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A STUDY ON CLINICO-EPIDEMIOLOGICAL FACTORS OF VENTILATOR ASSOCIATED PNEUMONIA IN A TERTIARY CARE CENTRE

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ABSTRACT

Background: Ventilator Associated Pneumonia (VAP) is a common and serious problem observed in patients who require treatment in intensive care units (ICU). VAP is defined as Pneumonia occurring more than 48 hours after intubation. **Objective:** To evaluate clinical and epidemiological risk factors involved in the development of VAP and to find out the common underlying aetiologies. **Methods:** A cross sectional study was conducted among 72 mechanically ventilated patients for more than 48 hours in the intensive care units. The clinical criteria used was modified Clinical Pulmonary Infection Score (CPIS). A score more than > 6 was used to diagnose VAP. Patients were classified into early or late onset pneumonia. Other risk factors contributing to development of VAP was also studied. **Results:** The incidence of VAP was 38.8% among 72 patients. Most common organisms isolated were Klebsiella Pneumoniae (39%) followed by Acinetobacter baumannii (21%), Pseudomonas aeruginosa (18%), MRSA (11%) , polymicrobial (7%) and Candida (4%). The risk of developing VAP was more in patients who were elderly and with Diabetes, CKD, septic shock . Majority had late onset VAP and about 10 (35.71%) patients died in VAP group. **Conclusions:** Klebsiella was the most common organism isolated from in our setting. Diabetes was an important risk factor. The incidence of VAP is directly proportional to the duration of mechanical ventilation. Patients who recovered from VAP (64.29%) was higher compared to those who died (35.71 %) probably due to early, appropriate antibiotics administration in adequate doses followed by de-escalation based on microbiological culture results and clinical response.

KEYWORDS

Ventilator Associated Pneumonia, Mechanical ventilation, Klebsiella Pneumoniae.

INTRODUCTION

Ventilator Associated Pneumonia (VAP) is the most common lethal infection observed in patients who require treatment in intensive care units. VAP is defined as pneumonia occurring amore than 48 hours after intubation.[1]

Ventilator associated pneumonia development is a multifactorial process that follows the disruption of respiratory system physiology caused by intubation. It is usually associated with higher mortality, morbidity and costs. Hence there is a need to solicit research for effective preventive measures. VAP can be used as an indicator of quality of care.[2]

In mechanically ventilated patients the incidence of VAP increases with duration of ventilation. The risk of VAP is highest early in the course of hospital stay and is estimated 3% per day during the first 5 days of ventilation, 2% per day during 5 to 10days and 1 % per day after 10 days of mechanical ventilation. Since most mechanical ventilation is short term, approximately half of all episodes of VAP occur within first 4 days of mechanical ventilation (MV). [3]

Ventilator associated pneumonia occurs in 9-27% of all intubated patients. Early onset VAP , defined as occurring less than 5 days of mechanical ventilation, usually has better prognosis and is caused by antibiotic sensitive bacteria. Late onset VAP is defined when it occurs at 5 days or more of mechanical ventilation and is caused by multi drug resistant pathogens and are associated with increased patient mortality and morbidity. Recent American Thoracic Society guidelines state that the key decision in initial empiric therapy is whether the patient has risk factors for multidrug resistant organisms, rather than the time of onset of VAP[4,5]

VAP rates range from 1.2 to 8.5 per 1000 ventilator days and are reliant on the definition used for diagnosis. [6] The presence of VAP increases hospital stay by an average of 7 -9 days per patient and also imposes an extra financial burden to the hospital. [7]

METHODS:

A cross sectional study was conducted among 72 mechanically ventilated patients for more than 48 hours in the intensive care units in a tertiary care hospital. The clinical history and examination of patients along with relevant blood investigations, ABG, blood and end otracheal aspiarte cultures and chest X-rays were studied. Chest X-rays were taken on the first day of mechanical ventilation, then after 48 hours, 5th and 7th day.To know if a patient was in the incubation period or not, we sent blood culture and sensitivity on the day of admission.The clinical criteria used included modified Clinical Pulmonary Infection Score (CPIS). We gave 0-2 points each for fever, leukocyte count, oxygenation status, quantity and purulence of tracheal secretions, type of radiographic abnormality and sputum culture and gram stain(Table 1). A score more than > 6 was used to diagnose VAP.[8,9]

Patients were classified into Early onset pneumonia if VAP develops in <5 days of intubation and Late onset pneumonia if it develops ≥5 days of intubation.

