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To Study Ventilator Associated Pneumonia Incidence, Risk Factors and Outcome in Patients on Mechanical Ventilation in Medical Intensive Care Unit

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A B S T R A C T

Patient's age group in our study ranged from 13 to 70 years. Mean age of VAP (Ventilator Associated Pneumonia) patients was 40 ± 15.87 years and that of NON VAP patients was 35.21 ± 13.33 years. Male dominance was found in our study. Among 30 VAP patients, 21 (70%) were male patients and 9 (30%) were female patients. Among 70 NON VAP patients, 42 (60%) were male patients and 28 (40%) were female patients. In present study out of 30 VAP patients 23 (76.67%) patients had associated comorbidity, and 7 (23.33%) patients did not. Presence of comorbid conditions like alcoholism (23.33%), diabetes (16.67%), hypertension (16.67%), chronic renal failure (10%) were significant statistically. Comorbid conditions contributed to development of VAP and mortality. So they should be treated vigorously. In present study mean duration of mechanical ventilation of VAP patients was 10.97 ± 4.70 days and that of NON VAP patients was 4.55 ± 2.64 days. There was direct relation between duration of mechanical ventilation and development of VAP. In our study gram negative microorganisms (90%) were common than Gram positive microorganisms (10%). *Pseudomonas* was the most common organism (33.33%) in our patients. causing late onset VAP (47.05%); whereas *Acinetobacter* was the most common cause for early onset VAP (53.84%). In present study almost all Gram negative microorganisms were sensitive to polymyxin-colistin group of antibiotics and Gram positive microbes were sensitive to linezolid and vancomycin. Antibiotics should be changed from broad spectrum to specific ones according to tracheal aspirate culture sensitivity reports. There was no significant difference between mortality in VAP and NON VAP patients. Mean duration of hospital stay of VAP patients was significantly more than NON VAP patients, indicating that presence of VAP increases morbidity of patients and cost of treatment.

Introduction

Mechanical ventilation is an essential, life-saving therapy for patients with critical illness and respiratory failure. Studies have estimated that more than 300,000 patients receive mechanical ventilation in the United States each year.

These patients are at high risk for complications and poor outcomes, including death. Ventilator-associated pneumonia (VAP), sepsis, Acute Respiratory Distress Syndrome (ARDS), pulmonary embolism, barotrauma, and pulmonary edema are among the complications that can occur in patients receiving mechanical ventilation. Mortality in patients with acute lung injury on mechanical ventilation has been estimated to range from 24% in persons 15–19 years of age to 60% for patients 85 years and older

The main aim of this study includes revealing incidence of Ventilator Associated Pneumonia, to study risk factors of Ventilator Associated Pneumonia and also to study outcome of Ventilator Associated Pneumonia.

Materials and Methods

Study design: Prospective study

Source of data

The study was carried out in a tertiary health care center. 100 patients on mechanical ventilator for more than 48 hours in medicine ICU were enrolled in study.

Duration of study

Two years from 1st December 2011 till 30th November 2013.

Inclusion criteria

1. Age > 12 yrs.
2. Patients who were on mechanical ventilation for more than 48 hrs.

Exclusion criteria

1. Patient who developed pneumonia within 48 hrs on ventilation.
2. Patient admitted with ARDS (Acute Respiratory Distress Syndrome), pneumonia, pulmonary tuberculosis at the time of admission.
3. Age < 12 yrs.

All relevant data from patient's medical records, bed side flow sheets including gender, age and admission diagnosis were noted. History of preexisting diseases like Diabetes Mellitus, Hypertension, Stroke, Ischemic Heart Disease, and previous admission to hospital and present symptomatology was listed and detailed physical examination was done. Details of medical interventions were recorded. These patients were prospectively followed for development of pneumonia.

The diagnosis of VAP was made according to clinical and laboratory findings (as per the CDC criteria) (Riza Hakan Erbay *et al.*, 2004) and the incidence was derived from the number of patients developing VAP out of 100 patients on ventilatory support for more than 48 hours in the ICU.

Diagnosis: 'Ventilator Associated Pneumonia' (VAP) is defined as the Clinical suspicion of pneumonia with occurrence of new and persistent radiographic infiltrate not otherwise explained, appearing on chest radiograph > 48hrs after onset of mechanical ventilation, along with any 2 of the following (Ibrahim *et al.*, 2001; Marini *et al.*, 1988; Trouillet *et al.*, 1998).

- i. Body Temperature > 38.3⁰C
- ii. Leukocytosis (>12,000WBC/cmm) or Leucopenia (< 4000WBC/cmm)
- iii. Purulent endotracheal secretions with Gram stain demonstration of bacteria and polymorphs.
- iv. Quantitative endotracheal aspirate cultures with growth >10⁶ colony forming units /ml

Investigations comprising complete blood count, biochemical tests including blood sugar, creatinine, and liver function tests, sputum Gram stain and culture, blood and pleural fluid culture were listed and analyzed, as per proforma.

Chest X-ray

On admission baseline chest X-ray was done just after intubation of each patient on mechanical ventilator. On follow up as patients developed signs of pneumonia chest X-ray were repeated. Development of new infiltrates, consolidation, cavitations, and pleural effusion were noted.

