



## STUDY OF CLINICAL AND MICROBIOLOGICAL PROFILE OF VENTILATOR ASSOCIATED PNEUMONIA

### General Medicine

**Dr. Chandrakant K. Patil** 3<sup>rd</sup> year medicine resident, Department of General Medicine, Sir Takhatsinhji Hospital and Govt. Medical College, Bhavnagar.

**Dr. Sunil J. Panjwani\*** M.D (Medicine) Associate Professor, Department of General Medicine, Sir Takhatsinhji Hospital and Govt. Medical College, Bhavnagar. \*Corresponding Author

### ABSTRACT

Ventilator associated pneumonia (VAP) is defined as pneumonia occurring more than 48 hours after endotracheal intubation/initiation of mechanical ventilation or pneumonia developing even after extubation. VAP developed during the first 4 days of mechanical ventilation is early onset, usually less severe mostly caused by antibiotic sensitive bacteria's and with better prognosis. Whereas late onset VAP develops 5 or more days after the initiation of mechanical ventilation, and is due to multidrug resistant (MDR) pathogens and is usually associated with increased morbidity and mortality. Common pathogens causing VAP includes Pseudomonas Spp. Escherichia coli, Klebsiella pneumonia and Staphylococcus aureus with varying prevalence. Due to the increased incidence of MDR organisms in intensive care units (ICU), early and correct diagnosis of VAP is mandatory for optimal antibiotic therapy. The present study was conducted on 50 patients with clinically suspected as VAP admitted to critical care unit of Sir T. General hospital, Bhavnagar under medicine department during one year period. This study will help to detect pathogens commonly associated in causation of VAP, also to determine their antibiotic susceptibility pattern. This study will also help to decrease the complications associated with VAP in critical care units.

### SUMMARY

- Out of 198 patients, 50 patients admitted to the critical care unit of Sir T, General hospital, Bhavnagar under medicine department on mechanical ventilation more than 48 hour were studied, of which 38 patients developed VAP.
- Detailed history, physical examination was done and patient was investigated with chest x ray, endotracheal aspirate culture and various blood reports.
- Incidence of VAP in our study is 19%.
- 22 out of 29 males and 16 out of 21 females develops VAP in present study.
- VAP was more common in age group of 46-55 year attributable to more number of cases admissions of that age group and underlying comorbid conditions.
- 14 (36.8%) patients had early onset VAP and 24 (63.1%) patients had late onset VAP.
- The prevalence of VAP was greater in patients with disease necessitating prolonged mechanical ventilation like poisoning, stroke, liver disease, COPD etc.
- The most common risk factors for VAP in our study were use of antacids, aspiration and chronic lung disease.
- Most common clinical features of VAP in our study were fever, crepitation and tachypnoea.
- The most common offending organisms isolated in our patients were Klebsiella (31.6%), Escherichia coli (23.7%) and Pseudomonas (18.4%).
- Most of the organisms showed resistance to commonly used antibiotics like Cephalosporins and Penicillins. They were sensitive to broad spectrum antibiotics like Meropenem (84.2%), Gentamycin (76.3%) and Amikacin (71%).
- The outcome of VAP patients was good after the change of antibiotics based on culture sensitivity report.
- Most of the patients with VAP had poor clinical outcome when compared to non VAP patients.
- 71.4 % patients with early onset VAP showed recovery but 28.6 % patients expired. 58.3 % patients with late onset VAP showed recovery and 41.6 % expired.
- Overall 63.2 % patients of VAP were recovered. 36.8 % patients of VAP were expired.
- Preventive strategies should be followed in critical care units to decrease the prevalence of VAP.

### KEYWORDS

### INTRODUCTION

VAP is significant cause of morbidity and mortality in critical ill patients. VAP occur only in patients who have been intubated and undergone mechanical ventilation for > 48 hour or after extubation. The risk of VAP increases with prolonged mechanical ventilation.

Early onset VAP is usually caused by antibiotic sensitive community acquired bacteria within first 96 hour of mechanical ventilation and had good prognosis. VAP that develops > 5 days after initiation of mechanical ventilation has an increased likelihood of being caused by multidrug resistant bacteria's with bad prognosis.

