ORIGINAL ARTICLE

Ventilator-Associated Pneumonia in a Tertiary Care Intensive Care Unit: Analysis of Incidence, Micro-Biological Profile, Resistant Pattern and Outcome

Sandeep Kumar[1], Malay Sarkar[2], D V Singh[3], R S Negi[4], Sunil Sharma[4], Sanjeev Prabhakar[5]

Authors' affiliation: [1]Senior Resident; [2]Professor and Head, Dept. of Pulmonary Medicine; [3]Professor and Head, Dept. of Microbiology; [4]Associate Professor; [5]Medical Officer, Dept. of Pulmonary Medicine, Indira Gandhi Medical College, Shimla
Correspondence: Dr. Malay Sarkar, Email: drsarkarmalay23@rediffmail.com

ABSTRACT

Background: Ventilator-associated pneumonia (VAP) is the most common nosocomial infection diagnosed in the intensive care unit (ICU). The aim is to determine the incidence, bacteriology and resistant pattern and 28 days mortality in intensive care unit.

Methods: This prospective study was conducted in intensive care unitfrom July 2017 through June 2018. All the patients who were on mechanical ventilation for >48 h in the ICU during the study period were enrolled. VAP was diagnosed according to the Centre for Disease Control (CDC) criteria. Fisher's exact test was applied to compare two or more set of variables.P-value less than 0.05 was considered to be statistically significant.

Results: A total of 117 patients were included in the study and VAP developed in 49 patients with an incidence of VAP 0.42% episodes of infection/1000 mechanical ventilation days(95% Confidence Interval: 0.32 to 0.514).These were predominantly caused by Gram-negative organisms and the most common organism isolated was Acinetobacter baumanii(12 isolates,40%). Acinetobacter baumanii infection was associated with prolonged ICU stay(P value 0.009).Colistin was the most effective drug in our study and found to be effective in >90% of the patients. The overall mortality of VAP patients in our study was 36.7%. Patients with underlying diabetes mellitus and hypertension had adverse outcome in comparison to the patients without underlying comorbidity (P value=0.017).

Conclusions: VAP continues to be a major threat to patients who are admitted for mechanical ventilation into the critical care unit, emphasizing the urgent need for infection control measures.

Key words: ventilator associated pneumonia, Acinetobacter baumannii, colistin

INTRODUCTION

Ventilator-associated pneumonia (VAP) is one of the most common nosocomial infection diagnosed in the intensive care units (ICU). VAP is defined as pneumonia that occurs 48 hours or more after endotracheal intubation or tracheostomy, caused by infectious agents not present or incubating at the time mechanical ventilation was started. VAP is of two types: early-onset and late-onset. Early-onset VAP occurs during their first four days of mechanical ventilation. It is usually less severe and is associated with a better prognosis. Early VAP is more likely caused by antibiotic sensitive bacteria. Late-onset VAP develops more than four days after initiation of mechanical ventilation, is caused by multidrug resistant (MDR) pathogens and associated with increased morbidity and mortality.[1]

The incidence of VAP ranges from 4 to 14/1000 ventilator days in the United States and 10 to 52.7/1000 days in developing countries.[2] The risk of developing VAP is estimated at around 3% per day during the first 5 days of ventilation, 2% per day during days 5 to 10 of ventilation, and 1% per day thereafter.[3,4] In contrast to infections of other organs (e.g., urinary tract and skin), for which mortality ranges from 1% to 4%, the mortality rate for VAP ranges from 20% to 50%, and can even be higher when lung infection is caused by high-risk pathogens.[5] Gram-negative bacteria are the most common pathogens causing HAP/VAP in Indian setting and should be routinely considered as the most common etiological agents of HAP/VAP.[6]

The principal risk factor for the development of VAP is the presence of an endotracheal tube. Endotracheal tube interferes with the normal protective upper airway reflexes, prevents effective coughing, and encourages micro aspiration of contaminated pharyngeal contents.[7]

Most studies report Acinetobacter species followed by P.aeruginosa as the most common organisms isolated from patients having HAP/VAP. The main aim of our study to determine the incidence ofVAP and to study the micro-biological profile and resistant pattern present in our institution.

