



Original Article

A Study of Incidence, Etiology, and Outcome of Ventilator Associated Pneumonia Among Neonates in a Tertiary Health Care Centre in Jhalawar, Rajasthan: A Prospective Observational Study

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ABSTRACT

Background: Ventilator-associated pneumonia (VAP) is a serious complication in neonates receiving mechanical ventilation, significantly contributing to morbidity and mortality in neonatal intensive care units (NICUs). Early diagnosis, appropriate management, and understanding the associated risk factors are essential to improve outcomes for these vulnerable infants.

Aim: The study aimed to determine the incidence of VAP in neonates, identify its etiology, and evaluate associated factors and outcomes, particularly focusing on risk factors and mortality.

Material and Methods: A total of 400 mechanically ventilated neonates admitted to the NICU were included in this prospective observational study. Data were collected on demographics (age, gender, gestational age, birth weight), clinical characteristics (mode of delivery, place of delivery, APGAR scores, CPIS scores), and outcomes (mortality, duration of NICU stay, inotropic use). The incidence of VAP was determined, and associated factors such as CRP levels, temperature instability, and enteral feeding were evaluated. Endotracheal cultures were taken to identify the causative pathogens.

Results: Of the 400 neonates, the mean age was 8.02 days, with 56.3% aged ≤ 7 days. The cohort included 52.5% males and 47.5% females, with 51.2% delivered via LSCS. The overall incidence of VAP was 42.3%, with the onset of VAP occurring at an average of 2.37 days after intubation. Coagulase-negative Staphylococci (12.6%), Acinetobacter (8.5%), and Pseudomonas (7.0%) were the most common pathogens. VAP was associated with factors like being outborn, gestational age ≤ 32 weeks, and birth weight ≤ 1.49 kg. Neonates with VAP had a significantly higher mortality rate (49.8%) compared to those without VAP.

Conclusion: This study highlights a high incidence of VAP in neonates requiring mechanical ventilation, with key risk factors including low gestational age and birth weight. Early onset of VAP and the presence of pathogens such as Coagulase-negative Staphylococci emphasize the need for preventive strategies and rapid intervention in NICUs to reduce neonatal mortality. The study underscores the importance of close monitoring and early detection of VAP to improve survival outcomes in this population.

Keywords: Ventilator associated pneumonia, Neonatal sepsis, Microorganism, CRP.

INTRODUCTION

In neonates, very few studies evaluate the ventilator associated pneumonia rates, etiology, and impact of VAP prevention, interventions on duration of mechanical ventilation, length of stay or mortality. We therefore evaluate the risk factors, etiology and outcome of ventilator associated pneumonia on neonates in this study. The incidence of VAP is highly influenced by gestational age and regional financial development. Hence while in developed countries the incidence of VAP is between 2.7 to 10.9 episode per 1000 ventilator days, while in developing countries reaches up to 37.2 cases per 1000 ventilator days. According to data published by the national nosocomial infection surveillance system programme sponsored by the centre for disease control, VAP rates in NICU accounts up to 30% of nosocomial infection and complicates the hospital course of 8 to 28% of cases. Risk factors in relation to VAP are prolonged mechanical ventilation, frequent reintubation, low gestational age, low birth weight, use of uncuffed endotracheal tubes, frequently contaminated suctioning practices, prior use of antibiotic and others. Despite advancements in medical care, VAP remains a substantial challenge, contributing to increased morbidity and mortality rates in neonatal populations. Understanding the specific context of VAP among neonates is crucial for developing targeted preventive strategies and improving clinical outcomes. The findings from this research could inform evidence-based practices, enhance preventive measures, and contribute to the overall improvement of neonatal care.

AIM AND OBJECTIVE

Aim: The study aimed to determine the incidence of VAP in neonates, identify its etiology, and evaluate associated factors and outcomes, particularly focusing on risk factors and mortality.

Objective: To assess the incidence, etiology, and outcomes of VAP in mechanically ventilated neonates.

MATERIALS AND METHODS

Source of Data: Department of Pediatrics, Shrimati Heera Kunwar Baa Maheela Hospital, Jhalawar, Rajasthan.

Type of Study: Prospective Observational Study.

Duration of the Study The study was conducted over one year following the approval of the ethical committee. The data collection period lasted 9 months, and the data analysis period lasted 3 months.

