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Original Research Paper

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A CLINICAL STUDY OF VENTILATOR ASSOCIATED PNEUMONIA IN A TERTIARY CARE CENTER

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ABSTRACT **Introduction:** Ventilator-associated pneumonia (VAP) is a nosocomial pneumonia in mechanically ventilated patients that develops 48hours after initiation of mechanical ventilation. Despite recent advances VAP complicates 8-28% of the patients receiving mechanical ventilation.1-5 **Objectives:** To determine the incidence, risk factors, clinical profile and outcome of VAP in a tertiary care hospital. **Methods:** 100 children between 1 month to 12 years of age who received mechanical ventilation for >48hours in PICU King George Hospital were enrolled in the study. The demographic details of the patients, underlying illness, duration of ventilation, medications administered and investigations performed and outcome of these children was noted. **Results:** Majority of children with VAP had a Clinical Pulmonary Infection score (CPIS) of>8.Incidence of VAP was 26%. Statistically significant difference was found with VAP in association with factors like purulent aspirate, un-cuffed ET tube, multiple intubations, and duration of mechanical ventilation>5days with gram negative bacilli(Acinetobacter and klebsiella) being the important causative agents. **Conclusion:** Awareness about the risk factors & their prevention will help in reducing VAP related morbidity and mortality. Early institution of empirical sensitive antibiotics improves outcomes in children with VAP and also helps to prevent the risk of multidrug resistance.

KEYWORDS : Ventilator associated pneumonia, risk factors, clinical profile, outcome.

INTRODUCTION:

Ventilator-associated Pneumonia (VAP) is nosocomial pneumonia in mechanically ventilated patients that develops more than 48 hours after the initiation of mechanical ventilator (MV) support. It is one of the leading causes of morbidity and mortality among hospital-acquired infections. The incidence of VAP is 3 to 10% in developed countries[6,7]. Studies from India have shown higher VAP rates of 6% to 46%.[8, 9] The mortality with VAP is 24 to 50% and can reach as high as 76% when high-risk pathogens cause lung infection.[2] When appropriately managed, incidence of VAP can be significantly reduced as majority of risk factors predisposing to VAP are preventable.

Patients developing VAP are usually treated empirically with antibiotics based on the possible pathogens.[10] Using appropriate antibiotics against the most prevalent organism improves the cure rate and survival and reduces the emergence of resistant strains.

The present study was undertaken in a tertiary care centre with significant burden of PICU patients requiring mechanical ventilation.

Knowledge about risk factors, organisms causing VAP, and their antibiotic sensitivity which changes frequently is essential for prevention and optimal management of VAP and reduce health care costs in developing countries.

METHODS:

The present study was a Prospective observational study conducted in a tertiary care hospital between June 2020 and July 2021.The study was approved by institutional ethics committee. Written informed consent was obtained from parents/care givers. 100 children of 1 month to 12 years of age admitted consecutively and mechanically ventilated were enrolled in the study.

Demographic details were taken and thorough physical examination were conducted in all these children.

All patients were investigated for the primary illness. Chest x-ray was taken in all patients soon after the onset of ventilation, during ventilation whenever there is a deterioration, prior to planned extubation and post extubation. Endotracheal aspirates were sent for culture and sensitivity after 48hrs of ventilation in all cases. Blood cultures were also done before initiating antibiotics & subsequently as per the need. Antibiotic regimen was modified if necessary after obtaining the culture and sensitivity pattern. Data collected was entered in a structured predesigned proforma. Results were tabulated and statistical analysis was done with Statistical package for social sciences (SPSS) version 15.

RESULTS:

Total of 100 children in the age group of 1 month to 12 years who received mechanical ventilation for more than 48 hours were enrolled in the study. Mean age of the children was 46.51 ± 38.84 with a range of 2 months to 180 months. Out of 100 children,59 were male (59%) and 41 were female (41%).

Details of the diseases with which the children were admitted is shown in Table 1

Table 1: Distribution of underlying diseases of VAP children

Diagnosis of enrolled patients	Number (%) N=100
Bronchopneumonia	16(16%)
Viral encephalitis	12(12%)
Aspiration pneumonia	12(12%)

Dengue	12(12%)
Sepsis	10(10%)
Pyogenic meningitis	7(7%)
Cerebral malaria	6(6%)
Congenital heart disease	5(5%)
Poisoning	5(5%)
Encephalopathy	4(4%)
TB meningitis	3(3%)
Others	8(8%)