For etiological diagnosis of VAP, endotracheal aspirate was taken and sent forculture and sensitivity as well as Gram staining. Other risk factors contributing to development of VAP like diabetes, hypertension, elderly, shock and other immunocompromised conditions were also be studied.

Table 1:Clinical pulmonary infection score (CPIS):

score	0	1	2
Tracheal secretions	Rare	Abundant	Purulent
Leucocyte count(mm3)	>4000 & <11,000	<4000 and >11000	<4000 and >11000 + band forms
Temperature (0C)	>36.5 & <38.4	>38.5 & <38.9	>39 or <36
PaO2/FiO2 ratio (mmHg)	>240 or ARDS	-	</= 240 & no ARDS

Chest X ray	No infiltrate	Diffuse infiltrate	Localized infiltrate
Culture of trachealaspirate	Negative	-	Positive

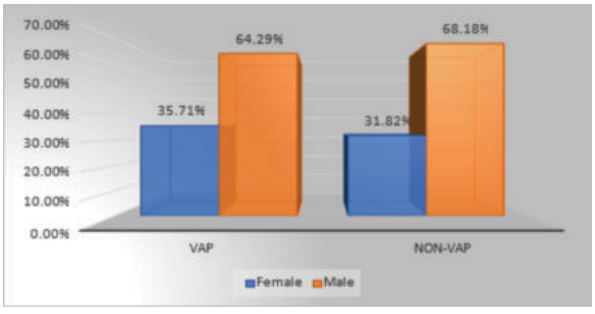
Statistical Analysis:
To study the incidence and etiology, frequency and percentage were applied. To analyze the risk factors of VAP, Chi-square test was applied.

RESULTS

A total of 72 patients admitted to the ICU of our hospital on Mechanical Ventilation were studied. The study included 24 female and 48 male patients, out of which 10(35.71%) females had VAP and 18(64.29%) males had VAP(table1; graph1).

Table 1: Sex distribution of VAP and Non-VAP

Sex	VAP		Non-VAP		Total	
	No.	%	No.	%	No.	%
Female	10	35.71%	14	31.82%	24	33.33%
Male	18	64.29%	30	68.18%	48	66.67%
Total	28	100%	40	100%	72	100%

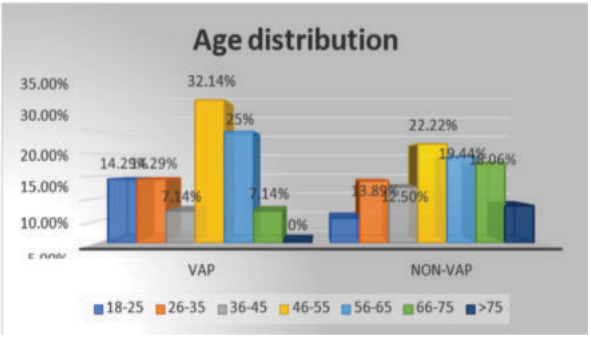


Graph 1: Sex distribution of VAP and Non-VAP

The age distribution of VAP was studied. In our study it was found that VAP was seen maximum in 46 to 55 years age group i.e. 32.14%, followed by 26 to 35 years and 18 to 25 years age group i.e. 14.29%(table2; graph 2). The mean age in patients with VAP was 47.07 ±15.38 years.