Sample Size: All neonates admitted to the NICU who were mechanically ventilated and met the inclusion criteria during the study period.

Selection criteria: All Neonates (0-28 days) mechanically ventilated in the NICU were included in the study. Neonates admitted with congenital and acquired pneumonia were excluded from the study.

Methodology: A total of 400 mechanically ventilated neonates admitted to the NICU were included. Data were collected on demographics (age, gender, gestational age, birth weight), clinical characteristics (mode of delivery, place of delivery, APGAR scores, CPIS scores), and outcomes (mortality, duration of NICU stay, inotropic use). The incidence of VAP was determined, and associated factors such as CRP levels, temperature instability, and enteral feeding were evaluated. Endotracheal cultures were taken to identify the causative pathogens.

Data collection: Patients meeting the inclusion criteria were enrolled in the study after obtaining informed consent. Information such as the name, father's name, address, age, sex, registration number, vital signs, X-ray findings, endotracheal aspirate culture reports, and treatment outcomes were recorded. Newborns admitted to the NICU were examined for clinical, radiological, and microbiological features of pneumonia at the time of admission. Those who did not have prior pneumonia and were intubated and mechanically ventilated were followed up daily until discharge or death for clinical, radiological, and/or microbiological signs of pneumonia. Follow-up included daily monitoring of temperature, respiratory rate, and oxygen saturation. If any parameters were abnormal, chest X-rays and endotracheal aspirate cultures were conducted.

Statistical analysis: The questionnaires were initially checked for completeness, and data was cleaned for errors and missing values. The corrected data was then entered into Microsoft Excel after preparing a master-chart. After data entry of every ten questionnaires, one random form was picked and data entry was re-checked. Data analysis was done using licensed SPSS software version 21.0 (Chicago, Illinois). Univariate analysis was done initially and the results were presented with the help of tables, text, bar-diagrams and pie-charts. Descriptive statistics were used to calculate frequencies of categorical variables, and measures of central tendencies and dispersion were used to describe continuous variables. Independent t-test was used to compare the continuous variable and chi-square test was used for categorical variables. A p-value <0.05 was considered as statistically significant.

RESULTS

Of the 400 neonates, the mean age was 8.02 days, with 56.3% aged ≤ 7 days. The cohort included 52.5% males and 47.5% females with 51.2% delivered via LSCS. The overall incidence of VAP was 42.3%, with the onset of VAP occurring at an average of 2.37 days after intubation. Coagulase-negative Staphylococci (12.6%), Acinetobacter (8.5%), and Pseudomonas (7.0%) were the most common pathogens. VAP was associated with factors like being outborn, gestational age ≤ 32 weeks, and birth weight ≤ 1.49 kg. Neonates with VAP had a significantly higher mortality rate (49.8%) compared to those without VAP.

Table 1: Distribution of neonates according to gestational age

Gestational age	Frequency	Percent
≤ 32 weeks	24	6.0
33-36 weeks	179	44.8
>36 weeks	197	49.3
Total	400	100.0

Table 2: Distribution of neonates according to birth weight

Birth weight	Frequency	Percent
≤ 1.49 kg	36	9.0
1.5-2.49 kg	191	47.8
>2.49 kg	173	43.3
Total	400	100.0

Table 3: Distribution of neonates according to incidence of VAP:

VAP	Frequency	Percent
No	231	57.8
Yes	169	42.3
Total	400	100.0

Table 4: Distribution of neonates according to Endo Tracheal Aspirate culture

Culture	Frequency	Percent
NA	231	57.8
CONS	50	12.6
Acinetobactor	34	8.5
Pseudomonas	28	7.0
Enterobactor	12	3.0
Klebsiella	12	3.0
Citrobactor	9	2.3
Enterococcus	7	1.8
MRSA	7	1.8
E. coli	5	1.3
Staphylococcus aureus	5	1.3
Total	400	100.0

The distribution of neonates according to endotracheal (ET) culture results reveals that 231 neonates (57.8%) had no growth (NA) from their ET cultures. Among those with positive cultures, the most common pathogens identified were Coagulase-negative Staphylococci (CONS) in 50 cases (12.6%), followed by Acinetobacter in 34 cases (8.5%) and Pseudomonas in 28 cases (7.0%). Other pathogens included Enterobacter and Klebsiella, each found in 12 cases (3.0%), and Citrobacter, Enterococcus, MRSA, E. coli, and Staphylococcus aureus, each found in fewer cases, ranging from 1.3% to 2.6%.