Details of interventions in these children is depicted in the Table 2

Table 2: Interventions performed in enrolled children

Variable	Value
Type of endotracheal tube used Cuffed, N(%) Uncuffed, N(%)	 41(41%) 59(59%)
Mean number of intubations(range)	1.94±1.19 (1-7)
Mean duration of mechanical ventilation in days(range)	5.05±2.30 (3-16)
Mean duration of ICU stay in days(range)	7.34±2.93 (3-16)
Presence of nasogastric tube, N(%)	18(18%)
Presence of Central venous catheter, N(%)	24(24%)
Use of PPI, N(%)	17(17%)

Based on CPIS score, incidence of VAP was 26%, non VAP was 74% with early VAP being 12 cases & late VAP was 14 cases. Various risk factors for VAP in the study are shown in Table 3

Table 3: Risk factors in study population

		VAP N= 26(%)	Non-VAP N=74(%)	P value
Age in years	<1 year 1-5 years 5-10yrs >10years	7(26.9%) 9(34.6%) 9(34.6%) 1(3.8%)	17(23%) 34(45.9%) 17(23%) 6(8.1%)	0.532
Gender	Male Female	12(46.15%) 14(53.84%)	47(63.51%) 27(36.48%)	0.1215
Endotracheal aspirate	Purulent Non purulent No aspirate	26(100%) 0 0	3(4.1%) 15(20.3%) 56(75.7%)	0.00
Endotracheal aspirate culture	Positive Negative	26(100%) 0	3(4%) 71(96%)	0.00
ET tube type	Cuffed Un-cuffed	6(23.1%) 20(76.9%)	35(47.3%) 39(52.7%)	0.038
No. of intubations	1-2 3-4 >5	8(30.76%) 14(53.84%) 4(15.38%)	71(95.94%) 3(1.3%) 0(0%)	0.000
Duration of ventilation		7.85±2.22	4.07±1.32	0.026
Central line insitu	Yes No	15(57.7%) 11(42.3%)	9(12.2%) 65(87.8%)	0.00
Use of PPI	Yes No	21(80.8%) 5(19.2%)	62(83.8%) 13(16.2%)	0.827

Acinetobacter was the most common organism isolated from endotracheal aspirates,10 cases with 6 being early VAP and 4 being late VAP. Next most common was pseudomonas with 7 cases, early 3 and late 4. Klebsiella was isolated in 5 cases with 2 in early VAP, 3 in late VAP, E. Coli in 2 cases, 1 in each. Staph aureus and enterobacter in 1 case each in late VAP.

All microbes isolated from ET aspirate culture were resistant to nearly all of the routinely used antibiotics. Acinetobacter was found to be multi resistant to penicillin, cephalosporin group of antibiotics, vancomycin and meropenem. It was found to be sensitive to only aminoglycosides like amikacin, gentamycin and other antibiotics like imipenem and levofloxacin. Pseudomonas was sensitive to only aminoglycosides like amikacin, gentamycin and other antibiotics like ceftazidime, cefepime, ciprofloxacin, levofloxacin, doripenam, imipenam, meropenam and piperacillin tazobactam. Klebsiella was sensitive to amikacin, gentamycin, amoxicillin clavulante, ciprofloxacin, levofloxacin, doripenam, imipenam, and meropenam. E.coli to amikacin, gentamycin, ciprofloxacin, levofloxacin, imipenam, and meropenam. Staphylococcus to ciprofloxacin, levofloxacin, linezolid, and vancomycin and Enterobacter to ciprofloxacin, levofloxacin, imipenam and meropenam.

Acinetobacter was the most common organism isolated in blood cultures of 5 VAP cases, followed by klebsiella in 2 cases and staph aureus in 1 case.

Out of 100 ventilated cases VAP contributed to 38.5%(10 cases) of mortality in the present study, whereas the mortality in non VAP was 35.1%.Out of 10 VAP deaths in the present study, deaths were secondary to gram negative infections with Acinetobacter(40%) being the most common followed by Klebsiella (30%), Pseudomonas (20%) and Enterobacter (10%).

DISCUSSION:

Mechanical Ventilator (MV) is an essential component of modern ICU care and it is associated with a considerable risk of VAP. Proper recognition of high risk patients and potential modifiable risk factors may outline preventive measures and institutional strategies to reduce the risk of infection. The incidence of VAP based on the Clinical Pulmonary Infection Score (CPIS) score in the present study was 26%. The incidence of VAP in various other studies was reported to range from 6.03% to 51% from Indian studies and 3% to 31% from developed countries.[6-9] Although there was a wide range of variation in the reported incidence rates of VAP at various centres, the present study correlates with various Indian studies. The difference in incidence rates could be mainly due to different criteria used for the diagnosis of VAP, difference in sample size and the underlying disease state requiring ventilator support.The incidence of VAP in the present study is comparable to the studies by Vedavathy S et al[12] from IGICH, Bengaluru and Patra et al[13] from PGI, Chandigarh (22.6%,30.5% respectively).While the incidence is high in the present study compared to the incidence of VAP in the study done by Balasubramanian P et al[8] from Mumbai and Mahantesh S et al[14] from Bengaluru (6.03,%,6.85% respectively), it is less compared to the study by Awastia S et al [15] from Uttar Pradesh and by Payal PM et al[9] from Vadodara (36.2 %, 46.4% respectively).