Risk factors for the development of VAP are old age, chronic lung disease, aspiration, reintubation, ARDS and premorbid conditions like diabetes, renal failure.

Common pathogens causing VAP includes Pseudomonas Spp. Escherichia coli, Klebsiella pneumonia and Staphylococcus aureus with varying prevalence.

Clinical manifestations of VAP includes fever, tachypnoea, tachycardia, worsening oxygenation, leucocytosis, increase in respiratory secretion and pulmonary consolidation on physical examination along with a new or changing radiographic infiltrate.

Investigations for VAP mainly includes complete blood examination, chest x ray and respiratory tract secretion for gram stain, culture and sensitivity.

Early diagnosis and adoption of practices known to prevent VAP can reduce mortality and decrease the development of MDR organisms. Figures quoted by the International Nosocomial Infection Control consortium suggest that overall rate of VAP is 13.6 per 1000 ventilator days. However the individual rate varies according to patient group, risk factors and hospital settings.

### AIM AND OBJECTIVES

#### AIM:

- Study of clinical and microbiological profile of ventilator associated pneumonia.

#### OBJECTIVES:

- To isolate and identify the causative organism of ventilator associated pneumonia in critical care patients on mechanical ventilator.
- To study the clinical features and complications of VAP.
- To determine the antibiotic susceptibility pattern in VAP patients.

### MATERIAL & METHOD

**Source of Data :** The patients admitted in critical care unit at Sir T.

General Hospital and Government Medical College, Bhavnagar; who were on mechanical ventilator for more than 48 hour, during the period from June 2018 to May 2019

**Sample Size:** 50 patients

**Sample procedure:** Observational prospective study.

**Duration:** June 2018- May 2019.

**Inclusion criteria:**

- Critical care patients who are intubated and on mechanical ventilation for more than 48 hours.
- Patients in whom VAP is clinically suspected.
- Patients with modified clinically pulmonary infection score is more than 6.

**Exclusion criteria:**

- Patients who developed pneumonia within 48 hours of mechanical ventilation.
- Age less than 12 years.

**METHOD:**

This prospective study was conducted on 50 patients of clinically suspected VAP, who were on mechanical ventilator for more than 48 hour admitted in critical care unit under medicine department at Sir Takhtasinhji General Hospital, Bhavnagar, during study period of 1 year, after taking written and informed consent of patients. All patients were subjected to detailed history and thorough clinical examination. Investigations conducted are complete blood picture, CRP, ESR, urine routine, blood sugar, chest x ray, endotracheal aspirate culture and sensitivity, blood culture and sensitivity and arterial blood gas analysis. All data were entered into standard proforma and analysed. Patients were evaluated clinically, radiologically and bacteriologically to determine the presence of pneumonia, isolate the causative microorganism and sensitivity to antibiotics and presence of comorbid conditions like DM, COPD, CKD, IHD etc. Study group divided into VAP and non VAP. All the data was collected and statistical analysis was done.

**OBSERVATION AND RESULT**

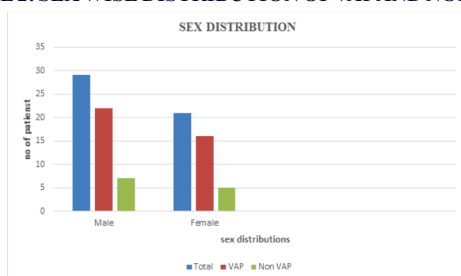
- The study was conducted on 50 patients who were on mechanical ventilation for more than 48 hour and clinically suspected as VAP admitted in critical care units under medicine department at Sir Takhtasinhji General Hospital, Bhavnagar, during the study period of 1 year.
- Out of 50, 38 patients were diagnosed to have VAP based on clinical pulmonary infection score (CPIS).

**TABLE 1: THE AGE DISTRIBUTION OF VAP AND NON VAP**

Age(years)	VAP		Non VAP		Total	
	No	%	No	%	No	%
15-25	4	66.6	2	33.3	6	100.0
26-35	6	100.0	0	0.0	6	100.0
36-45	7	70.0	3	30.0	10	100.0
46-55	8	72.7	3	27.3	11	100.0
56-65	7	77.8	2	22.2	9	100.0
66-75	4	80.0	1	20.0	5	100.0
76-85	2	66.7	1	33.3	3	100.0
Total	38	76.0	12	24.0	50	100.0

In our study, it was found that, the more VAP patients are seen in age group of 46-55 years but percentage wise it was higher in age group of 26-35 years.