Table 2: Age wise distribution of VAP and Non-VAP

AGE	VAP		Non-VAP		Total	
	No.	%	No.	%	No.	%
18-25	4	14.29%	0	0%	4	5.56%
26-35	4	14.29%	6	13.64%	10	13.89%
36-45	2	7.14%	7	15.91%	9	12.5%
46-55	9	32.14%	7	15.91%	16	22.22%
56-65	7	25%	7	15.91%	14	19.44%
66-75	2	7.14%	11	25%	13	18.06%
>75	0	0%	6	13.64%	6	8.33%
Total	28	100%	44	100%	72	100%



Graph 2: Age wise distribution of VAP and Non-VAP

Table 3 : Distribution of patients with VAP and Non-VAP

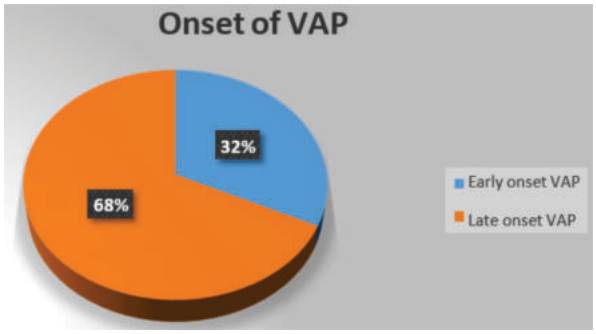
	No.	%
VAP	28	38.89%
Non-VAP	44	61.11%
Total	72	100%

Out of 72 patients, a total of 28 (38.89%) patients were diagnosed to have VAP.(table 3)

Majority of the patients in our study were found to have late onset VAP. i.e. 19 patients (67.86%).(Table 4; graph 4)

Table 4 : VAP and onset

	Frequency	Percent
Early onset	9	32.14%
Late onset	19	67.86%
Total	28	100%

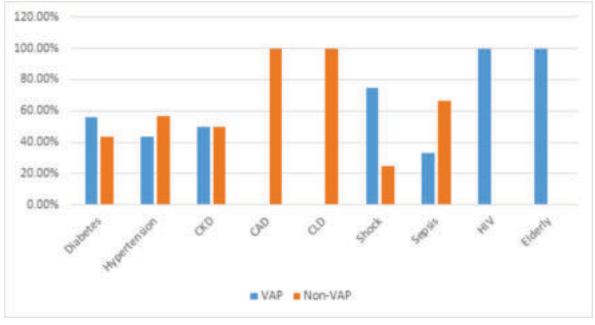


Graph 4: Onset of VAP

Table 5 : Causative organisms and VAP

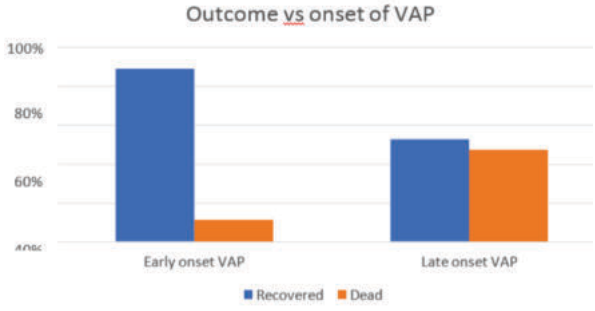
VAP	Present	
	No.	%
Pseudomonas	5	17.86%
Candida	1	3.57%
Klebsiella	11	39.28%
Polymicrobial	2	7.14%
A.baumannii	6	21.43%
MRSA	3	10.72%
Total	28	100%

Most common organisms isolated in our patients is Klebsiella pneumoniae (39%) followed by Acinetobacter baumannii(21%), Pseudomonas aeruginosa (18%), MRSA (11%) , polymicrobial(7%) and Candida(4%).(table5)



Graph 5: Comorbid illness and VAP

The association with co morbid illness was studied in our patients. It was found that the risk of developing VAP was more in patients who had medical illness like diabetes, CKD, shock and HIV and elderly patients than patients without them.(graph 5)