Endotracheal tube aspirate

On making a diagnosis of ventilator associated pneumonia, endotracheal tube aspirate was obtained for microbiological semiquantitative assay. Endotracheal aspirate was preferred over protected specimen brush (PSB) sampling and broncho-alveolar lavage (BAL),

After hand washing with soap and water for two minutes and wearing sterile gloves, 22-inch Ramson's 12F suction catheter was introduced through the endotracheal tube and advanced beyond the carina, to collect the lower respiratory tract secretions into a mucus trapper. After this, 2 ml of 0.9% saline was injected in the endotracheal tube with a sterile syringe to flush the exudates into a sterile

container for collection. The samples were immediately taken to the laboratory for processing. In the laboratory 0.001 ml of collected sample was directly inoculated on the blood agar, chocolate agar and McConkey's agar.

Following overnight incubation at 37⁰C, the media were examined for any growth and subsequently at 24, 48, 72, 96 hours and 7 days. A quantitative count of greater than 10⁶ CFU/ml was labeled as infection. The organisms detected on culture of tracheal aspirate were charted for the purpose of identifying the causative agent. Isolated colonies were subjected to Gram staining and biochemical tests for identification. Identification was carried out according to standard biochemical tests.

The patients diagnosed with VAP were started on initial empirical antibiotic therapy, which was guided by the fact whether a multi-drug resistant pathogen was expected. Later on, based on culture sensitivity reports the treatment was modified. The sensitivity pattern was studied by 'Kirby-Bauer disc diffusion method' according to the Clinical Laboratory Standards Institute (CLSI) guidelines. The tip of the endotracheal tube was also sent for microbiological assay as and when the patients were extubated as per clinical need.

Total leukocyte count was done as indicated by the admitting diagnosis or routinely at 48 hours or as indicated by chest X-ray findings.

The patients who developed VAP or met the above criteria within 96 hours of mechanical ventilation were categorized as early onset VAP and those who developed the same after this time period were categorized as late-onset VAP.

All the patients were managed with routine strategies for mechanical ventilation: semi-recumbent position at 45°, chlorhexidine oral care, deep vein thrombosis prophylaxis, active and passive chest physiotherapy. None of the patients were paralyzed.

The incidence of VAP was noted and each surrogate variable was analyzed. The surrogate variables that included risk factors for VAP were use of nasogastric tube feeding, IV sedative drugs, duration of mechanical ventilation, reintubation, and tracheostomy. Each of these variables were noted and compared between 2 groups – VAP and non-VAP. Peptic ulcer prophylaxis was given to all patients.

Comorbid conditions like hypertension, diabetes mellitus, chronic renal failure, ischemic heart disease, alcoholism and neurosurgical intervention were studied.

The patients were followed up from admission to MICU to till their final outcome i.e. either discharge or death. Resolution of the disease in the patient was defined as clinical improvement accompanied by normal temperature, decreased volume and transparency of tracheobronchial secretions and radiological confirmed elimination of the infiltrates. Pneumonia was called progressive if clinical and radiological picture was worsened and isolation of microorganism on semiquantitative method.

Measures assessed included the incidence of VAP, frequency of different pathogens isolated, their antibiotic sensitivity pattern, duration of mechanical ventilation and total duration of stay.

The data was entered and tabulated in Microsoft Excel. The statistics were analyzed using website. The obtained data

were subjected to the univariate analysis using the chi-square test. Comparison of data comprising mean± SD was done with the help of t-test. P-values less than 0.05 were considered as significant. We included the risk factors for z test; and age, duration of mechanical ventilation and duration of hospital stay for t-test (as it contains data comprising of mean ± SD).

Observations and results

Out of 100 patients on ventilator 30 (30%) patients developed VAP, i.e. Incidence of VAP in present study was 30%.

Maximum numbers of VAP patients (30%) were in 51-60 age group and minimum numbers (6.67%) were present in 61–70 year age group. Maximum (57.14%) numbers of NON VAP patients were in 21–40 age group and minimum (4.28%) numbers were in 61–70 age group.

Among 30 VAP patients, 21 (70%) were male patients and 9 (30%) were female patients.

Among 70 NON VAP patients, 42 (60%) were male patients and 28 (40%) were female patients.

Maximum numbers of VAP patients in our study group were of insecticide poisoning (36.67%). Amongst them 11 numbers of patients had a VAP (30.55%) and 25 patients had no VAP (69.44%).

Amongst cardiac insufficiency, hepatic encephalopathy and meningoencephalitis none of patient developed VAP.

Out of 30 VAP patients 13 (43.33%) patients developed early onset VAP; and 17(56.67%) patients developed late onset VAP.

Out of 30 VAP patients 23 patients (76.67%) had associated comorbidity, and 7 patients (23.33%) did not have any associated comorbidity.

Among 30 VAP patients, 7 patients were alcoholic (23.33%), 5 patients were hypertensive and diabetic (16.66%) each. Three patients (10%) suffered from chronic renal failure. Two patients (6.66%) had history of ischemic heart disease. One patient (3.33%) underwent neurosurgical intervention.

Impaired consciousness was the commonest risk factor for development of VAP i.e. out of 30 VAP patients 20 (66.67%) had impaired consciousness. Amongst 70 NON VAP only 16 patients (22.85%) had impaired consciousness

Use of IV sedatives was the least common risk factor, out of 30 VAP patients, only 2 patients (6.67%) were given IV sedatives. Among 82 patients who were on ventilator for less than 10 days, 16 (19.52%) patients developed VAP and 66 (80.48%) patients did not develop VAP.