**TABLE 2: SEX WISE DISTRIBUTION OF VAP AND NON VAP**



Our study included 29 (58%) males and 21 (42%) females, out of which 22 (75.9%) males and 16 (76.2%) females had VAP.

**TABLE 3: VAP AND ONSET**

VAP is divided into early onset and late onset VAP and their distribution as follows

VAP types	No	%
Early onset	14	36.8
Late onset	24	63.1
Total	38	100

**TABLE 4: RISK FACTORS AND VAP**

Risk factors	Early onset VAP		Late onset VAP		Total	
	No	%	No	%	No	%
Chronic lung disease	9	64.3	16	66.6	25	65.8
Aspiration	10	71.4	20	83.3	30	79.0
Reintubation	8	57.1	15	62.5	23	60.5
Prolonged paralysis	7	50.0	15	62.5	22	58.0
Diabetes	7	50.0	17	70.8	24	63.1
Sepsis	6	42.8	14	58.3	20	52.6
Antacids	12	85.7	18	75.0	30	79.0
Previous antibiotic therapy	5	35.7	12	50.0	17	44.7

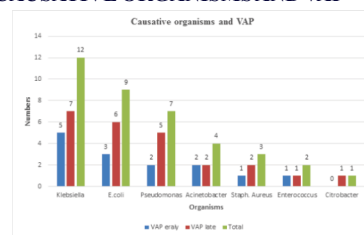
The commonest risk factor predisposing to early onset VAP was use of antacids (85.7%), followed by aspiration (71.4%) and chronic lung disease (64.3%).

**TABLE 5: CLINICAL FEATURES AND VAP**

Clinical features	VAP early onset		VAP late onset		Non VAP		Total	
	No	%	No	%	No	%	No	%
Fever	13	92.8	19	79.2	8	66.6	40	80.0
Tachypnoea	13	92.8	15	62.5	4	33.3	32	64.0
Fall in SPO <sub>2</sub>	10	71.4	18	75.0	5	41.6	33	66.0
Crepitation	11	78.6	18	75.0	4	33.3	33	76.0
Leucocytosis	10	71.4	15	62.5	9	75.0	34	68.0
Chest X ray (consolidation)								
a) Local	11	78.6	16	66.6	5	41.6	32	64.0
b) Diffuse	3	21.4	8	33.3	0	0.0	11	22.0
c) Total	14	100	24	100	5	41.6	43	86

Table 5 shows, clinical features and VAP. In early onset VAP most common clinical features were consolidation, fever and tachypnoea. In late onset VAP most common clinical features are consolidation, fever, fall of SPO<sub>2</sub> and crepitations. Overall consolidation and fever were most common clinical features.

**TABLE 6: CAUSATIVE ORGANISMS AND VAP**



Klebsiella was the most common organism isolated in VAP and also the most common organism in early onset and late onset VAP. Escherichia coli and Pseudomonas are next most common organisms.

**TABLE 7: ANTIBIOTIC SENSITIVITY PATTERN AND VAP**

Antibiotics	VAP early onset		VAP late onset		Total	
	No	%	No	%	No	%
Ceftazidime	6	42.8	10	41.6	16	42.1
Amikacin	8	57.1	19	79.2	27	71.0
Meropenem	10	71.4	22	91.6	32	84.2
Ceftriaxone	5	35.7	9	37.5	14	36.8
Ciprofloxacin	6	42.8	13	54.2	19	50.0
Ofloxacin	6	42.8	13	54.2	19	50.0
Piperacillin	8	57.1	17	70.8	25	65.8
Levofloxacin	7	50.0	11	45.8	18	47.4
Gentamycin	9	64.3	20	83.3	29	76.3
Amoxiclav	5	35.7	7	29.2	12	31.6
Cefotaxime	6	42.8	6	25.0	12	31.6

Commonest antibiotic for which most bacteria were sensitive in early onset VAP was meropenem (71.4%), followed by gentamycin (64.3%), amikacin (57.1%), piperacillin (57.4%), levofloxacin (50%) etc. Commonest antibiotic for which most bacteria were sensitive in late onset VAP was meropenem (91.6%). Others are gentamycin (83.3%), amikacin (79.2%), piperacillin (70.8%) etc. Overall meropenem and gentamycin are most sensitive antibiotics in both early and late onset VAP.