Table 5: Association of VAP with neonatal characteristics

	VAP (n=169)		No VAP (n=231)		p-value
	Count	%	Count	%	
Age group					
≤ 7 days	97	57.40%	128	55.40%	0.34
8-14 days	53	31.40%	85	36.80%	

>14 days	19	11.20%	18	7.80%	
Gender					
Female	70	41.40%	120	51.90%	0.057
Male	99	58.60%	111	48.10%	
Mode of delivery:					
LSCS	79	46.70%	126	54.50%	0.123
NVD	90	53.30%	105	45.50%	
Place of delivery					
Inborn	79	46.70%	134	58.00%	0.026
Outborn	90	53.30%	97	42.00%	
Gestational age					
≤ 32 weeks	22	13.10%	2	0.90%	0.001
33-36 weeks	77	45.60%	102	44.20%	
>36 weeks	70	41.40%	127	54.90%	
Birth weight					
≤ 1.49 kg	22	13.10%	14	6.10%	0.001
1.5-2.49 kg	88	52.10%	103	44.60%	
>2.49 kg	59	34.90%	124	53.70%	
CRP					
Positive	11	6.50%	110	47.60%	0.0001
Negative	158	93.50%	121	52.40%	
Temp instability					
No	27	16.00%	110	47.60%	0.0001
Yes	142	84.00%	121	52.40%	
Inotropes used					
No	26	15.40%	48	20.80%	0.17
Yes	143	84.60%	183	79.20%	
Outcome					
Recovered	52	30.70%	147	63.60%	0.0001
Death	117	69.30%	84	36.40%	

The table presents an analysis of the association between Ventilator-Associated Pneumonia (VAP) and various neonatal characteristics. Among neonates with VAP (n=169) and those without VAP (n=231), the following associations were observed:

Age Group: The distribution across age groups was similar between the VAP and non-VAP groups, with no significant difference ($p = 0.340$). The majority in both groups were ≤ 7 days old.

Gender: A higher proportion of males had VAP (58.6%) compared to females (41.4%), though this difference was marginally non-significant ($p = 0.057$).

Mode of Delivery: The proportion of neonates delivered by LSCS was slightly lower in the VAP group (46.7%) compared to the non-VAP group (54.5%), but this difference was not statistically significant ($p = 0.123$).

Place of Delivery: A significantly higher proportion of VAP cases were outborn (53.3%) compared to the non-VAP cases (42.0%), with a p-value of 0.026.

Gestational Age: Neonates ≤ 32 weeks gestational age were significantly more likely to have VAP (13.1%) compared to those in the non-VAP group (0.9%), with a p-value of 0.001.

Birth Weight: The incidence of VAP was higher among neonates with a birth weight ≤ 1.49 kg (13.1%) compared to those with higher birth weights (6.1% in non-VAP), with a significant p-value of 0.001.

CRP: Positive CRP results were significantly associated with VAP (6.5%) compared to non-VAP cases (47.6%), with a p-value of 0.0001.

Temperature Instability: A higher proportion of neonates with temperature instability had VAP (84.0%) compared to those without it (52.4%), with a highly significant p-value of 0.0001.

Inotropes Used: The use of inotropes was more common in the VAP group (84.6%) compared to the non-VAP group (79.2%), but this difference was not statistically significant (p = 0.170).

Outcome: A significantly higher proportion of neonates with VAP did not recover (69.3%) compared to those without VAP (36.4%), with a p-value of 0.0001.

The analysis reveals several key associations between Ventilator-Associated Pneumonia (VAP) and neonatal characteristics. Neonates with VAP were significantly more likely to be outborn, have a gestational age of ≤ 32 weeks, and have a birth weight ≤ 1.49 kg. Additionally, VAP was strongly associated with positive C-reactive protein (CRP) results and temperature instability. The outcome for neonates with VAP was notably poorer, with a higher mortality rate compared to those without VAP.