Among 18 patients who were on ventilator for more than 10 days, 14(77.78%) numbers of patients developed VAP and 4 (22.22%) patients did not develop VAP.

Gram negative microorganisms (90%) were more common than Gram positive microorganisms (10%) in our patients.

Pseudomonas was the most common organism in our patients (33.33%). It was the most common organism causing late onset VAP (47.05%); whereas *Acinetobacter* was the most common organism causing early onset VAP (53.84%). *Streptococci* were the least common organisms found in our set up (3.33%).

All Gram Negative microorganisms were sensitive to polymyxin and colistin antibiotics (100%). It was found that *Acinetobacter* was resistant to 4 out of 6 antibiotics used in our study.

Both Gram positive microorganisms were sensitive to linezolid. *Streptococci* were sensitive to linezolid, vancomycin, amoxicillin sulbactam, 3rd generation Cephalosporins.

Out of 30 patients who developed VAP, 16(53.33%) patients were discharged, 11(36.67%) patients succumbed to their illness. Three patients (10%) were referred to higher center.

Out of 70 NON VAP patients 44(62.86%) patients were discharged, 25(35.72%) patients succumbed to death and one patient (1.42%) was referred to higher center.

There was no significant difference between mortality in VAP and NON VAP patients, $p > 0.05$.

In our study it was found that out of 11 VAP patients who succumbed to death, 3 (23.07%) patients were from early onset VAP group and 8 (47.06%) patients were from late onset VAP group.

Mortality rate was maximum in diabetic patients. Out of 5 diabetic VAP patients 4 (80%) succumbed to death.

Mortality was least common in alcoholic patients. Out of 7 alcoholic patients only 1 patient (14.28%) succumbed to death whereas Ischemic heart disease and neurosurgical intervention was not associated with mortality. Out of 30 VAP patients, 9 patients (30%) had total duration of stay in hospital for less than 10 days whereas maximum numbers of patients i.e.

21 (70%) required staying for more than 10 days. On the other hand in NON VAP patients, 55 patients (78.57%) had total duration of stay in hospital for less than 10 days and remaining 15 patients (21.85%) required staying for more than 10 days.

Out of 30 VAP patients, 9 patients (30%) had total duration of stay in hospital for less than 10 days whereas maximum numbers of patients i.e. 21 (70%) required staying for more than 10 days.

On the other hand in NON VAP patients, 55 patients (78.57%) had total duration of stay in hospital for less than 10 days and remaining 15 patients (21.85%) required staying for more than 10 days.

This study was done to assess the incidence, risk factors and outcome of ventilator associated pneumonia. Our study included 100 patients on mechanical ventilator for more than 48 hours.

Incidence of ventilator associated pneumonia

Most studies on VAP in intensive care unit patients have been carried out in developed countries. VAP continues to complicate the course of 8 to 28% of the patients receiving mechanical ventilation (Jean Chastre and Jean-Yves Fagon, 2002).

Out of 100 ventilated patients 30 met with criteria for diagnosis of VAP (CDC Criteria), therefore the incidence of VAP in present study was 30%.

Fagon *et al.* (1996) found incidence of VAP (28%) in their study. Indian study by Alok Gupta *et al.* (2011) had 28.04% VAP incidence in their study. Thus, present study correlates with above studies.

The higher incidence of VAP in present study could be owing to presence of comorbid conditions like diabetes, chronic renal failure etc. The health seeking behavior of patients is different compared with that in developed world. Owing to limited resources, there is delay for medical help which may advance the disease. This leads to longer duration of Mechanical Ventilation, which is directly proportional to development of VAP (Panwar *et al.*, 2005).

Age-wise distribution of patients in MICU

Mean Age of VAP patients in present study group was 40 ± 15.87 years. Bimodal distribution of age was observed with the first peak between 21–40 years age group (admission comprising of insecticide poisonings, snake bite) and second peak from 51–60 years age (stroke and comorbid patients included in this group).

Mean age of NON VAP patients in our study group was 35.21 ± 13.33 years. Maximum numbers of patient were present in group of 21–40 years.

Age distribution of patients in VAP and NON VAP group was statistically insignificant, as $P > 0.05$.

HinaGadani *et al.* (2010) found mean age of VAP patients as 34 years.

Study by Alok Gupta *et al.* (2011) on VAP also had similar results with mean age was 39.9 years and bimodal distribution of age; first peak in 11–30 years and second peak in 51–60 years age group in their study population.

Thus present study correlates with the above studies.

Sex-wise distribution of patients in MICU

In our set up, male patients predominately (21) contributing 70% of study population whereas female patients (9) contributed 30%. Although the incidence of VAP was high in males, it was statistically non significant ($p=0.9$, $p >0.05$)

Studies by Fabin Jaimes *et al.* (2007) found male predominance; where 72% of VAP patients were male and 28% were female.

Kuo-Tung Huang *et al.* (2010) found 67% of male and 33% of female patients in their VAP study.

Among 70 NON VAP patients of our study, 42 patients (60%) were male and 28 patients (40%) were female.

Thus, our findings are consistent with above mentioned studies.

Disease profile of patients in MICU

The study cohort comprised of 100 patients of various diseases like, insecticide poisoning, neurological disorder, sepsis, snake bite etc.

Majority of the cases were of insecticide poisoning (36). Among them 11 (30.5%) patients were from VAP and 25 (69.44%) patients were from NON VAP group.