**TABLE 8: VAP AND CLINICAL OUTCOME**

Outcome	VAP early onset		VAP late onset		Total	
	No	%	No	%	No	%
Expired	4	28.6	10	41.6	14	36.8
Recovered	10	71.4	14	58.3	24	63.2

In early onset VAP totally 71.4% patients were recovered and 28.6% patients were expired. In late onset VAP 58.3 % patients were recovered and 41.6 % patients were expired. Overall 63.2% patients of VAP were recovered and discharged. 36.8 % patients of VAP were expired.

**DISCUSSION**

A total of 198 patients admitted to the critical care unit of Sir T. General Hospital, Bhavnagar during study period were kept on mechanical ventilation. Out of 198 patients 50 patients were on mechanical ventilation for more than 48 hours and clinically suspected as VAP. Out of 50 patients, 38 patients were diagnosed to have VAP based on CPIS.

**INCIDENCE:**

The incidence of VAP in our study was 19.2 % which is almost in accordance with other studies conducted by Trivedi et al, and Fagon et al (15 to 27%).

**AGE:**

In the present study, it was found that the maximum number of VAP patients was seen in age group of 46-55 years. The mean age is 47.7 years, which is similar in other Indian studies Rakshit, Joseph and Dey and western studies Alp and Rodrigues.

The higher incidence in the group of 46-55 years can be attributed to more number of patients getting admitted and undergoing ventilation in this age group. It may also be due to their associated co morbid condition.

**SEX:**

Our study included 29 (58%) males and 21 (42%) females, out of which 22 (75.9%) males and 16 (76.2%) females had VAP. There was no sex predilection to VAP in our study and was the same in other studies done by Wagh et al and Rodrigues et al.

**VAP AND ONSET:**

In the present study 63.1 % VAP cases were late onset, which is similar to other studies. The mean duration of ventilation in our study for VAP onset is 11 days which almost matches with other studies conducted by Heyland DK, et al and Cook DJ et al. This shows that VAP increases with the duration of mechanical ventilation. The risk of acquiring pneumonia appears to be increases with the duration of mechanical ventilation in a study done by Fagon et al and was found to be 7% at 10 days and 19% at 20 days.

VAP	Present study	Dey et al <sup>(42)</sup>	Abdel et al <sup>(38)</sup>
Early onset	36.8 %	47.7 %	42 %
Late onset	63.1 %	52 %	44 %

The mean duration of ventilation can effectively be reduced by administrating a proper weaning protocol.

**RISK FACTORS AND VAP:**

In our study most common risk factor for development of early VAP was use of antacids (85.7%), followed by aspiration (71.4 %) and chronic lung disease (64.3%).

In late onset VAP most common risk factors are aspiration (83.3 %), use of antacids (75%), diabetes (70.8%) and chronic lung disease (66.6%).

Overall aspiration, use of antacids and underlying comorbid illness are most common risk factors for VAP. Similar findings were reported by

Beck -Sague CM, Kaler W, Rello J, et al. Kalil AC, Metersky ML, Klompas M, et al.

**CLINICAL FEATURES AND VAP:**

Our study shows, in early onset VAP most common clinical features were consolidation (100%), fever (92.8%), tachypnoea (92.8%) and crepitations (78.6%). In late onset VAP most common clinical features were consolidation (100%), fever (79.2%), fall of SPO<sub>2</sub> (75%) and crepitations (75%). Overall consolidation and fever were the most common clinical features in VAP, which go in accordance with study by Chastre J, Fagan JY et al.

**CAUSATIVE ORGANISMS AND VAP:**

In our study the most frequently isolated organism in early and late onset VAP were Klebsiella (31.6%), Escherichia coli (23.7%) and Pseudomonas aeruginosa (18.4%).

