Research Article

Ventilator-associated pneumonia in a tertiary care intensive care unit: Analysis of incidence, risk factors and mortality

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Abstract

Background: Ventilator-associated pneumonia (VAP) is the most common nosocomial infection diagnosed in the intensive care unit (ICU) and in spite of advances in diagnostic techniques and management it remains a common cause of hospital morbidity and mortality. **Objective:** The primary objective of the following study is to determine the incidence, various risk factors and attributable mortality associated with VAP and secondary objective is to identify the various bacterial pathogens causing VAP in the ICU. **Materials and Methods:** This prospective observational study was carried out over a period of 1 year. VAP was diagnosed using the clinical pulmonary infection score. Endotracheal aspirate (ETA) and bronchoalveolar lavage (BAL) samples of suspected cases of VAP were collected from ICU patients and processed as per standard protocols. **Statistical Analysis:** Fisher's exact test was applied when to compare two or more set of variables were compared. **Results:** The incidence of VAP in our study was 57.14% and the incidence density of VAP was 31.7/1000 ventilator days. Trauma was the commonest underlying condition associated with VAP. The incidence of VAP increased as the duration of mechanical ventilation increased and there was a total agreement in bacteriology between semi-quantitative ETAs and BALs in our study. The overall mortality associated with VAP was observed to be 48.33%. **Conclusions:** The incidence of VAP was 57.14%. Study showed that the incidence of VAP is directly proportional to the duration of mechanical ventilation. The most common pathogens causing VAP were *Acinetobacter* spp. and *Pseudomonas aeruginosa* and were associated with a high fatality rate.

Keywords: Incidence, intensive care unit, mortality, risk factors, ventilator-associated pneumonia

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Introduction

Ventilator-associated pneumonia (VAP) is the most common nosocomial infection diagnosed in the intensive care units (ICUs). VAP is defined as pneumonia that occurs 48 h or more after endotracheal intubation or tracheostomy, caused by infectious agents not present or incubating at the time mechanical ventilation was started. It can be of two types: (i) early-onset VAP which is defined as VAP that occurs within the first 4 days of ventilation, and (ii) late-onset VAP which is defined as VAP that occurs more than 4 days after initiation of mechanical ventilation.[1]

Despite major advances in techniques in caring for patients whose respiratory tracts are instrumented and the routine use of efficient disinfection procedures for the respiratory equipment, nosocomial bacterial pneumonia continues to complicate the course of 7-41% of patients receiving continuous mechanical ventilation.[2] VAP requires rapid diagnosis and initiation of the appropriate antibiotic treatment, since studies have shown that the delayed administration of appropriate antibiotic

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therapy in patients with VAP has been associated with excess hospital mortality.[3] The incidence rates calculated using 1,000 ventilator days as denominator reflect more accurately VAP risks rates. VAP rates ranged from 4-14/1000 ventilator days in United States and 10-52.7/1000 days in developing countries.[4] A number of factors have been suspected or identified to increase the risk of VAP in various studies.[5] VAP causing pathogens also vary among different settings.[6] Therefore, knowledge of the incidence of VAP, associated risk factors and common pathogens causing VAP can help in development of effective preventive measures, which in turn will decrease the mortality and morbidity, duration of treatment and hospital stay associated with VAP.

The aim of our study was to determine the incidence of VAP, to assess the risk factors and attributable mortality associated with VAP and to find out the various bacterial pathogens causing VAP in the medical ICU of our institute.

Materials and Methods

A prospective observational study was conducted in the Department of Microbiology in association with 12 bedded multidisciplinary ICU of the Department of Pulmonary and Critical Care Medicine of our institute for the period of June 2009 to May 2010. Patients who received mechanical ventilation more than 48 h were included in our study. Modified clinical pulmonary infection score (CPIS) score was followed as a screening method to clinically diagnose VAP.[7] Detailed history including the name, age, sex, underlying clinical condition, date of admission to the ICU, date of indoor admission, any history of previous antibiotic intake, the treatment being administered in the ICU and clinical outcome of each patient was noted. Any lower respiratory tract infection that developed after 48 h of mechanical ventilation and was judged not to have been incubating before mechanical ventilation was taken as VAP. VAP rate was defined as the number of VAPs/1,000 ventilator days.[4] The diagnosis of VAP was based on clinical and microbiological criteria. A clinical suspicion of VAP was made in patients with modified CPIS score >6.[7] The diagnosis was confirmed when significant growth was obtained in the samples.

