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PREVALENCE PATTERN OF MORBIDITY AND MORTALITY IN VENTILATION ASSOCIATED PNEUMONIA (VAP) PATIENTS OF INTENSIVE CARE UNIT (ICU) IN MAHARASHTRA REGION.

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Abstract

Objective: To study the prevalence of morbidity & mortality in ventilation associated pneumonia (VAP) patients of intensive care unit (ICU). **Material and Methods:** The present study was conducted on 265 admitted patients of ICU during the period of July 2004 to June 2005 in Government Medical College & Hospital. A total of 100 patients on mechanical ventilation were followed-up prospectively. The microbiological test results were reported to the clinician immediately for appropriate antibiotic administration helping the betterment of the patient. Patients were followed-up twice a week on day 4 and day 7. The end-point was betterment with removal of patient from ventilation or death of the patient. **Results:** Out of the total 100 patients studied, 97 were colonized either with monomicrobial or polymicrobial pathogens. Out of these 97 colonized patients, 57 developed ventilation-associated pneumonia (VAP) with incidence of 58.76% among colonized patients. The overall mortality was 57% of the total studied patients. The mortality in patients colonizing trachea and developing VAP was 54.39%, whereas, the mortality in those only colonizing, but not developing VAP was 41.86%. Maximum 77.4% deaths were in the poisoning cases. Colonization rate among OPP cases was 97.44%, VAP rate was 64.10% and death rate was 43.59%. **Conclusion:** Knowledge about the colonization in mechanically ventilated patients, developing into VAP and their antimicrobial susceptibility pattern at the institute level by prospective study will definitely be useful in formulating its antibiotic policy and the optimal management of the patients by decreasing the incidence of morbidity and mortality amongst VAP.

Keywords: Ventilation-associated pneumonia, morbidity and mortality, colonization.

INTRODUCTION:

Hospital-acquired pneumonia is the most common nosocomial infection reported among mechanically ventilated patients admitted in the ICU, where it is labeled as 'Ventilation-associated pneumonia' (VAP), with highest mortality & morbidity in spite of the availability of potent broad-spectrum antimicrobial agents, multifaceted supportive care modalities, and the use of preventive measures.**(1,2)** The mortality rate in VAP ranges from 24% to 80% in several studies**(3,4)** with 2 to 10 fold higher risk of death in ICU-ventilated patients.**(5)** The primary risk

factor for development of VAP is mechanical ventilation with its requisite endo-tracheal intubation.**(6)** To label the presence of organisms in the trachea as 'colonization' or 'pneumonia' is not a very simple task.**(7,8)** VAP is usually seen in patients who are mechanically ventilated for more than 48 hrs. with one of the following features according to Johanson *et al*.**(6,9,10)** (New or progressive pulmonary infiltrate on X-ray chest, Fever > 38 ° C, Polymorphonuclear Leukocytosis > 10,000 / cu.mm., Purulent tracheobronchial secretions).

The high mortality associated with VAP in the medical ICU has led to strategies, which encourage rapid institution of broad-spectrum antibiotics.**(11)** The literature supports the view that inadequate antibiotics for 48-72 hrs. is associated with an increased mortality.**(11)** Several studies have shown that proper antimicrobial treatment of patients with VAP get better the outcome. **(9,12)** The selection of empiric antibiotic therapy should be based on whether the patient has received prior antimicrobial therapy and on the duration of mechanical ventilation.**(13)** So the present study was conducted for effectiveness of antimicrobial therapy by seeing the prevalence of morbidity & mortality pattern of VAP amongst intensive care unit patients.

MATERIALS & METHODS:

The present study was conducted in 5-bedded Intensive Care Unit (ICU), Government Medical College & Hospital, Aurangabad (Maharashtra). A total of 265 patients were admitted in the ICU during the study period from july 2004 to june 2005.

