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Original Research Article

To study the ventilator associated pneumonia in the ICU patients in a tertiary care hospital: Incidence, risk factors and etiological agents

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ABSTRACT

Introduction: Ventilator Associated Pneumonia (VAP) is the second most common nosocomial infection in the United States, with high mortality and morbidity. Duration of hospital stay increased in average of 7 to 9 days with increase in treatment cost of $40,000 per patient. However, clinical evidence on the incidence of this infection is poor, especially from ICUs in India.

Aim: To study the incidence, risk factors and etiological agents in ICU patients developing VAP in a tertiary care hospital in India.

Materials and Methods: In this study, patients who were kept on ventilator for more than 48 hours in ICU were enrolled. To clinically diagnose VAP, the modified clinical pulmonary infection score (CPIS) and clinical criteria were used as a screening tool. A full clinical history of the patients was documented, as well as the date of admission to the ICU, the date of initiation of mechanical ventilation, and the method of access to the patients' airway. A standard PROFORMA was used and the collected data was observed and analysed further.

Results: In the present study out of 45 patients enrolled for the study, only 6 patients (13.3%) showed VAP. The presence of early VAP was observed in 3 patients whereas late VAP was also observed in 3 patients. The male and female patients exhibited similar incidences of VAP. The patients with an age group more than 70 years showed a maximum (37.5%) prevalence of VAP. Clinical features like fever and increased amount of secretions were found to be associated with the occurrence of VAP. Smoking and diseases like hypertension, kidney disease, malignancy and chronic lung disease were non-significantly associated with VAP. Whereas disease states like coma and enteral nutrition were found to be significantly associated with VAP. Acinetobacter and Klebsiella were the most common organisms isolated in our institution.

Conclusion: VAP remains a significant concern to patients admitted to an ICU for mechanical ventilation, highlighting the critical need for preventive measures.

1. Introduction

Pneumonia causes 11% to 15% of all hospital-associated infections (HAIs) and 27% of all infections in the medical intensive care unit (MICU), respectively.[1] Ventilator-associated pneumonia (VAP) is most common in mechanically ventilated patients.[2] Intubated patients who developed VAP make up 9-27% of this number.[3,4]

VAP occurs 48 hours after tracheal intubation in mechanically ventilated patients. Early-onset VAP is defined as pneumonia that occurs within 4 days and is usually attributed to antibiotic sensitive pathogens and carries a better prognosis. Late-onset VAP is pneumonia that occurs after 4 days of intubation and is mostly caused by multidrug-resistant (MDR) pathogens and is associated with increased mortality and morbidity.[4] Endotracheal intubation

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and artificial ventilation are risk factors because they conflict with the body's natural defence mechanisms.[2,5]

VAP is related to an increase in multidrug-resistant infections, antibiotic use, mechanical ventilation time, ICU and hospital duration of stay,[6] among other things. VAP rates vary depending on the term used for diagnosis, ranging from 1.2 to 8.5 per 1,000 ventilator days.[7]

VAP rates are influenced by a number of non-modifiable and modifiable risk factors. Non-modifiable risk factors include male gender, advanced age (over 60 years), history of COPD, tracheostomy, recent neurologic surgery, multi-organ system failure, and coma. Supine positioning, gastric over-distension, ventilator circuit colonisation, low ETT cuff strain, and repeated patient transfers are all modifiable risk factors.[8]

VAP is a significant growing issue in health-care facilities, driving up the cost of patient care and time spent in the hospital, as well as patient morbidity. The cost of healthcare is increased by more than $40,000 per hospitalised patient due to VAP.[9]

There are no gold standard criteria for the diagnosis of VAP. It complicates the evaluation of case definitions and systematic approach to confirmation. The diagnostic evaluation is made complex by variable sensitivity and specificity of available clinical criteria. It restricts the ability to compare studies and the use of VAP rates as a quality-of-care indicator.[10] (The number of VAP episodes per 1000 ventilator days is known as the VAP rate.)

Antibiotic therapy should not be delayed in order to conduct diagnostic tests, as any delay in starting effective antibiotic therapy will increase the risk of VAP-related mortality. Based on local microbiological evidence, patient characteristics, and the sensitivity pattern of expected pathogens at the hospital, this initial empirical therapy can be updated. The increased likelihood of inadequate initial empiric antimicrobial treatment of infections is the cause of rising antimicrobial resistance.[11]

This study's main purpose was to determine the incidence of VAP in ICU patients, risk factors, and various pathogens associated with it. By knowing the most common pathogens and their susceptibility pattern in our ICUs, we can create a local antibiogram that helps in the initiation of appropriate empirical antimicrobial. Moreover, by knowing the risk factors associated with VAP, we can reduce VAP incidence in ICU settings and decrease the length of ICU stay, thereby reducing morbidity and mortality.