Graph 6 : Outcome vs Onset of VAP

In Early onset VAP 1 patient (11.11%) was dead and 8 patients were alive (88.88%). 19 patients(67.86%) were affected by late onset VAP, among which 9 patients (28%) were dead and 10 patients (52.63%) were recovered.(graph 6)

Table 6 : Duration of ventilator vs outcome

Outcome	Duration of ventilator (days)		p- value
	Mean	SD	
Recovered	8.33	3.7	0.43
Dead	9.42	4.82	

In our study mean duration of ventilator was significantly high in VAP patients compare to Non-VAP patients. (p – 0.001). Among the patients duration of ventilator was not significant in relation to outcome. (p >0.05). The mean duration of ICU stay was significantly high in VAP patients (18.25 ±4.74 days) compare to Non-VAP patients (9.72 ±3.17 days). (p – 0.0001).

The duration of ICU stay among the patients with VAP was similar in those who recovered and dies with treatment. (p- 0.71). In our study, 18(64.29%) patients recovered after treatment in VAP patients. 10(35.71%) patients died in VAP group. 35(79.55%) patients in Non-VAP group recovered after treatment .(table 6)

DISCUSSION

Nosocomial infections denote a major health problem in our society. Ventilator associated pneumonia is considered to be one of the most worrisome problem in every ICU set up. Nosocomial pneumonia is a particularly common problem in intubated patients getting mechanical ventilation in ICU.

Noticeable effort has been taken to develop and improve preventive measures to reduce the incidence of VAP. The preventive strategy is based on modifiable risk factors. Aim to reduce the risk of VAP by several pharmacological and non- pharmacological measures available. Endotracheal intubation and prevention of microaspiration of pathogens to the lower airways will be the ultimate measure, that should be taken.

This study was undertaken to determine the incidence, outcome and risk factors associated with ventilator associated pneumonia in our setup.

According to this study around 38.89% was the incidence of VAP. The prevalence of VAP was 28 cases per 72 patients depending on the population studied. In an ICU on any given day about 10% of patients will develop pneumonia, VAP in the majority of cases.

VAP is diagnosed by clinicians using the Clinical Pulmonary Infection Score(CPIS). A score more than 6 is predictive of VAP.After viewing the aforementioned values in the same patient at the same time, the majority of doctors would almost likely assume VAP and start therapy with a broad-spectrum antibiotic while awaiting culture findings. The optimum treatment plan for patients is created by combining information from the CPIS, information from the microbiologic analysis of bronchoalveolar lavage and sound clinical judgment. [8,9]

From our study, distribution of organisms was Pseudomonas (5 patients) 17.86% , MRSA (3 patients) 10.72%, Acinetobacter baumannii (6 patients) 21.43%, Polymicrobial (2 patients)

7.14%, Klebsiella pneumoniae (11 patients) 39% and Candida (1 patient) 3.5%.Rakshit and colleagues observed that the incidence of VAP is directly proportional to the duration of MV. They also found that Gram-negative bacteria followed by methicillin resistant Staphylococcus aureus (MRSA) are among the commonest incriminating organisms.[10]

Chastre and Fagon[11] gathered microbiological data from 24 published investigations that made use of bronchoscopic diagnostic techniques. Overall, aerobic gram-negative bacilli accounted for 58 % of isolates, while gram-positive cocci made up the remaining 35 percent.