Out of 19 cerebrovascular accident patients, 9 (47%) patients developed VAP and 10 (52.63%) patients did not develop VAP. Out of 16 neuromuscular snake bite patients, only 2 (12.5%) patients developed VAP whereas 14 (87.5%) patients did not.

There were 12 sepsis patients, out of them 4 (33.33%) patients were from VAP category and 8 patients (66.67%) from NON VAP category. There were 4 patients of

complicated malaria; among them only one patient (25%) had VAP and rest 3 (75%) patients had no VAP.

There were 3 patients of cardiac insufficiency and hepatic encephalopathy each and 2 patients of meningoencephalitis, none of them (0%) developed VAP.

There were 2 patients of Guillain- Barre syndrome, out of them 1 (50%) patient developed VAP. Out of 2 patients of tubercular meningitis with obstructive hydrocephalous only one (50%) patient developed VAP. There was only one patient of tetanus who developed VAP (100%).

Distribution of clinical spectrum was insignificant between VAP and NON VAP patients, $P>0.05$.

Incidence of VAP was greater either in patients who required prolonged mechanical ventilation (e.g. Guillain- Barre syndrome, Tetanus, organophosphorus poisoning, etc.) or in patients with neurological disorder who had impaired consciousness and inadequate cough reflexes which predisposed them for development of VAP.

Out of 30 VAP patients in our study- 36.67% patients were of insecticide poisoning, 30% patients were of cerebrovascular accident, 13.33% patients were of sepsis, 6.67% patients were of neuromuscular snake bite. There were 3.33% patients of complicated malaria, Guillain-Barre syndrome, tubercular meningitis with obstructive hydrocephalous and tetanus each.

Panwar *et al.* (2005) found that out of 24 VAP patients, 25% patients were of poisoning, 25% of the patients were of neurological complications, 8.33% patients were of sepsis, 4.16% patients were of complicated malaria, and 8.33% patients

were of Tetanus. None of the snake bite patient developed VAP in their study.

Disease profile studied by Noyal Mariya Joseph *et al.* (2009) in VAP patients had almost similar results. They found that out of 36 VAP patients 28% of patients were of poisoning, 11% patients were of snake bite and 2.77% patients were of Tetanus. In their study 2.77% patients of cardiac insufficiency developed VAP. Thus, the present study findings are consistent with above mentioned studies.

Time of onset of VAP

We studied our VAP patients according to time of onset of VAP, into early and late onset and found that both groups comprised roughly equal number of patients. Those who developed VAP within 96 hours of mechanical ventilation were categorized as having “early onset VAP” and those who developed after 96 hours were classified as “late onset VAP”. We found that 13(43.33%) patients developed early onset VAP and 17(56.67%) patients developed late onset VAP. This distribution was statistically insignificant, $P > 0.05$.

Onset of VAP in present study is similar to study by Noyal Mariya Joseph *et al.* (2009) where 41.7% cases were early onset VAP and 58.3% of the cases were late onset VAP.

Study by Panwar *et al.* (2005) found 33.33% patients developed early onset of VAP and 66.67% patients developed late onset VAP. Thus, our findings are consistent with above mentioned studies.

Comorbidity associated with VAP patients

In present study 23 (76.67%) VAP patients had associated comorbid conditions whereas

7 patients (23.33%) did not. It was statistically significant; $P < 0.05$. Maximum numbers of patients (76.67%) who developed VAP had some associated comorbid condition.

In present study 7 (23.33%) patients were alcoholic, 5 (16.67%) patients were diabetic and hypertensive each. 3 (10%) patients were suffering from chronic renal failure. Two (6.67%) patients had history of ischemic heart disease and 1 (3.33%) patient underwent neurosurgical intervention.

Study by Kuo-Tung Huang *et al.* (2010) found that out of 42 VAP patients, 12 (28.6%) were hypertensive, 11 (26.2%) patients were diabetic, 4 (9.5%) patients had ischemic heart disease and 6 (14.3%) patients suffered from chronic renal failure.

Fabian Jaimes *et al.* (2006) studied alcoholism, diabetic statutes, ischemic heart disease, and chronic renal failure as a comorbid conditions for development of VAP in their study. Thus, the present study findings are consistent with above mentioned studies.

Patients who developed VAP were more likely to be suffering from condition causing immunosuppression such as diabetes mellitus, chronic renal disease etc. It is studied that hyperglycemia affects neutrophils function, and trials suggest that keeping the blood sugar close to normal with exogenous insulin may have beneficial effects, including decreased risk of infection (Longo *et al.*, 2011).

Risk factors for development of VAP

Impaired consciousness

Level of consciousness has a significant impact on the incidence of VAP. In our

study impaired consciousness was the most common risk factor for development of VAP.

Out of 30 VAP patients 20 patients had impaired consciousness (66.67%) whereas out of 70 NON VAP patients only 16 patients (22.85%) had impaired consciousness. It was highly significant statistically, $P < 0.001$.

Study by Hina Gadani *et al.* (2010) found that incidence of VAP was significantly higher in stuporous patients (62.5%) than that of in conscious (37.75%) patients.

Study by Noyal Mariya Joseph *et al.* (2009) found that out of 36 VAP patients 8 (23%) patients had impaired consciousness whereas out of 164 NON VAP patients only 14 (8.5%) patients had impaired consciousness.

Thus, our findings are consistent with above mentioned studies.