2. Materials and Methods

A hospital-based Prospective observational study was conducted in the Intensive care unit of the Department of Respiratory Medicine, Critical Care and Sleep Medicine at Sri Venkateshwaraa Medical College Hospital& Research Centre, Ariyur, Puducherry (SVMCH & RC) from October 2019 to September 2020. All patients who were kept on ventilators for more than 48 hours in ICU at SVMCH&RC setup were enrolled and followed up. Both male and female adult patients who were kept on the ventilator were included in this study. 45 consecutive patients were followed up in our study.

2.1. Sample size

In a study (Mohan et al., 2013), the occurrence of Enterobacter aerogenes was 3% among VAP patients. The sample size was calculated using the following formula (Charan and Biswas, 2013):[12,13]

$n=4*pq/d^{2,}$

where n: Sample size

d: Margin of error

p=prevalence, q=1-p

n=4*0.03*0.97/(0.06*0.06)=32

Assuming 80% power, 5% significance level with 95% confidence interval as well as assuming 0.06 margin of error, the required sample size is 32 subjects

2.2. Inclusion criteria

1. All patients above 16 years of age.
2. All patients intubated or tracheostomized after ICU admission and on ventilator for more than 48 hours.
3. No change in antibiotics for the past 48 hours.

2.3. Exclusion criteria

1. Those patients already intubated or tracheostomized at the time of ICU admission.
2. Those who developed pneumonia within 48hrs of admission or intubation.
3. Those diagnosed with pneumonia at the time of admission.
4. Those diagnosed with Acute Respiratory Distress Syndrome at the time of admission.
5. Those who were reintubated after extubation during their stay in our medical facility.

2.4. Procedure

To clinically diagnose VAP, the modified clinical pulmonary infection score (CPIS) and clinical criteria were used as a screening tool. A full clinical history of the patients was documented, as well as the date of admission to the ICU, the date of mechanical ventilation initiation, and the mode of access to the patients' airway, such as orotracheal or tracheostomy, as well as systemic antibiotic therapy. The ventilator mode and settings, as well as any changes in settings, were evaluated daily in each patient. Patients' vital signs, general and physical examination, oxygen saturation were monitored regularly. Baseline investigations like complete blood count, blood culture, the culture of endotracheal tube and sensitivity, and chest X-ray were

taken into consideration. The number of ventilator days, length of stay in ICUs and outcome of the patients was noted.

1. A PROFORMA was used and the collected data was observed and analysed further. A Master chart was prepared on its basis with each patient details and parameters. A distinction could be made as Early OR Late VAP as per the definitions below.
2. **Early-onset VAP** is defined as pneumonia that occurs within 4 days.
3. **Late-onset VAP** is pneumonia that occurs after 4 days of intubation.

2.5. Statistical analysis

The data is described in frequency, percentages, and mean standard deviation. When comparing categorical variables, the Chi-square test was used, and when comparing continuous variables, the Unpaired t-test was used. The 0.05 p-value was deemed meaningful. SPSS 16.0 was used to conduct all of the analyses (Chicago, Inc., USA).

3. Results

The incidence of VAP was found to be 13.3% (95%CI=0.07-0.30). The study observed that early and late VAP was exhibited by 3 patients each.

The incidence of VAP was observed to be higher in the age>70 years (37.5%). There was no significant (p>0.05) association of incidence of VAP with age and gender.(Table 2)

Almost all VAP patients were febrile. The presence of bronchial breath sounds was a useful clinical finding in patients with VAP. The presence of purulent secretions was significantly associated with VAP (p=0.003). None of the other clinical features was associated (p>0.05) with the depiction of VAP. An increase in O2 requirement was not seen in most of the VAP cases in our study.(Table 3)

The association of incidence of VAP with smoking habit showed no significant association. (p>0.05).