Endotracheal aspirate (ETA) and bronchoalveolar lavage (BAL) samples were collected from all patients admitted in the ICU requiring mechanical ventilation for more than 48 h.[8] Patients who were already on ventilation before admission to the ICU or those who died within 48 h were excluded. ETA samples were collected from each patient on 2nd 4th and 7th day while BAL was collected once from each patient. All the samples were transported to the laboratory immediately. Gram stain preparations were made from all ETA and BAL samples and examined first under low power (×10 objectives) to determine the presence and type of cells in the specimen and then observed under oil immersion field (×100 objective). The relative number of micro-organisms and their morphologies were recorded.[9] All the samples were inoculated on blood agar, MacConkey agar and chocolate agar. Semi-quantitative cultures were done.[10] The MacConkey plates were incubated at 37°C while blood agar and chocolate agar were incubated at 37°C in the presence of 5-10% carbon dioxide. Growth $>10^5$ CFU/ml was taken as the cut-off threshold for ETAs while growth $>10^4$ CFU/ml was taken as the cut-off for BALs.[11,12] Samples showing growth less than these thresholds were assumed to be due to colonization or contamination. In case of significant growth, the isolated colonies were subjected to gram stain and biochemical tests for identification. Identification was carried out according to standard biochemical tests.[13]

Statistical analysis

The statistical analysis was performed using standard tests. Fisher's exact test was applied when two or more set of variables were compared. $P < 0.05$ was considered to be statistically significant.

Results

A total of 105 patients, who were on mechanical ventilation for more than 48 h were included in our study. A total of 60 patients fulfilled the clinical and microbiological criteria for the diagnosis of VAP. The incidence of VAP in our study was 57.14% and the incidence density of VAP was 31.7/1000 ventilator days. Out of the 60 cases, 21 (35%) were categorized under early onset group and 39 (65%) under the late onset group. In relation to gender the incidence of VAP was more among males (65%) than females (35%) and in different age groups the incidence of VAP was highest in patients more than 55 years of age (73.68%). When considering the development of VAP in relation to the underlying condition in our study it was seen that trauma was the most common underlying condition as shown in Table 1. Patients admitted to the ICU after trauma were at the highest risk of developing VAP with 76% of patients developing pneumonia. The incidence of VAP increased in patients who were on mechanical ventilation for >15 days (85.17%) as compared to those who were ventilated for less than ≤15 days (50%) [$P < 0.01$]. Out of the 60 patients who developed VAP 12 (20%) were on a broad spectrum antibiotics in the preceding

7 days as compared to 5 (11.2%) from non VAP group. There was a total agreement in bacteriology between semi-quantitative ETAs and BALs in our study.

The majority, i.e. 95.7% of bacterial isolates were found to be Gram-negative bacilli. *Acinetobacter* spp. accounted for 34.28% of VAP cases followed by *Pseudomonas aeruginosa* which was responsible for 25.71% cases. Other Gram-negative bacilli isolated were *Klebsiella pneumoniae*, *Citrobacter freundii*, *Enterobacter* spp., and *Escherichia coli* [Table 2]. Out of the total 70 isolates only 3 isolates were Gram-positive bacteria of which 2 were *Staphylococcus aureus* and 1 *was Enterococcus* spp. Among the total 60 episodes of VAP reported, 10 episodes of VAP were polymicrobial and 50 episodes were monomicrobial. In the monomicrobial episodes, Gram-negative isolates accounted for 96% (48/50) and even in polymicrobial episodes of VAP Gram-negative isolates were predominant accounting for 90% (9/10).

The overall mortality associated with VAP was observed to be 48.33%. Mortality in non VAP group was significantly low at 20%. As these two groups were not similar in other aspects, so the excess mortality could not be attributed entirely to VAP. Severity adjusted mortality could not be calculated. We noted that the mortality associated with VAP was highest in the age group of >55 years (64.29%), followed by 46-55 years (54.54%), 36-45 years (50%), 15-25 years (36.36%) and 26-35 years (30%) respectively.

Discussion

Overall incidence of VAP was 57.14% in our study. This figure is at the higher end of the range of 15-58% as reported by other investigators.[1] 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, to the use of preventive strategies. The incidence density of VAP in our study was 31.7/1000 ventilator days which were was high but comparable to ICUs in other developing countries.[4] The higher incidence of VAP in our study can be attributed to the fact that the total number of cases in the study and the study duration were less as compared to other studies showing lower incidence. One more reason for this high incidence can be the lack of adequate nursing staff (nurse to patient ratio should ideally be 1:1 as compared to 1:4 in our institute) which may have adversely affected the quality of care given to patients. There is now a growing evidence that high work load and low staffing level increase the risk for negative patients outcomes such as death and healthcar-associated infections.[14]

When considering the development of VAP in relation to the underlying condition, we observed that trauma was the most common. Many studies have shown that injured patients (head injury and multiple fractures) are at increased risk for VAP relative to medical patients.[5,15,16] Another risk factor, which was evaluated in this study was the duration of mechanical ventilation. It was observed that the incidence of VAP increased in patients who were on mechanical ventilation for >15 days (85.17%) as compared to those who were ventilated for less than ≤15 days (50% [$P < 0.01$]). Thus, the incidence of VAP increases with the duration of