Case Selection

Patients with more than 48 hours of mechanical ventilation (MV) with endotracheal tube were included in the study.**(7)** Patients on mechanical ventilation for 48 hours or less or who developed pneumonia within 48 hours of MV were excluded from the study. In addition, patients with fulminant pneumonia and pulmonary edema were excluded from the study. All the patients were given antibiotic prophylaxis with administration of gentamicin.

A total of 100 patients on mechanical ventilation with intubation tube fulfilling the inclusion criteria were followed-up prospectively. Exclusion criteria were severe immunosuppression (organ transplantation, AIDS) and evidence of pulmonary infection or suspicion of gross aspiration at admission.**(14)** Informed consent was obtained from the patient or the nearest relative of the patient. According to Johanson *et al* criteria, the episodes of ventilation-associated pneumonia were diagnosed. **(9)** The end-point was betterment with removal of patient from ventilation or death of the patient.

Data collection

The details of Patients fulfilling the inclusion criteria were recorded in the specially designed proforma which includes patient's name, age, sex, registration number and detail history was taken. Major complaints, underlying disease, indication for intubation, general & systemic examination, and results of routine investigations with X-ray chest reporting were noted. Patients receiving antibiotics with its duration of administration was also recorded.

Patients were followed-up twice a week on day 4 and day 7. During the follow-up visits, special note about the duration of MV, CBC, X-ray chest, rise in temperature and extra pulmonary focus, if any was noted.

Collection and transport of Endotracheal-aspirate (EA)

On the day of intubation of the patient, the tracheal swab was taken for the presence of bacterial colonization. The endotracheal aspirate of the patient was taken within the first 24 hours of intubation using a sterile mucus extractor (trap) under all aseptic precautions. On subsequent visits on day four and seven as well, the endotracheal aspirates were collected similarly and then transported immediately to laboratory in the Department of Microbiology. The results were reported to the clinician immediately for appropriate antibiotic administration helping the betterment of the patient.

RESULTS:

During the one-year study period, from July 2004 to June 2005, a total of 265 patients were admitted in the medical ICU. Out of which 100 patients mechanically ventilated (MV) with intubation tube for more than 48 hours were included in the study to evaluate the morbidity and mortality pattern of VAP. The study group comprised of 64 males and 36 female patients.

Out of the total 100 patients studied, 97 were colonized either with monomicrobial or polymicrobial pathogens. Out of these 97 colonized patients, 57 developed ventilation-associated pneumonia (VAP) with incidence of 58.76% among colonized patients. In all, 3 patients were not colonized by the microorganisms, either on day 1 or day 5 of intubation and showed signs of recovery. Thus, these 3 patients were extubated and discharged on day 6 with complete recovery from the symptoms they presented with, at the time of admission.

The incidence of VAP in the present study was seen in 57 patients (57%) out of 100 patients studied. Most of the patients, 31 (54.4%) of the total 57 patients were in the age-group 21-40 years. Mean age of patients with VAP was 31.7 years. Total four patients were at extremes of age. The numbers of males affected were almost twice 64.9% compared to females 35.1%. (Table-1)

Table 1 : Age and Sex Wise Distribution of VAP

AGE (years)	MALE	FEMALE	TOTAL
0-10	0	1	1
11-20	5	2	7
21-30	12	7	19
31-40	7	5	12
41-50	3	2	5
51-60	7	0	7
61-70	1	2	3
71-80	2	1	3
TOTAL	**37**	**20**	**57**

Out of 57 developing VAP, 44 patients developed on day 7 of mechanical ventilation in the ICU. Only 13 patients developed VAP on day 4 of MV. Considering the cut-off day as fourth day after mechanical ventilation (MV) for defining early and late-onset VAP, 13 (22.8%)

patients developed early-onset and 44 (77.2%) patients developed late-onset VAP.

Of the total episodes of ventilator-associated pneumonia, 48 (84.2%) showed polymicrobial (two or more than two organisms) growth. Only 9 patients (15.8%) developed VAP due to the monomicrobial organism. Of the 48 patients who developed VAP due to polymicrobial organisms, 9 (18.6%) patients developed on day 4, while with increase in duration of MV to day 7, 39 (81.4%) more new patients developed VAP.