This may be due to the higher chances of aspiration in patients with impaired level of consciousness and impaired cough reflexes.¹

Enteral feeding

Our study found RT feeding as a major factor present in 53.33% of VAP patients whereas in 70 NON VAP patients only 5 patients (7.14%) were given RT feeding. It was highly significant statistically, $p < 0.001$. Study by Noyal Mariya Joseph *et al.* (2009) who found RT feeding as risk factor for development of VAP in 42% patients. Study by Ranjit *et al.* (2011) found enteral feeding risk factor for development of VAP in 40.42% patients. Thus, our findings are consistent with above mentioned studies.

Enteral nutrition is generally regarded as beneficial in critically ill patients but it is

considered as risk factor for development of VAP, mainly because of an increased risk of aspiration of gastric contents as shown in studies conducted by Ferrer *et al.* (1999). Among the methods that have been advocated for reducing aspiration, feeding the patient in a semi recumbent position has been useful (Drakulovic *et al.*, 1999).

Reintubation

In present study population out of 30 VAP patients, 7 (23.33%) patients were reintubated and among 70 NON VAP patients only one (1.42%) patient was reintubated. Most patients in our study group were re-intubated for falling oxygen saturation, accidental self-extubation by patient and rarely as an elective procedure.

Reintubation was statistically significant in VAP patients than in NON VAP patients, $p < 0.05$.

Study by Rajasekhar *et al.* (2006) found reintubation as a risk factor in 36% patients. Study by Chiranjay Mukhopadhyay *et al.* (2010) found it as a risk factor in 42% patients.

Thus, our findings are consistent with above mentioned studies.

The increased incidence of VAP following reintubation was probably related to an enhanced risk of aspiration of the colonized oropharyngeal contents during each episode of intubation, by patient with subglottic dysfunction after several days of intubation (Jean Chastre and Jean-Yves Fagon, 2002). The findings of increased risk of VAP with reintubation imply that this procedure should not be included as a routine protocol in all mechanically ventilated patients; also it is safer to intubate patients (who have been extubated for some reason) as soon as

possible to minimize the risk of aspiration during the interval between extubation and reintubation.

Tracheostomy

It was found to be another independent risk factor for development of VAP.

In present study group, out of 30 VAP patients 5 (16.67%) patients required tracheostomy and prolonged ventilation whereas out of 70 NON VAP patients, 2 patients (2.85%) required tracheostomy.

It was not statistically significant $p > 0.05$.

Tracheostomy is considered as risk factor in study by Ibrahim *et al.* (2001) and Apostolopouou *et al.* (2003). It is probable the leakage, of pooled secretions around the tracheostomy tube into the trachea which increases colonization and leads to VAP. Presence of tracheostomy tube within the trachea may produce reflex mucus secretion which provide mucus receptors for bacterial adherence and serve as a bridge between the bacteria and respiratory epithelium (Noyal Mariya Joseph *et al.*, 2009).

However, some studies state that early and planned tracheostomy (within less than 7 days of intubation) protects mechanically ventilated patients from VAP (Panwar *et al.*, 2005). Our patients rather had tracheostomies between 7 and 14 days who needed prolonged ventilation.

Administration of intravenous sedatives to patients on Mechanical Ventilator might impair their cough reflexes, increasing the risk of aspiration and subsequently predisposing them for development of VAP.

In present study we had 2 (6.67%) patients amongst total 30 VAP patients who were given IV sedatives.

There was no significant association between use of IV sedatives and incidence of VAP, $p > 0.05$.

Noyal Mariya Joseph *et al.* (2009) had studied, use of IV sedatives as a risk factor for the development of VAP.

Dirks *et al.* (1987) in their study, comparing sucralfate versus antacids or H₂ blockers, had found that agents elevating gastric pH increased the risk of VAP by favoring gastric colonization with Gram negative bacilli.

Most of the patients who developed VAP in our study were on H₂ blockers and were given semirecumbent ($>30^\circ$) position.

Effect of duration of mechanical ventilation on incidence of VAP

The relation between the duration of endotracheal intubation and development of VAP has been examined by several authors.

In present study group among 82 patients who were ventilated for less than 10 days, 16 (19.52%) patients developed VAP and 66 (80.48%) patients did not develop VAP whereas among 18 patients who were ventilated for more than 10 days, 14 (77.78%) numbers of patients developed VAP and 4 (22.22%) patients did not.

Mean duration of mechanical ventilation of VAP patients was 10.97 ± 4.70 days and that of NON VAP patients was 4.55 ± 2.64 days. There was significant association between duration of mechanical ventilation and development of VAP, $p < 0.001$.

Hina Gadani *et al.* (2010) found that mean duration of mechanical ventilation was 19 days for VAP patients and 11 days for NON VAP patients.

Panwar *et al.* (2005) has also emphasized a direct correlation between the duration of mechanical ventilation and development of VAP.

Thus, our findings are consistent with above mentioned studies. The incidence of VAP is directly proportional to the duration of mechanical ventilation. Therefore, duration of ventilation has to be reduced to get rid of morbidity and mortality associated with mechanical ventilation which can be achieved by proper weaning protocols and titrating sedation regimen as per the need of patients.

Among the various methods of weaning, spontaneous breath trial has been proved to be very effective as compared with intermittent mandatory ventilation (IMV), as IMV promotes respiratory fatigue (Marini *et al.*, 1988; Imsand *et al.*, 1994). Once a daily trial of spontaneous breathing and prolonged period of rest may be the most effective methods of weaning to recondition respiratory muscles that may have been weakened during mechanical ventilation (Faulkner, 1985; Rochester *et al.*, 1988).