MATERIAL AND METHODS

This was a prospective observational study, conducted in the adult ICU of a tertiary care hospital in North India from July 2017 to June 2018. All patients over 18 years of age, who were intubated and mechanically ventilated for more than 48 h, were included in the study. Patients who developed pneumonia within 48 hours of mechanical ventilation were excluded from the study. All the enrolled patients were monitored daily for the development of VAP using clinical and microbiological criteria until either their discharge or death. A data collection sheet was used for the detailed history including name, age, sex, underlying clinical condition, and date of admission to the ICU, duration of hospitalization and mechanical ventilation, details of antibiotic therapy, use of steroids, position of patient, use of sedatives, presence of neurological disorder, impaired consciousness, and other important parameters. Patient was subjected to chest radiograph at the time of connecting the patient to the ventilator and after 48 hours of mechanical ventilation and thereafter.

Endotracheal aspirate (ETA) was collected from all patients admitted in the ICU/HDU/RICU, who were mechanically ventilated for more than 48 hours. Respiratory samples were collected by deep sterile endotracheal suctioning and transported to the laboratory immediately. The endotracheal aspirates culture subsequently was done whenever indicated. A quantitative endotracheal aspirate culture showing $\geq 10^5$ CFU/ ml was considered significant and was reported. However, the diagnosis of VAP was done on the basis of CDC's defined criteria.

All samples were sent for Gram staining and culture. The aspirate specimens showing presence of <10 squamous epithelial cells and >25 neutrophils per low power field were included in the study. Quantitative culture of the endotracheal aspirate was performed for identification of VAP pathogens. Endotracheal aspirates were homogenized by vortexing for one minute. Endotracheal aspirates were serially diluted in sterile normal saline as 1/10, 1/100,1/1000. Nichrome loop calibrated to contain 1/100 and 1/1000 ml of endotracheal aspirate was used for quantitative culture. The streaming technique was used to inoculate agar media. Culture of the sample was done on Blood agar and MacConkey agar, which was incubated aerobically overnight at 37^0C. Microbial growth was identified by ID/AST method. In case of any growth of microorganism present, further evaluation was done for sensitivity pattern. The organisms isolated by culture of the ETA from VAP patients were identified based on standard microbiological technique. The patients were followed up to 28 days to know the outcome.

Statistical Analysis: The collected data was compiled in Microsoft Excel 2010 and statistical analysis of the pre-coded data was done using SPSS (Statistical Programme for Social Sciences) software 15 version and Open Epi Software Version 2.3. The statistical analysis was performed using standard tests. Data were summarized using the mean and standard deviations for quantitative variables and frequency and percentage for qualitative variables. Fisher's exact test or Chi square test of statistic were applied when two or more set of variables were compared. P value less than 0.05was considered to be statistically significant.

RESULTS

A total of 117 patients fulfilling the inclusion criteria were included in the study. The mean age of the patient enrolled in the study was 52.5 ± 16.6 years. Majority of patients (70 %) were males. A total of 49 patients developed VAP with an incidence of 41.89% (95% Confidence Interval: 0.32 to 0.51). Out of 49 patients developing VAP only 30 patients were considered for the study due to unavailability of complete data of remaining patients.

Out of 30 VAP patients 53.3% were smokers. Majority (68.7%) of smokers were having smoking index of more than 100. Majority (63.3%) of patients had ICU stay of less than 14 days and 36.7% of patients had ICU stay of more than 14 days. Most of the patients (80%) had a medical illness that leads to ICU hospitalisation.(Table 1) Majority (30%) of the patients had COPD as a primary disease. Around one-third of the patients had diabetes as their co-morbidity.

Acinetobacter baumanni was the most common (40%) organism isolated on culture, followed by Pseudomonas aeruginosa (30%). Colistin was the most sensitive drug against the isolated Gram-negative bacilli in more than 90% of the patients. Staphylococcus aureus was isolated from one patient, which was MRSA, sensitive to Teicoplanin, Vancomycin and Linezolid.