The most common category was poisoning (66 %), mainly organophosphorus (OPP) accounting 39% and the strychnine poisoning 27% of the cases. The numbers of neural cases with Guillain-Barre Syndrome (GBS) were 14, while 10 patients presented each with chronic obstructive pulmonary disease (COPD), 6 with acute renal failure (ARF) and, 4 with acute respiratory distress syndrome (ARDS). (Table-2) Thus, almost all the cases included were of non-infective etiologies. Almost all of the patients had received prophylactic antibiotics after intubation, which consisted mainly of Inj. Ampicillin and Inj.Cefotaxime.

Maximum 77.4% deaths were in the poisoning cases. Thirty-nine patients in the study group were of OPP. Out of the 25 of these developing VAP, 17 patients died. 1 patient did not colonize with any of the organisms and was discharged on day 5 with complete recovery. Thus, colonization rate among OPP cases was 97.44%, VAP rate was 64.10% and death rate was 43.59%. 7 patients died without developing VAP in out of total 14 patients of OPP who did not developed VAP. The reasons for death in these patients varied from cardiac arrest to respiratory failure. Out of the remaining 7 patients, 1 was discharge on day 5 after recovery, 2 were discharged against medical advice after about a week after admission and 4 recovered after appropriate antimicrobials.

Twenty-seven patients in the study group were of strychnine poisoning. Out of the 14 of these developing VAP, 7 patients died. Thus, colonization rate among strychnine poisoning cases was 100%, VAP rate was 51.85% and death rate was 25.93%.5 died due to respiratory failure and cardiac arrest in out of the 13 patients of Strychnine poisoning who did not developing VAP. Total 8 patients recovered after adequate management with broad-spectrum antibiotics, nutritional supplement and supportive care.

Of the total 14 patients of GBS studied, 7 developed VAP. Of these, 3 patients died of VAP due to polymicrobial. 1 patient did not colonize with any organisms and was discharged on day 5 with complete recovery. Thus, colonization rate among cases of GBS was 100%, VAP rate was 50% and death rate was 21.43%. Of the 7 patients of GBS not developing VAP, 1 patient was discharged on day 5 after recovery, 2 patients died of cardiac arrest and remaining 4 patients recovered well without any residual complications.

Ten patients in the study group were of chronic obstructive pulmonary disease (COPD). Out of the 6 of these developing VAP, 2 patients died. Thus, colonization rate among COPD cases was 100%, VAP rate was 60% and death rate was 20%. Of the 4 patients of COPD not developing VAP, 2 died due to respiratory arrest, while the other two recovered and were discharged.

Of the total 6 patients of ARF studied, 3 developed VAP. Of these, 1 patient died on day 7 with late-onset VAP due to polymicrobial. 1

patient did not colonize with any organisms and was discharged on day 5 with complete recovery. Thus, colonization rate among cases of ARF was 83.33%, VAP rate was 50% and death rate was 16.67%. Of the 3 non-VAP patients of ARF, 1 died due to respiratory failure and 1 patient was shifted to the dialysis unit for further management. 1 patient was extubated and discharged on day 5 after recovery.

Table 2 : Death Comparison between VAP and NON-VAP Patients.

Disease	Patients developing VAP	Death in VAP patients	NON-VAP patients	Death in NON-VAP patients	Total Deaths
OPP (39)	25	**17**	14	**07**	**24**
Strychnine poisoning (27)	14	**07**	13	**05**	**12**
GBS (14)	07	**03**	07	**02**	**05**
COPD (10)	06	**02**	04	**02**	**04**
ARF (06)	03	**01**	03	**01**	**02**
ARDS (04)	02	**01**	02	**01**	**02**
TOTAL (100)	**57**	**31**	**43**	**18**	**49**

Total 4 patients in the study group were of acute respiratory distress syndrome (ARDS). Out of the 2 of these developing VAP, 1 patient died on day 4 with early-onset VAP due to monomicrobial. Thus, colonization rate among ARDS cases was 100%, VAP rate was 50% and death rate was 25%. Of the 2 non-VAP patients of ARDS, 1 died due acute respiratory failure and 1 patient recovered and was discharged. (Table-2)

DISCUSSION:

Ventilation-associated pneumonia (VAP) is the commonest complication in patients mechanically ventilated with endotracheal intubation tube. A wide range of microorganisms causes the potential problem of VAP. **(2,4,14,15,16)**

In the present study, colonization occurred in 97 patients out of the total 100 patients studied. Hence, total colonization rate was found to be 97%.