Organism	Present study No. %	Rajendran R, Girish N et al No. %	Rakshit et al No. %
Klebsiella	12 (31.6)	20 (23.8)	7 (29.4)
Escherichia coli	9 (23.7)	18 (21.4)	3 (12.6)
Pseudomonas	7 (18.4)	12 (14.2)	11 (46)
Acinetobacter	4 (10.5)	11 (13.9)	2 (8.2)

The organisms causing VAP were different in different study groups mainly because of geographical variation. The present study helped to know the commonest organisms causing VAP at our hospital.

**ANTIBIOTIC SENSITIVITY PATTERN AND VAP:**

In our study the commonest antibiotic for which most bacteria were sensitive in early onset VAP was meropenem (71.4%), followed by gentamycin (64.3%), amikacin (57.1%), piperacillin (57.4%), levofloxacin (50%) etc. The commonest antibiotic for which most bacteria were sensitive in late onset VAP was meropenem (91.6%). Others are gentamycin (83.3%), amikacin (79.2%), piperacillin (70.8%) etc. Overall meropenem and gentamycin are the most sensitive antibiotics in both early and late onset VAP. This is mainly attributed due to most common organism causing VAP were gram negative organisms.

Antibiotics	Sensitivities (number and %)	
	Present study	Harsha, Virendra et al.
Meropenem	32 (84.2)	16 (66.6)
Gentamycin	29 (76.3)	16 (66.6)
Amikacin	27 (71.0)	20 (83.3)
Piperacillin	25 (65.8)	19 (79.2)
Levofloxacin	18 (47.4)	13 (54.2)
Ciprofloxacin	19 (50.0)	16 (66.6)
Cefotaxime	12 (31.6)	5 (20.8)

As most of bacteria isolated were resistant to various antibiotics, which results in the development of MDR pathogens. This is mainly because of prolonged stay in hospital, use of corticosteroids and prior use of antibiotics, inappropriate empirical antibiotic therapy and underlying morbidity. Ranjan et al. observed that prior use of antibiotics increases the risk of acquiring drug resistant pathogens. Similarly, Joseph et al. stated that prior antibiotic therapy was independent risk factor for VAP by MDR pathogens. The organisms isolated in the present study were predominantly gram negative. The antibiotics such as meropenem, gentamycin and amikacin have been found to be good antibiotic options for VAP to start with till culture reports are available.

**VAP AND CLINICAL OUTCOME:**

The overall mortality in our study was 36.8 %. In early onset VAP it was 28.6% and in late onset VAP was 41.6%. In other studies mortality varied from 30% to 50%. The mortality in VAP patient was significantly higher than non VAP patient. Gupta et al and Panwar et al found the same type result.

Higher rate of mortality in late onset VAP in our study is because of longer duration of mechanical ventilation and underlying co-morbid conditions.

Authors	Study year	Mortality rate of VAP (%)
Kerver et al	1986-87	30
Torres et al	1987-88	33
Fagon et al	1989-94	53
Rakshit et al	2003-04	37
Present study	2018-19	36

The reason for high prevalence of VAP in our study was may be due to small number of cases, the presence of co morbid illness and most of the patients were seriously ill. The health seeking behaviour in our patients is different when compared to that of the western population. By the time the patient is referred to the tertiary care centre his/her underlying disease would have progressed and may be irreversible. This may necessitate longer duration of mechanical ventilation which is directly proportional to the development of VAP, so the higher mortality.

## CONCLUSION

- VAP is a serious problem in CCU leading to prolonged hospitalization, its associated financial implication and high mortality rate.
- The causative pathogens of VAP may vary depending on country, region and hospital.
- Most common organisms isolated in VAP in present study were Klebsiella, Escherichia coli and Pseudomonas.
- Most common underlying risk factors are use of antacids, aspiration and underlying comorbid illness.
- Knowledge of the susceptibility pattern of the local pathogens causing VAP can guide the clinician to choose the appropriate empirical antibiotics.
- Most of the isolated organisms in our study are susceptible to meropenem, gentamycin and amikacin.
- The increase prevalence of late onset VAP in our study is mainly because of underlying comorbid illness.
- The MDR pathogens are increasing in our CCU.
- The emergence of MDR pathogens can be prevented by adopting an antibiotic policy and dose de-escalation regimens.
- Further studies are needed to under the condition of CCUs in detail.

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