Table 2: Distribution of organisms isolated from patients with VAP

Bacterial isolates	Number	Percentage
Gram positive bacteria		
Staphylococcus aureus	2	2.85
Enterococcus spp.	1	1.43
Gram negative bacteria		
Acinetobacter baumannii	23	32.86
Acinetobacter lwoffii	1	1.42
Pseudomonas aeruginosa	18	25.71
Klebsiella pneumoniae	15	21.43
Citrobacter freundii	6	8.58
Enterobacter spp.	3	4.28
Escherichia coli	1	1.43
Total	70	100

VAP: Ventilator-associated pneumonia

Table 1: Patients with VAP according to age groups and underlying clinical condition

Underlying clinical conditions	Total no. of patients (105)	Patients developing VAP in different age groups (in years)					Total no. of patients developing VAP (60)	Percentage of patients developing VAP
		15-25	26-35	36-45	46-55	>55		
Post-operative	11	1	2	2	-	-	5	45.5
COPD	7	-	-	-	1	3	4	57
Trauma	21	3	7	4	1	1	16	76.2
Neurological illness	11	-	1	1	1	3	6	11.5
Poisoning	17	6	2	2	-	-	10	58.8
Snake bite	9	3	1	-	-	-	4	44.4
Respiratory failure	9	-	-	1	3	1	5	55.5
Miscellaneous*	20	5	1	-	2	2	10	50

*Diabetes mellitus, malignancy, liver diseases, renal failure, etc., VAP: Ventilator-associated pneumonia; COPD: Chronic obstructive pulmonary disease

mechanical ventilation. These findings were similar to an Italian study that icluded 724 ICU patients and showed that the frequency of VAP rose from 5% for patients receiving mechanical ventilation for 1 day to 69% for those receiving mechanical ventilation for more than 30 days.[17,18]

One more risk factor, which was evaluated in our study was the administration of broad spectrum antibiotics in the preceding 7 days. It was observed that out of the 60 patients who developed VAP, 12 (20%) were on a broad spectrum antibiotics in preceding 7 days as compared to 5 (11.2%) in the non VAP group ($P > 0.05$ which was, however not statistically significant). Furthermore, prolonged antibiotic administration to ICU patients for primary infection is thought to favour selection and subsequent colonization with resistant pathogens responsible for super infection. A sentinel study of VAP in a French ICU noted that prior antimicrobial therapy markedly increased the rate of VAP caused by *P. aeruginosa* and *Acinetobacter* spp. These two pathogens accounted for 65% of VAP cases among patients who have previously received antibiotics, compared with only 19% of VAP cases among antibiotic-naïve patients.[2] In our study also these two pathogens were responsible for 60% VAP cases. *Acinetobacter* spp. accounted for the highest number of cases followed by *P. aeruginosa*. Similarly, Joseph *et al*. also reported *Acinetobacter* spp. and *P. aeruginosa* as the predominant organisms causing VAP.[19] In another study by Gupta *et al*., the most common pathogen was *P. aeruginosa*.[20]

Airway intubation is associated with increased frequency of Gram-negative bacterial colonization of upper and lower respiratory tract with subsequent overgrowth and pneumonia. Non fermenters such as *Pseudomonas* spp. and *Acinetobacter* spp. were significantly associated with late onset VAP as observed by other workers but in our study even in patients with early onset VAP, *Acinetobacter* was the most common pathogen.[19,21,22] In their study Giantsou *et al*. also observed that potentially multiresistant *P. aeruginosa* was the most commonly isolated pathogen in both early onset and late onset VAP.[23]

In the present study, two types of samples, i.e. ETA and BAL were taken for each patient. Both methods produced comparable results. Wu *et al*. also showed that quantitative cultures of ETAs were comparable to those using invasive bronchoscopic methods.[24] VAP has been associated with mortality rates of 24-76% at a variety of institutions. Patients with VAP appear to have a 2-10 fold higher risk of death compared to ventilated patients without pneumonia.[25] The overall mortality in patients with VAP in our study was 48.33% while in the non VAP patients the mortality was 20% ($P < 0.05$). This figure is comparable to that of the study done by Mukhopadhyay *et al.* in which the overall mortality rate among patients with VAP was 47.3%.[21]

Conclusion

VAP is a serious problem in the ICU leading to longer hospital stay higher treatment costs and increased mortality and morbidity. Prolonged mechanical ventilation is an important risk factor. In addition, prior use of antibiotics increases the risk of acquiring drug resistant pathogens. Effective nursing care and adequate staffing also impact on VAP prevention. Better knowledge of local patterns of pathogens causing VAP can help facilitate treatment choices. Local data collected the similar studies can assist in making informed treatment choices.

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