non-VAP group in which 39(55.7%) out of 70 were <37 weeks of gestation, so prematurity (Gestational age < 37 weeks) is highly significant in predicting development of VAP ((OR 8.47; 95% CI 2.37-30.32; p-<0.001).

4. Out of the total 35 VAP cases 7(20.0%) were Very Low Birth Weight (VLBW) (<1500grams) while only one case (1.4%) out of 70 in the Non-VAP group was VLBW. VLBW (<1500 grams) is highly significant both clinically & statistically in predicting development of VAP (OR 135.3; 95%CI 12.3-485.5; p- <0.001).

5. Out of 35 VAP cases 11(31.4%) had a primary diagnosis of birth asphyxia while in Non-VAP group 36(51.4%) had birth asphyxia, which is statistically insignificant (OR 0.43; 95% CI 0.18-1.02; p-0.052).

6. Out of 35 VAP cases 17(48.6%) had a primary diagnosis of Respiratory distress syndrome while in Non-VAP group 30(42.9%) had RDS, which is statistically insignificant (OR 1.26; 95% CI 0.56-2.84; p-0.579).

7. The age in hours at the time of initiation of mechanical ventilation in VAP group (Mean±SD 7.6±5.57; 95% CI 5.66-9.48) and Non-VAP group (Mean±SD 6.7±5.26; 95% CI 5.43-7.94) was statistically insignificant as a predictor of development of VAP, p-value 0.427.

8. Duration of Mechanical ventilation in days in VAP group (Mean±SD 15±4.3; 95% CI 13.52-16.48) and Non-VAP group (Mean±SD 5.7±2.32; 95% CI 5.15-6.25) is statistically an important risk factor in predicting development of VAP, p-value <0.001.

9. Hospital stay in days in VAP group (Mean±SD 25.1±7.46; 95%CI 22.5-27.71) and Non-VAP group (Mean±SD 10.3±3.10; 95% CI 9.58-11.05) is statistically very significant risk factor in predicting VAP, p-value<0.001.

10. Frequency of changing endotracheal tubes in VAP group was(Mean±SD)4.5±1.5; 95% CI 4.03-5.06 and in Non VAP group was(Mean±SD)1.2±1.06; 95% CI 0.96-1.47(p-value<.001). (Table 1)

Table 1. Comparison based on number of Re-intubation attempts among VAP and Non-VAP Neonates

No. of Re-intubation Attempts	Mean	SD	95% CI	P-value
VAP	4.5	1.50	4.03-5.06	<0.001
Non-VAP	1.2	1.06	0.96-1.47	

11. Multivariate logistic regression analysis revealed that prematurity(p-0.012), duration of mechanical ventilation (p-0.001) and VLBW (<1500 grams) (p-0.003) were only three single independent and statistically significant risk factors for development of VAP.(Table2)

Table 2. Multivariate logistic regression analysis of risk factors

Risk Factor	Odds Ratio	95% CI	P-value
Prematurity (Gestational Age < 37 weeks)	4.51	1.69-11.19	0.012
VLBW (Birth Weight < 1500 grams)	7.69	2.01-29.56	0.003
Nasogastric Tube Use	0.31	0.13-7.62	0.159
Mechanical Ventilation Duration (Days)	6.51	1.91-14.02	0.001
Hospital Stay (Days)	0.96	0.37-2.65	0.976
No. of Re-intubation Attempts	0.54	0.06-4.63	0.576

12. Endotracheal aspirate (ETA) culture came positive in 32 VAP cases (91.4%) and blood culture came positive in only 12 VAP cases (34.3%). Most common bacteria isolated from ETA of VAP patients was Klebsiella spp. (34.3%), E.coli (22.9%) and Acinetobacter (17.1%), the rarest organism grown was Citrobacter (5.7%).(Table 3)

Table 3. Organisms isolated from endotracheal aspirate and blood cultures

Organism	ETA		Blood	
	No.	%age	No.	%age
Klebsiella	12	34.3	2	5.7
E.coli	8	22.9	1	2.9
Acinetobacter	6	17.1	1	2.9
Staphyloccus aureus	4	11.4	7	20.0
Citrobacter	2	5.7	1	2.9
Total	32	91.4	12	34.3

13. Outcome of neonates in VAP and non VAP groups is given in table 4. Mortality rates among the VAP group was 9/35 (25.7%) and Non-VAP group was 15/70 (21.4%), which was statistically insignificant (OR 1.27; 95%CI 0.49-3.28; p-0.622).