Microbiological profile in early and late onset VAP patients in MICU

In present study, we observed that Gram negative organisms (90%) were the predominant causative flora in VAP patients, with *Pseudomonas* being the commonest (33.33%) followed by *Acinetobacter* (26.67%), *Klebsiella* (13.33%) and *E. coli* (6.67%). There was 10% contribution from polymicrobial flora infection.

In present study *Acinetobacter* (53.84%) was the most common organism in early onset VAP and *Pseudomonas* (47.05%) was most common in late onset of VAP.

This is similar to trends reported previously. The study by Mandakini Pawar *et al.* (2003) showed a similar predominance of Gram negative organisms. Rajasekhar *et al.* (2006) in their study found that most frequently isolated organisms were *Acinetobacter* and *Pseudomonas*. The predominant organisms in the early onset VAP group were *Acinetobacter* and *Klebsiella*. In the late onset group *Pseudomonas* was the most predominant organism. In present study we found only 10% Gram positive organisms which is in accordance with study by Noyal Mariya Joseph *et al.* (2009) who found 14.9% Gram positive organisms in their study.

Microorganisms responsible for VAP may differ according to the population of patients in the ICU, the durations of hospital and ICU stays, and the specific diagnostic methods used. The microbial flora associated with VAP represents the common organisms present in the gut, oropharynx and environment (i.e. Gram negative). Colonization in patients on ventilator has been recognized as an important source for these Gram negative infections.

Antibiotic sensitivity pattern

In our study group most of the Gram negative microorganisms were sensitive to polymyxin, colistin, imipenem and piperacillin- tazobactam antibiotics, whereas most of the Gram positive microorganisms were sensitive to linezolid and vancomycin.

Pseudomonas was isolated in 10 samples and was found to be maximally susceptible to polymyxine and colistin. *Pseudomonas* showed favourable susceptibility pattern to Imipenem and piperacilline- tazobactam. Whereas it was fairly resistant to drug such

as 3rd generation cephalosporins, amikacin and ciprofloxacin.

Acinetobacter was isolated in 8 samples and showed maximum susceptibility to polymyxine and colistin. It was moderately susceptible to imipenem and was highly resistant to piperacillin-tazobactam, 3rd generation cephalosporins, amikacin and ciprofloxacin.

Klebsiella was isolated in 4 samples and was highly susceptible to polymyxine, colistin, imipenem and piperacillin-tazobactam. It showed fairly susceptibility 3rd generation cephalosporins, amikacin and ciprofloxacin.

E. coli was isolated in 2 samples it was maximum susceptible to polymyxine, colistin, imipenem and amikacin. *E. coli* showed favourable susceptibility to piperacillin-tazobactam 3rd generation cephalosporins and ciprofloxacin.

MRSA was isolated in 2 samples and all isolates were resistant to amoxicillin sulbactam and 3rd generation cephalosporins. They showed excellent sensitivity to linezolid and fair susceptibility to vancomycin.

Streptococci were isolated in 1 sample. They were susceptible to linezolid, vancomycin, amoxicillin sulbactam and 3rd generation cephalosporins.

polymicrobial flora were mostly susceptible to polymyxin colistin. They were fairly susceptible to imipenem and amikacin and resistant to rest of antibiotics. The sensitivity results are similar to study by Alok Gupta *et al.* (2011) and by Vishal Anand Gupta *et al.* (2013).

Since ventilator associated pneumonia accounts for significant morbidity and

mortality, broad spectrum antibiotics are used empirically and this further enhances the chance for individual patients to be colonized with resistant organisms. Strict antibiotic policies have to be laid down for the ICU so as to restrict the use of empiric broad spectrum antibiotics. This will reduce the frequency of colonization. The knowledge of common organisms in ICU and their antibiotic susceptibility is important for institution of appropriate antimicrobial therapies. Over use of third generation cephalosporins in a hospital setting as first line therapy has been the cause for increased resistance to these drugs. Hence a combination of betalactam/betalactamase inhibitor such as piperacillin/tazobactam, ticarcillin/clavulanate has been found to be effective for prevention of colonization (Trouillet *et al.*, 1998).

Outcome of vap patients in MICU

Mortality rate for VAP patients ranges from 24 to 50% and can reach 76% in some specific settings.

In present study out of 30 VAP patients, 16 (53.33%) patients were discharged, 11 (36.67%) patients succumbed to their illness and 3 (10%) patients were referred to higher center for further treatment. Among 70 NON VAP patients 44 (62.85%) patients got discharge, 25 (35.72%) patients succumbed to death and one (1.42%) patient was referred to higher center.

Study by Kollef *et al.* (1999) found mortality rate of 37.5% in their study of ventilator associated pneumonia. Study by Panwar *et al.* 2005) found mortality rate of 37% in VAP patients. Study by Alok Gupta *et al.* (2011) observed 32.71% mortality in their study population. Thus, our findings are consistent with above mentioned studies.

In present study mortality in VAP group was 35.72% and the difference was not statistically significant ($p > 0.05$), while in NON VAP group, it was 36.67%.