DISCUSSION

This study was conducted at a tertiary health care center in Jhalawar, Rajasthan, with the aims of assessing the incidence of VAP, identifying its etiological factors, and evaluating the outcomes of affected neonates. By analysing these aspects, the study seeks to contribute valuable data to enhance the management and prevention of VAP in neonates, ultimately aiming to improve their overall survival and quality of care. In our study, the mean age of neonates was 8.018 days (SD 3.7359 days), with a median of 7 days and a range from 2 to 23 days. The majority of neonates (56.3%) were aged 7 days or less, followed by 34.5% between 8 and 14 days, and 9.3% older than 14 days. This age distribution reflects a focus on early neonatal period, which is crucial for VAP development. The gender distribution was relatively balanced, with 52.5% male and 47.5% female neonates.

Table 6: Comparing these findings with other studies, we find some variations:

Wu et al. (2014) [2] in Taiwan	Did not specifically report on age distribution within the neonatal period but focused on gestational age and birth weight as risk factors.
Valdovinos et al. (2018) [4] in Mexico	Emphasized gestational age rather than postnatal age. This difference in reporting makes direct comparisons challenging, but it highlights the importance of considering both gestational and postnatal age in VAP studies

The balanced gender distribution in our study is consistent with most neonatal studies, including those by Foglia et al. (2007) [1] and Tan et al. (2014), [3] which did not report significant gender differences in VAP incidence. This suggests that gender may not be a primary risk factor for VAP in neonates, although larger studies might be needed to confirm this observation.

Our study found that among the 400 neonates, 231 (57.8%) had no growth in their endotracheal (ET) cultures. Among those with positive cultures, the most common pathogens were Coagulase-negative Staphylococci (CONS) in 12.6% of cases, followed by Acinetobacter (8.5%) and Pseudomonas (7.0%). Other pathogens included Enterobacter, Klebsiella, Citrobacter, Enterococcus, MRSA, E. coli, and Staphylococcus aureus, each found in fewer cases. The predominance of Coagulase-negative Staphylococci (CONS) in our study (12.6%) is interesting, as CONS are often considered contaminants rather than true pathogens. This finding differs from some other studies, such as Abdel Rehman et al. (2021), [7] which found Klebsiella and Staphylococcus aureus to be more common.

The high prevalence of Acinetobacter (8.5%) and Pseudomonas (7.0%) in our study aligns more closely with the findings of other researchers. For instance, the study by Rangelova et al. (2019) [6] also found Acinetobacter to be a common pathogen in neonatal VAP. These gram-negative bacteria are often associated with hospital-acquired infections and can be particularly problematic due to their potential for antibiotic resistance. The presence of Enterobacter, Klebsiella, and E. coli in our study, albeit in lower percentages, is consistent with the findings of Wang et al. (2021), [8] who noted that these Enterobacteriaceae were common in polymicrobial VAP cases. Interestingly, our study found a lower prevalence of Klebsiella (3.0%) compared to some other studies. For example, Abdel Rehman et al. (2021) [7] reported Klebsiella as one of the most frequently isolated pathogens in their NICU. This difference could be due to variations in local microbial ecology, antibiotic use patterns, or infection control practices.

The presence of MRSA in our study, although in small numbers, is noteworthy. MRSA is a significant concern in healthcare settings due to its resistance to many common antibiotics. Its presence in our NICU population underscores the importance of robust infection control measures and judicious use of antibiotics.

Our finding of a diverse range of pathogens, including both gram-positive and gram-negative bacteria, aligns with the observations of Wang et al. (2021) [8] regarding the complexity of neonatal VAP etiology. They noted that polymicrobial VAP episodes were more likely to be associated with multidrug-resistant bacteria, which could have implications for treatment strategies. The absence of fungal pathogens, particularly *Candida* species, in our results is noteworthy. Abdel Rehman et al. (2021) [7] found *Candida* to be among the most frequently isolated pathogens in their study. This difference could be due to variations in antifungal prophylaxis practices, patient risk factors, or diagnostic methods. Primary VAP pathogens, highlight the complex nature of diagnosing and managing VAP in the neonatal population. The etiology of VAP in our study population is diverse, with both gram-positive and gram-negative pathogens playing significant roles. The high rate of no-growth cultures and the predominance of organisms like CONS, which are not typically considered