Table 4. Showing association of outcome with VAP in study Neonates

Outcome	VAP		Non-VAP		P-value
	No.	%age	No.	%age	
MORTALITY	9	25.7	15	21.4	
SURVIVAL	26	74.3	55	78.6	0.622
Total	35	100	70	100	
Odds Ratio=1.27 ; 95% CI=0.49-3.28					

DISCISSION

The incidence of ventilator associated pneumonia in our study was 33.33% or 37.9 cases per 1000 days of mechanical ventilation. This incidence is comparable to the incidence of VAP in earlier neonatal studies as Apisarnthanarak. A, Holzmann-Pazgal, et al (28.3%) or 6.5 per 1000 ventilator days (EGA<28 weeks) and 4 per 1000 ventilator days (EGA>28 weeks); Witaya Petdachai et al (50% or 70.3 cases per 1000 ventilator days); Tian-Ming Yuan, Li-Hua Chen et al (20.1%); E.Foglie, M.D Meier, et al (9.6%); S.Tripathi, G.K Malik, et al (30.6% or 37.2 cases per 1000 days of mechanical ventilation); Park JH, KimCS, et al (16.5%);Kawanishi F, Yoshinaga M et al, (9.66 for the every 7-day group and 8.08 for the every 14-day group per 1000 ventilator days). This variation is due to differences in diagnostic criteria used, aseptic precautions in intensive care units and variable sensitivity and specificity of diagnostic tests. Most studies in VAP have used objective diagnostic criteria based on the combination of quantitative culture samples obtained with fiberoptic bronchoscopy using the protective specimen brushing (PSB) or the bronchoalveolar lavage (BAL). Both these methods have been shown in literature to have a specificity and sensitivity of greater than 95% in the diagnosis of VAP. The quantitative bacteriologic methods have increased the reliability of sputum specimens for the diagnosis of lower respiratory tract infections when compared with conventional qualitative cultures because of more careful collection of sputum and the method of dilution which eliminates contaminating oropharyngeal secretions. Since the technique of PSB and BAL are not readily available to us in our NICU, the endotracheal aspirate technique was used as an alternative diagnostic tool for VAP. It may be helpful for delineating the causative organism and can thus reduce the overuse of antibiotics in NICU. Moreover, it is a simple, inexpensive and non-invasive technique and suited to the set-up where cost becomes a major limiting factor. In our study, very low birth weight (<1500 grams), prematurity (gestational age <37 completed weeks), duration of mechanical ventilation, number of re-intubation attempts and length of NICU stay were significantly associated with VAP in bivariate analysis. Multiple regression analysis revealed that prematurity (p value= 0.012), duration of mechanical ventilation (p=0.0060 and very low birth weight <1500 grams (p=0.032) were three single independent and statistically significant risk factors for predicting ventilator associated pneumonia. Various studies done on neonates have shown the same results, S.Tripathi, G.K Malik, et al (2009) revealed that duration of mechanical ventilation (p=0.021) and Very low birth weight (p=0.042) were two single independent and statistically significant risk factors for predicting VAP; Ramya Srinivasan, J.asselin, et al (2009) revealed that patients with VAP had greater need for mechanical ventilation (12 vs. 22 median ventilator free days), longer ICU length of stay (6 vs13 median ICU free days); Deng C, Li X, Zou Y, et al (2011) revealed that birth weight, mechanical ventilation (MV), parenteral alimentation, dexamethasone and other respiratory disease were associated

with the development of VAP. In our study as far as etiological organisms are concerned, gram negative predominance was observed as a causative factor of VAP. Most common organisms isolated on endotracheal aspirate culture were Klebsiella spp. (37.5%) followed by E.coli (21.8%) and Acinetobacter (15.6%). Similar observations were made by S.Tripathi, G.K Malik, et al (2009) found Klebsiella spp. (32%), E.coli (23.2%) and Acinetobacter (17.8%) being the other two common organisms; Ramya Srinivasan, J.asselin, et al (2009) found that most common VAP organisms identified were Gram negative bacteria (42%), Staphylococcus aureus (22%), and Haemophilus influenzae (11%).In our study out of total 105 cases enrolled 24 babies died (22.91%), out of which 9/35 died in VAP group (25.7%) and 15/70 died in Non-VAP group (21.4%), which is statistically insignificant (p=0.622), similar observations were made by other studies Witaya Petdachai, et al (2004) (29.4% among VAP group); Tian-Ming Yuan, Li-Hua Chen et al (2006) rate of VAP group was 13.5% (7/52) vs. 12.1% in controls (p>0.05); E.Foglie, M.D Meier, et al (2007) mortality rates for VAP (20%) or uninfected patients (21%) were found; S.Tripathi, G.K Malik, et al (2009) mortality rates were higher in patients with VAP (40%) and lower in Non-VAP cases (22.06%) (p=0.058), overall mortality was (27.5%).

Conclusion

This study concludes that VAP is a potentially lethal & common problem among mechanically ventilated patients in NICU. The endotracheal aspirate of patients on ventilators should be sent routinely for culture and if the patient develops VAP, antibiotics should be changed as per report. By using aseptic precautions while handling ventilated patients and empirical antibiotics as per the endotracheal aspirate sensitivity pattern of NICU in the patients who develop VAP, we may be able to improve the outcome rate of the patients on mechanical ventilation.

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