Table.1 Incidence of VAP

	Number of Cases (N)	Percentage (%)
VAP	30	30%
NON VAP	70	70%
TOTAL	100	100

Table.2 Age-wise distribution of patients in MICU

Age in Years	Number of VAP Patients N (%)	Number of non VAP Patients N (%)
13-20	3 (10%)	08 (11.42%)
21-30	7 (23.33%)	20(28.57%)
31-40	6 (20%)	20(28.57%)
41-50	3 (10%)	12(17.14)
51-60	9 (30%)	07(10%)
61-70	2 (6.67%)	03(4.28%)
MEAN ± SD	40± 15.87 years	35.21± 13.33 years
P Value by t Test	p >0.05, INSIGNIFICANT	

Age distribution: insignificant; patients were equally distributed in both groups.

Table.3 Sex-wise distribution of patients in MICU

Sex	Total number of patients	Number of VAP Patients N (%)	Number of Non VAP patients N (%)
Male	63	21(70%)	42(60%)
Female	37	09(30%)	28(40%)
Total	100	30	70
Chi square Test=0.9, DF=1, p > 0.05			

Sex distribution: insignificant; both groups were equally distributed.

Table.4 Disease profile of patients in MICU

Disease profile	Total number patients on ventilator	Number of VAP patients N (%)	Nuber of non VAP Patients N (%)	Percentage of VAP patients (out of 30 vap patients)
Insecticide poisoning	36	11(30.55%)	25(69.44%)	36.67%
Cerebrovascular accident	19	09(47.36%)	10(52.63%)	30%
Neuroparalytic snake bite	16	02(12.5%)	14(87.5%)	6.67%
Sepsis	12	04(33.33%)	8(66.67%)	13.33%
Complicated malaria	4	01(25%)	3(75%)	3.33%
Cardiac insufficiency	3	00	3(100%)	0
Hepatic encephalopathy	3	00	3(100%)	0
Meningoencephalitis	2	00	2(100%)	0
Gb syndrom	2	01(50%)	1(50%)	3.33%
Tbm with hydrocephalous	2	01(50%)	1(50%)	3.33%
Tetanus	1	01(100%)	0	3.33%
TOTAL	100	30	70	100%

Chi -square Test=5.47, DF=4, p > 0.05

Insignificant: distribution of clinical spectrum was insignificant between VAP and NON VAP groups

Table.5 Time of onset of VAP

Onset of VAP	Number of VAP patients N (%)
Early vap (48-96hours)	13 (43.33%)
Late vap (>96 hours)	17 (56.67%)
Total	30 (100%)

Chi square Test, p > 0.05, DF=1 Insignificant

Table.6 Associated comorbid conditions in VAP patients

Comorbidity	VAP PATIENTSN (%)
Alcoholism	07 (23.33%)
Hypertension	05 (16.67%)
Diabetes mellitus	05 (16.67%)
Chronic renal failure	03 (10%)
Ischemic heart disease	02 (6.67%)
Neurosurgical intervention	01 (3.33%)
No comorbidity	07(23.33%)
Total	30 (100%)

Chi-square Test,p < 0.05, DF=1, Significant.

Presence of comorbid condition was significant in VAP patients.

Table.7 Risk factors for development of VAP in MICU patients

Risk Factors	Number of VAP Patients N (30)	Number of Non VAP Patients N (70)	P Value By Z Test
Impaired consciousness	20 (66.67%)	16 (22.85%)	P< 0.001**
RT feeding	16 (53.33%)	05 (7.14%)	P< 0.001**
Reintubation	07 (23.33%)	01 (1.42%)	P< 0.05*
Tracheostomy	05 (16.67%)	02 (2.85%)	P> 0.05 ^
IV sedatives	02 (6.67%)	04 (5.71%)	P>0.05^

** Highly Significant; * significant; ^ Not Significant.

Table.8 Effect of duration of mechanical ventilation on incidence of VAP

Duration of Mechanical Ventilation	VAP Patients(30) N (%)	Non VAP Patients (70) N (%)	Total Patients (100)
< 10 Days	16(19.52%)	66 (80.48%)	82
>10 Days	14(77.78%)	04 (22.22%)	18
Mean ±SD	10.97± 4.70 days	4.55± 2.64 days	6.48± 4.47 days
Chi- Square Test= 23.86, DF= 1, p< 0.001, Highly Significant			

There was significant difference between duration of mechanical ventilation in VAP and NON VAP patients

Table.9 Microbiological profile of early and late onset VAP patients in MICU

Microorganism	Early onset (n)	Percent	Late onset (n)	Percent	Total	Percent
<i>Pseudomonas</i>	2	15.38%	8	47.05%	10	33.33%
<i>Acinetobacter</i>	7	53.84%	1	5.88%	8	26.67%
<i>Klebsiella</i>	1	7.69%	3	17.64%	4	13.33%
Polymicrobial flora	1	7.69%	2	11.76%	3	10%
<i>E. coli</i>	0	0	2	11.76%	2	6.67%
MRSA	1	7.69%	1	5.88%	2	6.67%
<i>Streptococci</i>	1	7.69%	0	00%	1	3.33%
Total	13		17		30	100%