Early onset VAP, which occurs within the first 4 days of mechanical ventilation, is more likely caused by antibiotic sensitive bacteria and usually carries a better prognosis. Late onset VAP (more than 5 days) is more likely caused by multidrug-resistant (MDR) pathogens, with increased patient mortality and morbidity[5].In the present study 46.1% cases had early VAP and 53.8% cases had late VAP. This is comparable to the studies by Mahantesh S et al[14] (36.48% early, 63.51% in late VAP) Patra PK et al[13] (41.1% early, 58.9% late VAP) and by Hamid et al[16](23.3% early,76.67% late VAP). Various risk factors were studied by comparing the group with VAP and those without VAP. Age of presentation was categorized into

four groups(<1 yr, 1-5 yrs, 5-10yrs and >10yrs).There was no significant association of VAP with respect to the age of presentation (p value 0.532) and similar finding was noted in the study by Mahantesh et al[14]and by Vedavathy S et al[12].Galal YS et al[18] Study reported that patients with VAP were significantly younger(<1yr) and also girls had significantly higher VAP compared to boys. Though male population predominated in total number of VAP cases in the present study, sex distribution(male: female ratio 1.4:1) was also not significantly associated with occurrence of VAP (p value 0.1215).The results are in agreement with that of Patra PK et al[13]and Vedavathy S et al.[12] Though the central nervous system cases and respiratory cases were more among the study population in the present study,the primary diagnosis was not significantly associated with the occurrence of VAP.In a study done by Galal YS et al,[18] a significantly higher VAP patients presented with coma and multiorgan failure and the primary diagnosis differed significantly between VAP and non-VAP groups. The character, amount and bacteriological positivity rate of the endotracheal aspirates from the intubated patients was evaluated for association with VAP. It was found that presence of purulent aspirates, moderate to heavy aspirates and positive aspirate cultures were significantly associated with occurrence of VAP (p value 0.00). This suggests that whenever the clinicians observe these findings in mechanically ventilated children in ICU, with the suspicion of VAP they should promptly consider early initiation of empirical antibiotics based on the antibiotic susceptibility pattern at their centre. Presence of uncuffed endotracheal tube was significantly associated with occurrence of VAP(p value 0.038) in the present study. The type of endotracheal tube used whether cuffed or uncuffed was found to be a risk factor for development of VAP by Spray et al.[19] Use of low volume high pressure cuffs reduced the rate of VAP to 56% and high-volume low-pressure cuffs further lowered it to 20%.[19] Vedavathy S et al found no significant difference in the type of ET tube and the development of VAP.[12] Re-intubations in patients on mechanical ventilator is an important risk factor for development of VAP.[20] When the number of intubations were evaluated, in the present study, VAP was significantly associated(p value 0.00) with higher number of intubations(3 or more intubations).

It was observed that 82.35% children with history of 3-4 intubations and 100% of children with ≥5 intubations had developed VAP in the present study. This finding is consistent with that of Torres et al study, who demonstrated that the pneumonia rate was 47% for re-intubated patients compared with the 4% for control subjects.[21] Similar results were reported by Elward AM et al.[6]Re-intubation was an independent risk factor for the development of VAP as observed by Patra PK et al[13] and Khalid Amro et al[17]Thus, re-intubations in patients on mechanical ventilation definitely increases the risk of developing VAP.The risk of VAP increases with emergency unplanned re-intubation and with multiple attempts. However, data on the circumstances surrounding reintubation was not collected in this study.