In this study, Acinetobacter was associated with prolonged ICU stay and the result was statistically significant. Other risk factors like age, comorbidities and reintubation were not related to the type of organism isolated.

Table 1: relationship between risk factors and outcome

Association	Total (n=30)	Outcome		P Value
		Survived (n=19)	Dead (n=11)	
Age				
< 50 Years	11	9	2	0.14
>50 Years	19	10	9	
Sex				
Male	21	12	9	0.41
Female	9	7	2	
Duration of ICU stay				
<14 days	19	11	8	0.34
>14 days	11	8	3	
Smoker				
smoker	16	7	9	0.26
Non smoker	14	12	2	
Previous Hospitalization				
yes	6	3	3	0.64
No	24	16	8	
Type of admission				
Medical	24	15	9	1.00
Surgical	6	4	2	
Comorbidity				
No comorbidity	17	14	3	0.01
Diabetes	6	4	2	
Hypertension	2	0	2	
DM + HT	5	1	4	
Steroid				
Given	15	10	5	1.00
Not given	15	9	6	
Sedation				
Given	27	18	9	0.53
Not given	3	1	2	
Impaired consciousness				
Present	17	10	7	0.45
Absent	13	9	4	
Type of intubation				
Emergency	22	13	8	1.00
Elective	8	5	3	
Reintubation				
Done	13	7	6	1.00
Not done	17	12	5	

Table 2: Organisms found in cultures of samples of Endotracheal Secretions

Organism Found	Cases (n=30 (%)
Acinetobacter baumanni	12 (40.0)
Pseudomonas aeruginosa	10 (30.0)
Staphylococcus aureus	1 (3.3)
Klebsiella pneumonia	4 (13.3)
Enterobacter sp.	3 (10.0)

In the age group of less than 50 years, majority (81.8%) of the patients survived, whereas in the age group of more than 50 years only 52.6% patients survived. Around three-fourth of females survived while among males, only one-half of the patients survived. Out of 19 patients staying in ICU for less than 14 days, 57.9% survived while 72.7% patients survived in the group of more than 14 days stay. (Table 1)

Majority (85.7%) of the patients from non-smoker group survived and in smoker group only 43.8% survived. 62.5% patients of underlying medical condition and 66.7% patients of underlying surgical cause survived. Most of the patients in whom there was no associated co-morbidity, survived (82.4%) and outcome in patients with both hypertension and diabetes was worse (20%) and this correlation was found to be statistically significant (p value 0.017).

DISCUSSION

VAP is a common complication associated with invasive ventilatory support and contributes to a significant morbidity and mortality in patients admitted to ICU.

Endotracheal aspiration (single catheter technique) is the most commonly used method of endotracheal sampling in ICUs all over the world. However, this technique has low sensitivity and specificity for the diagnosis of VAP, as the upper respiratory tract is frequently colonized with potential pathogens, even in the absence of pneumonia.

The incidence of VAP ranges from 4 to 14/1000 ventilator days in the United States and 10 to 52.7/1000 days in developing countries. In our study, incidence rate was 41.8%.Gadani et al. showed 37 % incidence rate.[8] But other studies have shown variable incidence rates in India. Deshmukh et al. reported the incidence of 78%[9], whereas Rit et al. had shown incidence rate of 20%.[10]

Divergence of incidence can be attributed to several factors such as differences in the study population, differences in the definition of VAP, e.g. clinically versus microbiologically oriented and possibly, differences in prevalence of comorbidities and variable adoption of preventive strategies in ICUs. Intubated COPD patients are more prone to VAP and have an increased mortality and duration of mechanical ventilation. This may be the reason for high incidence of VAP in our study.

In our study, mean age of the patients was 52 years. Majority of the patients (30%) had COPD as a primary disease, so the mean age was high. The results were similar to other studies with high mean age and male predominance. In contrast, study done by Gadani et al. had much lower mean age of 34 years[8], probably because majority of the patients included in the study were of poisoning.

The commonest pathogen isolated in our study was Acinetobacter baumanii, observed in 40% of VAP cases. Mathai et al. isolated A. baumanii in 53.2% of VAP cases.[11] We reported Pseudomonas aeruginosa as the second commonest organism. However, Gadani et al had reported Pseudomonas aeruginosa as the commonest pathogen causing VAP[8].