Coma was the only risk factor significantly associated with the incidence of VAP. The incidence of VAP was 42.9% in coma patients and 7.9% in without coma. The presence of Diabetes, Hypertension, Chronic kidney disease, chronic lung disease and malignancy were not significantly associated with increased incidence of VAP. The 4 patients with malignancy did not develop VAP but this was insignificant statistically.(Table 4)

The use of steroids did not seem to increase the risk of VAP. Thus, one study showed that low dose steroids (200-300mg/day of hydrocortisone) could be used without increasing the risk of pneumonia. Increased incidence of VAP has not seen with immunosuppressant drug therapy and none of the patients on immunosuppressant therapy developed VAP. All the 3 patients with solid organ transplant did not develop VAP. Recent surgery (neurosurgery and abdominal surgery) and blood transfusion was also not a risk factor for the development of VAP. There was no evidence that early enteral feeding was linked to the development of VAP. Restrictive blood transfusion was given in our patients and was not found to be a risk factor for VAP.(Table 5)

All six patients with VAP had a Modified CPIS of ≥6. Acinetobacter and Klebsiella were the most common organisms isolated (33% each). Pseudomonas aeruginosa and candida tropicalis were isolated in 16.66% each.(Table 6)

4. Discussion

In the intensive care unit (ICU), Ventilator-Associated Pneumonia (VAP) is the second most common nosocomial infection (ICU).[2] VAP, which causes significant mortality and morbidity, is difficult to diagnose and treat. VAP is connected to a range of risk factors and is a major issue in health-care facilities, raising the cost of patient care as well as the hours spent caring for patients, hospital length of stay, and patient morbidity.[9,10] Incidence of MDR pathogens associated with VAP has been increasing.[7] There is no gold standard criteria for the diagnosis of VAP. It makes it difficult to compare studies and use VAP rates as a quality-of-care indicator.[10]

The incidence of the VAP in our setting was 13.3% which was lower compared with previous studies where incidence was 28-29%.[13] The incidence of early and late-onset VAP was found to be 50% each, which was similar to that reported in a previous study.[14] The lower incidence of VAP in our study may be due to initiation of the Non-invasive ventilator support in majority of the patients, initiation of appropriate empirical antimicrobial therapy, strict implementation of VAP bundle and hand hygiene.

In our study, the mean age of patients was 58.16 years, the minimum and maximum ages being 25 years and 82 years respectively. The maximum number of patients in our study were in the 50-60 years age group (31%). The incidence of VAP in our study was observed to be highest in the age group >70 years (37.5%). There was no significant (p>0.05) association of incidence of VAP with age.[15]

Our study population consisted more of males (66%) compared to females (33%). In our study, the incidence of VAP was similar in males (13.3%) and females (13.3%). There was no significant association of incidence of VAP with gender.

Clinical features of VAP include fever, presence of bronchial breathing or rales, increase in amount or purulence of secretion, and increase in O2 requirement. Bronchial breath sound was a useful clinical finding present in patients with VAP. The presence of purulent secretion was significantly associated with VAP (p=0.003). None of the other clinical features was associated (p>0.05) with the depiction of VAP. An increase in O2 requirement was

Table 1: Modified clinical pulmonary infection scoring system

Modified CPIS points	**0**	**1**	**2**
Tracheal secretions	Rare	Abundant	Purulent
Leukocyte count/mm ^{3}	>4,000 and < 11,000	<4,000 and > 11,000	<4,000 or > 11,000 + >50% bandforms
Temperature (^{0} C)	>36.5 and <38.4	>38.5 and <38.9	> 39 or <36
Pa02/FI02 ratio	>240 or ARDS	–	< 240 and no ARDS
Chest radiograph	No infiltrate	Diffuse infiltrate	Localized infiltrate
Microbiology	Negative		Positive

Table 2: Association of incidence of VAP with Age and gender

Parameters		**No. of patients**	**No. with VAP**	**% with VAP**	**p-value**
Age in years	<50	10	0	0	0.110
	50-60	14	2	14.3	
	61-70	13	1	7.7	
	>70	8	3	37.5	
Gender	Male	30	4	13.3	1.000
	Female	15	2	13.3	

Table 3: Association of incidence of VAP with clinical features

Clinical features		**No. of patients**	**No. with VAP**	**% with VAP**	**p-value**
Fever	Yes	21	5	23.8	0.08
	No	24	1	4.2	
Rales	Yes	9	2	22.2	0.38
	No	36	4	11.1	
Bronchial breath sound	Yes	4	3	75	0.0001*
	No	41	3	7.3	
Increase in the amount of secretion	Yes	30	6	20	0.06
	No	15	0	0	
Increase in purulence of secretion	Yes	20	6	30	0.003*
	No	25	0	0	
Increase in O_2 requirement	Yes	10	2	20	0.48
	No	35	4	11.4	