Presence of central venous catheter is also a significant risk factor for developing VAP. Out of 24 children with central venous catheter, 15(62.5%) developed VAP(p value 0.00) in the present study. Similar findings were reported by Elwald Ma et al[6]and Vedavathy S et al.[12]

In the present study, nasogastric tube and early enteral feeding was significantly associated with occurrence of VAP(p value 0.00). Out of 18 children with nasogastric tube, 13 children (72.22%) developed VAP. Mahantesh S et al[14] also found that nasogastric tube in situ is a risk- factor for VAP. In contrast, Vedavathy S et al and Patra PK et al studies showed that nasogastric tube is not a risk factor for VAP.[12,13] Some studies have suggested to bypass the stomach by using a jejunal tube instead of a gastric tube in critically ill children.[22] These issues are however, still controversial and require further study before definite recommendations can be made regarding the use of nasogastric tube for feeding in critically ill children. Use of Proton pump inhibitors (PPIs) in mechanically ventilated children in the present study was not significantly associated with occurrence of VAP (p value 0.827). There is lot of inconsistencies in the literature about the use of H_2 receptor blockers and PPIs as risk factors for VAP. Elwald MA et al observed that H_2RBs act as risk factor for VAP.[6] H_2RBs and antacids were identified as independent risk factors for ICU acquired VAP in various other studies.

Acinetobacter(38.46%) was the most common organism isolated from endotracheal aspirates in early onset VAP and late onset VAP followed by Pseudomonas(26.92%), Klebsiella(19.23%) and Staphylococcus aureus(1 case of late VAP). These results were similar to the studies done by Mahantesh et al, Balasubramanian P et al and Patra PK et al who reported Pseudomonas as the second most common isolate after Acinetobacter.[8,13,14] In Europe and North America, Staphylococcus aureus predominated in most of the ET aspirate cultures.[23,24] This microbial flora reflects the common organisms present in the gut, oropharynx and environment. Increased use of advanced diagnostic and interventional procedures in hospital ICUs is responsible for the emergence of Acinetobacter as an important pathogen in ICUs.

Concomitant endotracheal and blood culture positivity was seen in 8(30.7%) out of 26 VAP cases. Among these, 5 cases of early onset VAP isolated Acinetobacter and 1 case of early VAP each isolated klebsiella & Staph aureus from both endotracheal aspirate and blood culture. Primary blood pathogen might be the culprit in causing VAP in such cases. Though 38(38.5%) cases expired in the VAP group it was statistically insignificant as mortality in non VAP was observed to be 35.1%(35 cases). 40% of deaths in the present study were due to gram negative organisms Acinetobcter being the commonest. However in Patra et al study, all the deaths in the group with Noscomial pneumonia were secondary to gram negative infections with Pseudomonas contributing to 57.1% deaths.[13]

All microbes isolated from ET aspirate culture were resistant to nearly all of the routinely used antibiotics. They pose a great therapeutic problem for the clinician because of the resistance of these bugs to major group of antibiotics. In the present study as well, Acinetobacter was found to be multi resistant to penicillin, cephalosporin group of antibiotics, vancomycin and meropenem. It is found to be sensitive to only aminoglycosides like amikacin, gentamycin and other antibiotics like imipenem and levofloxacin. Increased use of advanced diagnostic and interventional procedures in hospital ICUs is responsible for the emergence of Acinetobacter as an important nosocomial pathogen in the ICUs. Improper use of high-grade antibiotics for common infections in hospitals could also be responsible for emergence of multi drug resistance. Hence every institute should have a proper antibiotic stewardship committee to monitor the indiscriminate use of high-grade antibiotics and also evaluate the local antibiograms regularly to prevent antibiotic resistance. Knowledge about the most common bacterial isolates in ICUs and their antibiotic sensitivities will help us in planning appropriate empirical antibiotics for treating hospital acquired VAPs.

Another important consideration is that the mere presence of bacterial isolate in endotracheal aspirates doesn't mean infection, as it could be bacterial colonization as well. Hence the clinician should take into consideration the overall clinical context of the patient like presence of fever, leucocytosis, associated radiological infiltrates and purulent copious aspirates before considering the bacterial isolate as infection.

CONCLUSION:

VAP is an important nosocomial infection in IPCU with an incidence of 26% and with a high mortality rate of 38.5%. Gram negative bacilli (Acinetobacter and Klebsiella) were the most important causative agents and were nearly resistant to commonly used antibiotics. Multiple intubations, uncuffed ET tube, duration of mechanical ventilation, purulent and copious endotracheal aspirates, central venous line and NG tube were associated with increased risk of VAP. Awareness about all these risk factors is helpful in reducing VAP related morbidity and mortality. Further research about risk factors and diagnosis of VAP in PICU is needed. Early institution of empirical sensitive antibiotics and strictly following antibiotic stewardship programmes can help in preventing multidrug resistance and improve outcomes in children with VAP.

Limitations:

The major limitation of the present study was the inability to use newer techniques (such as Bronchoalveolar Lavage or Protected specimen brush technique) due to resource constraints in the diagnosis of VAP and lack of appropriate sample size due to time constraints.

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