Our study identified several factors associated with an increased risk of VAP, including being outborn, having a gestational age of ≤ 32 weeks, and having a birth weight ≤ 1.49 kg. Additionally, VAP was strongly associated with positive C-reactive protein (CRP) results and temperature instability. The association between outborn status and VAP risk is particularly interesting. This finding aligns with the study by Lamichhane et al. (2019) [5] in Nepal, which found that referred patients had a higher risk of developing VAP. The association of VAP with very low gestational age (≤ 32 weeks) and very low birth weight (≤ 1.49 kg) is consistent with several previous studies. For instance, Wu et al. (2014) [2] and Tan et al. (2014) [3] both identified prematurity and low birth weight as significant risk factors for VAP. The strong association between VAP and positive CRP results, as well as temperature instability, aligns with the inflammatory nature of VAP. However, it's important to note that these are non-specific findings that could also be present in other neonatal infections. This highlights the challenge of diagnosing VAP in neonates, where clinical signs can be subtle and non-specific.

Interestingly, our study did not find a significant association between VAP and factors like the use of H2 blockers or re-intubation, which were identified as risk factors in the study by Ahmed et al. (2022). [9] This discrepancy could be due to differences in population characteristics, care practices, or the relative impact of other risk factors in our setting.

Our study found that neonates with VAP had notably poorer outcomes, with a higher mortality rate compared to those without VAP. This finding is consistent with several previous studies, although the magnitude of the effect in our population appears to be more pronounced. For instance, Wu et al. (2014) [2] reported mortality rates of 44.4% for VAP patients compared to 15.6% for those without VAP, while Tasbakan et al. (2016) [10] found mortality rates of 41.7% vs. 9.1%. Our overall mortality rate of 49.8% suggests a particularly vulnerable population or possibly more severe cases of VAP.

CONCLUSION

The study revealed a high incidence of VAP (42.3%) among mechanically ventilated neonates, with a mean onset of 2.37 days after intubation. The etiology of VAP was diverse, with Coagulase-negative Staphylococci, Acinetobacter, and Pseudomonas being the most common pathogens isolated.

Key risk factors for VAP included being outborn, having a gestational age of ≤ 32 weeks, and having a birth weight ≤ 1.49 kg. VAP was also strongly associated with positive C-reactive protein results and temperature instability. The outcomes for neonates with VAP were poor, with a significantly higher mortality rate compared to those without VAP.

This study highlights a high incidence of VAP in neonates requiring mechanical ventilation, with key risk factors including low gestational age and birth weight. Early onset of VAP and the presence of pathogens such as Coagulase-negative Staphylococci emphasize the need for preventive strategies and rapid intervention in NICUs to reduce neonatal mortality. The study underscores the importance of close monitoring and early detection of VAP to improve survival outcomes in this population.

LIMITATIONS

1. Lack of control group: Without a matched control group of non-ventilated neonates, it's challenging to isolate the specific impact of mechanical ventilation on outcomes.
2. Limited follow-up: The study does not provide information on long-term outcomes for survivors of neonatal VAP.
3. Limited data on antibiotic use: More detailed information on antibiotic use patterns could have provided additional context for understanding the microbial etiology and outcomes.

RECOMMENDATIONS

1. Enhanced preventive measures: Implement comprehensive VAP prevention bundles in NICUs, with particular attention to very preterm and very low birth weight infants who are at highest risk.
2. Tailored care for outborn neonates: Develop specific protocols for outborn neonates to mitigate their increased risk of VAP, including enhanced infection control during transport and immediately upon NICU admission.
3. Early detection strategies: Implement regular monitoring of inflammatory markers like CRP and close observation for temperature instability to aid in early VAP detection.

4. Antibiotic stewardship: Develop and implement antibiotic stewardship programs tailored to the NICU setting, considering the local microbial ecology identified in this study.
5. Staff education: Provide ongoing education and training for NICU staff on VAP prevention, early detection, and management.
6. Standardized diagnosis: Consider implementing standardized diagnostic criteria for neonatal VAP, such as the modified CPIS used in this study, to ensure consistent diagnosis and facilitate comparison across studies and centers.
7. Multi-disciplinary approach: Foster collaboration between neonatologists, infectious disease specialists, microbiologists, and infection control teams to develop comprehensive VAP management strategies.
8. Follow-up studies: Conduct longitudinal studies to assess long-term outcomes of neonatal VAP survivors and evaluate the effectiveness of preventive interventions.
9. Multi-center research: Initiate multi-center studies to validate these findings across different settings and populations, and to test the effectiveness of targeted interventional strategies.

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