Various studies have reported differential colonization rates of trachea by varying pathogenic microorganisms, most commonly by the Gram-negative bacteria. **(7,8,14)** Delclaux *et al* in a study showed 66%, Johanson *et al* found 84.6% and Albert *et al* reported 85% overall colonization rate in their study group.**(17,9,7)**

Incidence of VAP

The incidence of VAP as reported by various workers varied from 9 to 78 %, depending on the severity of illness, type of patients studied, prophylactic antibiotic administration, the techniques & criteria used to diagnose the pneumonia.**(3,7,18,19)** This is due to diverse study design, various methods of specimen

collection and different diagnostic methodologies.

In present study incidence of VAP was 57%. Salata et al have shown 41% , Kollef et al 9.3%, Craven et al 21%, and Akca et al 31%.**(8,15,20,21)** In the present study, total 57% patients developed ventilator-associated pneumonia (VAP).The increased incidence of VAP in the present study might be due to longer period of MV averaging 13 days. It is a known fact that as the duration of ventilation increases, the chances of developing pneumonia also increases.

Age and Sex Distribution

Fagon *et al* in their study on surgical and medical ICU patients, using PSB for diagnosis found that majority of patients were of older age group (65 ± 10.5 years). **(4)** Similarly, George *et al* in their study on mechanical ventilation (MV) patients in medical ICU using PSB and BAL for diagnosis reported a mean age of 57 years (± 2.7 years) for VAP patients.**(2)** In both the above mentioned studies the underlying conditions that necessitated ventilation included chronic obstructive pulmonary disease, congestive cardiac failure, renal failure and shock. Conditions such as poisoning, CNS diseases like GBS and neuromuscular diseases accounted for only a minority of VAP cases.

In contrast, the present study of patients developing VAP included only 10.5% patients with an underlying diagnosis of COPD, 5.3% with ARF and 3.5% patients with ARDS. Involvement of CNS with most cases of poisoning comprised 80.7% of patients developing VAP. In a study conducted by Latorre *et al* the mean age of the patients was 17 years.**(3)** On the other hand, Craven *et al* found the mean age of 55 years in their study group.**(20)** In the present study, the mean age of patients developing VAP was observed to be - 31.7 years. Most of the patients in the present study were clustered in the young age group of 21-40 years, comprising of 56.1% of the patients. This subset of population is generally considered to be healthy and with a lesser predisposition to illness as compared to the older age groups. In our study, only four patients were at the extremes of life developing VAP. There were three between the age group 71-80 years and one patient with age less than 1 year. These patients were more likely to be in an immunocompromised state and therefore more prone to infection. This might explain the younger age group of VAP patients in the present study. In the present study, males accounted for 64.9% of VAP cases. Chastre *et al* also reported higher 52.8% of male patients and George *et al* reported 87.18% incidence of the male patients developing VAP in their study group.**(16,2)** Akca *et al* also reported more males 166 (63.9%) as compared to females 94 (36.1%), in their study on VAP.**(21)**

Early & late onset VAP

In the present study, the tracheal aspirates were followed up on days 1, 4 and 7 of intubation to evaluate the colonizing organisms causing VAP. In our study, considering day 4 for early and late-onset VAP, 22.8% patients developed early-onset VAP, while 77.2% patients developed late-onset VAP.