Table 4: Association of incidence of VAP with the disease as risk factors

Risk factors		**No. of patients**	**No. with VAP**	**% with VAP**	**p-value**
Diabetes	Yes	19	4	21.1	0.19
	No	26	2	7.7	
Hypertension	Yes	31	5	16.1	0.41
	No	14	1	7.1	
Chronic kidney disease	Yes	12	1	8.3	0.55
	No	33	5	15.2	
Chronic lung disease	Yes	8	1	12.5	0.93
	No	37	5	13.5	
Malignancy	Yes	4	0	0	0.41
	No	41	6	14.6	
Coma	Yes	7	3	42.9	0.01
	No	38	3	7.9	

Table 5: Association of incidence of VAP with other risk factors

Other risk factors		No. of patients	No. with VAP	% with VAP	p-value [1]
Enteral nutrition	Yes	45	6	13.3	-
	No	0	0	0	
Blood transfusion	Yes	16	1	6.2	0.29
	No	29	5	17.2	
Immunosuppressant drugs	Yes	7	0	0	0.25
	No	38	6	15.8	
Solid-organ transplant	Yes	3	0	0	0.48
	No	42	6	14.3	
Tracheostomy	Yes	1	0	0	0.69
	No	44	6	13.6	
Prolonged steroid use (> 7days)	Yes	9	1	11.1	0.82
	No	36	5	13.9	
Abdominal surgery	Yes	3	0	0	0.48
	No	42	6	14.3	
Recent neurological surgery	Yes	2	1	50	0.11
	No	43	5	11.6	

Table 6: Distribution of organism isolated (Endotracheal aspirate culture) in VAP cases

Organism	No. (n=6)	%
Acinetobacter	2	33.33
Candida tropicalis	1	16.66
Klebsiella	2	33.33
Pseudomonas aeruginosa	1	16.66

not seen in most of the VAP cases. Hence, clinically, the presence of bronchial breath sound and increase in purulence of secretion were significantly associated with the incidence of VAP.

Several studies have analysed various risk factors such as shock, coma, antibiotic usage for at least 1 month before admission, nasogastric tube, bronchoscopy-tracheostomy, reintubation, intubation lasting for more than 5 days, and smoking that have a significant correlation with the development of VAP.[16,17] We studied the correlation of 15 risk factors with the incidence of VAP. Out of the risk factors we evaluated, coma was the only factor that was significantly (p=0.008) associated with the incidence of VAP. 22% of our study population were smokers and there was no significant (p=0.72) association of occurrence of VAP with smoking. Among the patients we studied, comorbid disease conditions such as diabetes (p=0.19), hypertension (p=0.41), chronic kidney disease (p=0.55), chronic lung disease (p=0.99) and malignancy (p=0.41) were not significantly associated with the incidence of VAP. We sought the association of other risk factors in ICU patients with VAP, such as blood transfusion and enteral nutrition, but neither of them showed significant association (p>0.05). Both the prolonged use of steroids (p= 0.82) and immunosuppressant therapy (p=0.25) were not found to be associated with an increased risk of VAP. Recent surgery (neurosurgery and abdominal surgery) and solid organ transplant were also not significant risk factor for the development of VAP (p>0.05). Only one of the patients in our study was tracheostomized and no significant association was found between tracheostomy and the occurrence of VAP (p=0.69).

Pseudomonas aeruginosa and Candida tropicalis were the most common pathogens attributed to early-onset VAP. Acinetobacter and Klebsiella were the most common pathogens causing late-onset VAP. Multidrug-resistant pathogens (MDR) are becoming more common among VAP patients, according to recent reports. Pseudomonas was found to be the most common organism in previous studies. However, Acinetobacter and Klebsiella were found to be the most common organisms causing VAP in our study.[17]

Blood culture was positive in 2 VAP cases only (33%). Acinetobacter & Klebsiella species were the common pathogens isolated. The mortality rate was found to be higher (50%) among patients in whom the same species was isolated in both ET aspirate and blood culture.

The association of incidence of VAP with modified CPIS score showed that all the six patients with VAP had a Modified CPIS of ≥6.

5. Conclusion

VAP is a widespread nosocomial infection that occurs in mechanically ventilated patients in India, and it remains to pose a serious problem to intensive care physicians. Knowing the major risk factors for VAP will aid in the implementation of quick and efficient prevention

methods such as non-invasive ventilation, vigilance during emergency intubation, decreasing re-intubation, avoiding tracheostomy as much as possible, and reducing sedation.

6. Conflict of Interest

No conflict of interest.

7. Source of Funding

None.

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