Table.10 Antibiotic sensitivity pattern in Gram negative organisms

Organisms	Polymyxin Colistin N (%)	Imipenem N (%)	Piperacillin Tazobactam N (%)	3 rd Generation Cephalosporins N (%)	Amikacin N (%)	Ciprofloxacin N (%)
<i>Pseudomonas</i> (10)	10 (100%)	8 (80%)	5 (50%)	4 (40%)	3 (30%)	3 (30%)
<i>Acinetobacter</i> (8)	8 (100%)	4 (50%)	0	0	0	0
<i>Klebsiella</i> (4)	4 (100%)	4 (100%)	4(100%)	3 (75%)	3 (75%)	3 (75%)
<i>E. coli</i> (2)	2 (100%)	2 (100%)	1 (50%)	1 (50%)	2 (100%)	1 (50%)

Table.11 Antibiotic sensitivity pattern in Gram positive organisms

Organisms	Linezolid N (%)	Vancomycin N (%)	Amoxicillin sulbactam N (%)	3 rd generation cephalosporins N (%)
MRSA 2	2 (100%)	1(50%)	0 (0%)	0
Streptococci 1	1 (100%)	1 (100%)	1 (100%)	1 (100%)

Table.12 Outcome of patients in MICU

Outcome	Number of VAP patients	Percentage	Number of non VAP patients	Percentage
Discharge	16	53.33%	44	62.86%
Death	11	36.67%	25	35.72%
Referred	03	10%	01	1.42%
Total	30	100%	70	100%

Chi-square Test $p > 0.05$, DF =1, Insignificant.

Table.13 Mortality with respect to onset of VAP in micu patients

VAP Onset	Total Number of Patients	VAP Mortality	Percentage
Early VAP	13	3	23.07%
Late VAP	17	8	47.06%
Total	30	11	

Table.14 Mortality with respect to associated comorbidity

Comorbidity	VAP N	VAP Mortality N (%)
Alcoholism	07	1(14.28%)
HTN	05	2(40%)
DM	05	4(80%)
CRF	03	2(66.66%)
IHD	02	0
Neurosurgical intervention	01	0
No comorbidity	07	2(28.57%)
Total	30	11

Table.15 Total duration of hospital stay of ventilated patients

Total Duration of Hospital Stay in Days	VAP Patients (30) N (%)	Non VAP Patients (70) N (%)	Total Patients (100) N (%)
< 10	09 (30%)	55 (78.57%)	64 (64%)
10-20	17 (56.67%)	13 (18.57%)	30 (30%)
>20	04 (13.33%)	02 (2.85%)	06 (06%)
MEAN±SD	13.53± 6.74 days	7.3± 4.77 days	9.17±6.12 days

Chi-square Test, $p < 0.001$, DF=1, Highly Significant

Similarly study by Hina Gadani *et al.* (2010) and study by Panwar *et al.* (2005) found that difference between mortality rates of VAP and NON VAP patients was statistically significant.

Mortality with respect to onset of VAP in MICU patients

In present study it was found that out of 11 VAP patients who succumbed to death, 3 patients (23.07%) were from early onset VAP group and 8 patients (47.06%) were from late onset VAP group suggesting that early onset VAP had good prognosis as compared with late onset VAP.

A similar high mortality rate associated with late onset VAP (66.67%) than early onset VAP (20%) was observed in study by Hina Gadani *et al.* (2010).

Studies have shown that previous antibiotics use decreases mortality in early onset of VAP but markedly increases multi drug resistant pathogens leading to increased mortality in late onset VAP (Park, 2005).

The de-escalation strategy fully endorsed by American Thoracic Society, which means initiation of a broad spectrum antibiotic and changing to a narrow spectrum according to antibiotic sensitivity reports will reduce inappropriate antibiotic use and subsequently the drug resistant pathogens (American Thoracic Society and Infectious Diseases Society of America, 2005).

Mortality with respect to associated comorbidity

In present study it was observed that out of 5 diabetic patients 4 patients (80%) died, out of 3 chronic renal failure

patients 2 patients (66.67%) succumbed to death and among 5 hypertensive patients 2 (40%) patients had death. So mortality rate was the highest in diabetic patients. Alcoholic patients had less (14.28%) mortality rate.

It was observed that no mortality was found in patients having history of ischemic heart disease and who underwent neurosurgical intervention. VAP patients having no associated comorbidity had 28.57% mortality rate. Study done by Kuo-Tung Huang *et al.* (2010) on early predictor of outcome of VAP, they found similar mortality rates among VAP patients having associated comorbidity. They found out that mortality rate was 20% in hypertensive and diabetic patients, 30% in chronic renal disease patients and no mortality in ischemic heart disease patients. Associated comorbid conditions contributed to mortality rate in VAP patients (Longo *et al.*, 2011).

Total duration of hospital stay of ventilated patients

In our study, out of 30 VAP patients, 9 (30%) patients had total duration of hospital stay for less than 10 days whereas maximum numbers of patients i.e. 21 (70%) required staying for more than 10 days. On the other hand in NONVAP patients, 55 (78.57%) patients had total duration of hospital stay for less than 10 days and remaining 15 patients (21.85%) required staying for more than 10 days.

Mean duration of MICU stay of VAP patients was 13.53 ± 6.74 days and NON VAP patients was 7.3 ± 4.77 days. It was highly significant statistically, $P < 0.001$.

Study by Ranjit and Bhattarai (2011) found that VAP group patients had significantly longer duration of ICU stay. They found

mean duration of hospital stay of VAP patients was 29 ± 17.88 days and that of NON VAP patients was 9.22 ± 5.14 days.

Study by Riza Hakan *et al.* (2004) found that hospital stay increased by 5.9 days in patients who developed VAP. Thus, the present study findings are consistent with above mentioned studies.

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