Table 3: Correlation of risk factors with Acinetobacter versus other microorganisms.

Risk factor	Acinetobacter	Other Micro-organism	P value
Age			
<50 Years	4	7	1
>50 Years	8	11	
Duration of ICU stay			
<14 Days	4	15	0.009
>14 Days	8	3	
Comorbidity			
Present	4	9	0.136
Absent	8	9	
Re-intubation			
Done	8	5	0.061
Not done	4	13	

The preponderance of Gram-negative non-fermenters in the patients with VAP may be due to the fact that Gram-negative bacilli commonly colonizes upper airways in intubated patients, and aspiration of these colonizers into the lower airways lead to the VAP development.

We also reported statistically significant association (P value=0.009) between isolation of A. baumaniion ETT culture and increased duration of ICU stay (more than 14 days). Ellis et al. also showed a significant risk with longer ICU stay and prior antibiotic use for infection with Acinetobacter.[12] Dash et al. demonstrated advanced age, in-patients, longer duration of hospital stay, associated comorbidities, and invasive procedures as significant risk factors for Acinetobacter spp.[13]

Some other studies have shown methicillin-sensitive Staphylococcus aureus (MSSA) or methicillin-resistant Staphylococcus aureus (MRSA) as the major pathogens, especially in early onset VAP. But in our study, Staphylococcus aureus was the least common; which indicates that the causative pathogens vary in different ICU environment. The epidemiological knowledge of the local microbiological pattern can help in deciding early, appropriate and broad-spectrum antibiotic.

Regarding the susceptibility profiles of the etiologic pathogens of the VAP patients in our study, Colistin emerged as the most effective antibiotic, which was found to be sensitive in around 90% of our patients, followed by Meropenem and Ceftazidime. In a study by Rit et al, Colistin was found to be the most effective antibiotic followed by Piperacillin/Tazobactum combination and then Imipenem.[10] This confers the high incidence of MDR pathogens in ICU environment. In a study by Gu et al, colistin emerged as effective and safe as β-lactams for the treatment of VAP caused by MDR Gram negative bacilli.[14] Also, they showed that colistin combined therapy does not provide better outcomes compared with colistin monotherapy.

Patients of VAP with underlying diabetes mellitus and hypertension had adverse outcome in comparison to the patients without underlying comorbidity and it was statistically significant (P value=0.017). Study done by Dhadke et al. showed poor outcome among patients with associated comorbidities[15]. Huang et al. (2010) on early predictor of outcome of VAP, found higher morality rates among VAP patients having associated comorbidity.[16] They found out that morality rate was 20% in hypertensive and diabetic patients. Kornum et al. in their study which included 2,931 pneumonia patients concluded that type 2 diabetes mellitus and admission hyperglycemia are predictors of increased pneumonia-related mortality.[17] The biological mechanisms responsible for increased mortality in diabetic patients who are hospitalized for pneumonia include harmful effects of hyperglycemia and decreased leucocyte function.

The overall mortality of VAP patients in our study was 36.7%. Ranjan et al.[18] and Gadani et al.[8] had shown much higher mortality rates of 48.3% and 54% in the VAP patients. The possible reason for the less mortality rate in our study may be the fact that we assessed the outcome only for 28 days, and long term outcome was not included in the study.

VAP occurs in a considerable number of patients in our setup and is responsible for increased mortality, morbidity and longer duration of hospitalization.

LIMITATIONS

The main limitation of our study was a small sample size.Acute physiology and chronic health evaluation scores were not assessed in our study, which would have been helpful in assessing the severity of the illness.We observed the patients for 28 days. Our study could not provide data beyond 28 days.In our study, endotracheal aspirate was cultured on aerobic bacterial media only, so the presence of fungi, virus and anaerobic bacteria could not be assessed.

CONCLUSION

Awareness of the risk factors documented in this study may help identifying the patients at higher risk of developing VAP and implementing preventive measures during the management.This study highlights the need for urgent infection control, planning, and which need to be diagnosed as early as possible.

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