The result of our study relates well to the study carried out by Trouilliet *et al* who, in their study of 135 episodes of VAP found 25.2% of early-onset VAP and 74.8% episodes of late-onset

VAP.**(18)** Akca *et al* found 33.3% episodes of late-onset VAP and 66.6% of early-onset VAP in their study group.**(21)** No prophylactic antibiotic therapy was given to any of their patients. They stated that in patients receiving prophylactic antibiotics the incidence of early-onset VAP is lower. Prod'hom *et al* observed, early-onset pneumonia (within first 4 days) represented 45% of all pneumonia episodes.**(22)** Heyland *et al* in a multicenter study on 1,014 reported an incidence of 23.9% early-onset (< 7 days) and 23.6% late-onset (> 7 days) VAP. **(23)** The low incidence of VAP in these studies could be due to greater specificity of criteria for diagnosis, clinical criteria and quantitative culture of PSB.

Monomicrobial versus Polymicrobial VAP

Various workers have reported polymicrobial etiology of VAP, which might be due to the aspiration of the oropharyngeal contents into the respiratory tract.(4,10,16)

Fagon et al reported 40% of the cases of VAP to be of polymicrobial etiology.(4) De Latorre et al found a very high polymicrobial incidence of 83.3% among the patients with VAP.(3) Chastre et al studied microbiology of VAP in patients with ARDS and without ARDS using QC of PSB and BAL, reported polymicrobial etiology in 55% of VAP cases in ARDS and 60% of VAP cases without ARDS.(16)

In the present study, the incidence of polymicrobial VAP was 84.2% versus only 15.8% VAP due to monomicrobial etiology.

Underlying diseases

Johanson *et al* found that of the patients who developed pneumonia, 24% had respiratory diseases, and 26% had drug overdose as the underlying condition.**(9)** Delclaux *et al* reported a very high incidence 60% of VAP in patients suffering ARDS. **(17)** Altered sensorium can also play an important role in the development of VAP, as the chances of aspiration are more in such a state.**(24)** This may be the reason for the patients with poisoning developing VAP. This explains the high incidence 57% of VAP in the present study.

Mortality

Results of several studies from 1986 to 2001 have confirmed that observation despite variation of population studied overall mortality rates for patients with or without VAP were respectively, 71% versus 28%, 33% versus 19%, 55% versus 25%. **(4,10,20)**

Chastre *et al* reported a higher mortality for VAP cases 47% compared to 28% for non-VAP cases.**(19)** A study by Heyland *et al* [23] has reported a mortality rate of 23.7% in patients with VAP.**(23)** Fagon *et al* using clinical and microbiological criteria reported a mortality rate of 71% in patients of VAP.**(4)** Fagon *et al* [4] also reported that morality in patients with ventilator-associated pneumonia was two-fold higher than non-VAP cases.**(4)** Torres *et al* has reported an overall mortality of 33 %, whereas, Rello *et al* observed a statistically significant increase in the mortality of patients, who received inappropriate initial antibiotic therapy, inspite of a change in the treatment after culture results.**(10,25)**

In our present study, the overall mortality was 57% of the total studied patients. The mortality in patients colonizing trachea and developing VAP was 54.39%, whereas, the mortality in those only colonizing, but not developing VAP was 41.86%. The high mortality rate in those not

developing VAP could be explained, mostly due to the underlying disease and cardiac and/or respiratory failure.

Kollef *et al* in their study found mortality among patients with VAP (43.8%) not significantly different from the mortality rate among patients without VAP (37.6%).**(15)** Kollef *et al* in their study found that patients with VAP had a significantly longer duration of MV (23.5 ± 18.4 days) compared to those without VAP (12.5 ± 9.1 days).**(15)**

CONCLUSION:

Clinicians need to adapt the treatment recommendations and preventive measures to their respective institutes, as the routes of infection and agents causing pneumonia vary considerably among health-care facilities. **(26)**

Therefore, knowledge about the commonest etiological pathogens colonizing trachea in mechanically ventilated patients, developing into VAP and their antimicrobial susceptibility pattern at the institute level by prospective study will definitely be useful in formulating its antibiotic policy & the optimal management of the patients by decreasing the incidence of morbidity and mortality related to VAP.

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