In a study done by Andrade and colleagues the incidence of VAP was found to be 24.59 per 1000 ventilator days and the mortality rate was 32.1%. The major pathogens isolated were Pseudomonas, Staphylococcus aureus and Enterobacteriaceae and were found to be resistant to Imipenem, Oxacillin and third and fourth generation cephalosporins.[12] In a study done by Katherson and his colleagues found that the incidence of VAP was comparable to that found in the National Nosocomial Infection Surveillance System and Klebsiella was the most common organism. The incidence of VAP was found to increase with the duration of MV[13] .Similarly Trivedi et al[14] reported an incidence of 9.3% of nosocomial pneumonia and 38% had ventilator associated pneumonia. Commonest isolates were Pseudomonas (55%), Acinetobacter (20%), Staph aureus (16.5%) and Klebsiella (15%). Total mortality was 21.3%. VAP is associated with crude mortality rate of 20-70%.

It was found that the risk of developing VAP was more in patients who had medical illness like diabetes, CKD, shock and HIV and elderly patients than patients without them.

In our hospital among patients who developed VAP two- thirds were males (64%) and one third were females (31%). This is because of increased number of male patients being admitted. Also male gender as such is a risk factor for the development of VAP. In our study, most of the VAP patients are around the age group 46 to 55 years old, next comes 56 to 65 age group . The higher incidence of VAP in the middle age group can be attributed to more number of patients getting admitted and undergoing mechanical ventilation in this age group.

Early onset VAP is pneumonia follows after 2 days of mechanical ventilation. While late onset VAP arises 5 days after intubation. Among the 28 patients studied 9(32.14%) had early onset VAP and 19(67.86%) had late onset VAP.Among those 9 who developed early onset VAP 1(11.11%) expired. In late onset group 9(28%) were expired. The probability of getting VAP increases with the duration of mechanical ventilation.

It has been found that the risk for VAP increased from 5% in patients receiving one day of respiratory assistance to 68.8% in patients receiving more than 30 days. In our study late onset VAP ,is more severe and has high mortality compared to early onset VAP.

The incidence of VAP is straight away related to the duration of mechanical ventilation in our study. The mean duration of ICU stay was significantly high in VAP patients approximately 18 days compared to non-VAP patients .

There is a significant association that patients had to be on mechanical ventilation for prolonged periods following development of VAP have increased mortality. Late onset VAP have seen to have increased mortality, morbidity, stay in hospital and increased cost utilization.

In a study done by Katherson and his colleagues found that the incidence of VAP was comparable to that found in the National Nosocomial Infection Surveillance System and Klebsiella was the most common organism. The incidence of VAP was found to increase with the duration of MV.[13]

In our study, 18(64.29%) patients recovered after treatment in VAP patients. 10(35.71%) patients died in VAP group. Thirty five (79.55%) patients in Non-VAP group recovered after treatment. Rakshit et al in their study had 37% mortality in VAP patients.[10]

In a study done by Andrade and colleagues the incidence of VAP was found to be 24.59 per 1000 ventilator days and the mortality rate was 32.1%.[12] In a study done by Alp and his associates VAP was the leading cause of morbidity and mortality in intensive care units with incidence of 7% to 70 and the mortality rates of 20–75%.[15]

In our study we observed that in Early onset VAP 1 patient (11.11%) was dead and 8 patients were alive (88.88%). 19 patients(67.86%) were affected by late onset VAP, among which 9 patients (28%) were dead and 10 patients (52.63%) were recovered.

Risk factors for mortality in VAP [16,17,18] include: Increased age,increased duration of intubation, unconsciousness; multiple comorbidities; cerebrovascular incident; multiple trauma; bacteremia; enteral nutrition; immune suppression; peripheral and central venous catheters and increased APACHE II Score.

The related conditions which are considered as significant risk factors in our study were diabetes mellitus (56.25%), hypertension(43.47%). About 75% had shock in VAP patients. Majority of the VAP episodes were of late onset type.

CONCLUSION

VAP occurs commonly in ICU set up. It is concomitant with significant morbidity in critically ill patients. The incidence of VAP is directly proportional to the duration of mechanical ventilation. The mean duration of ICU stay was significantly high in VAP patients (approximately 18 days) compared to non-VAP patients . There was a significant association that patients had to be on mechanical ventilation for prolonged periods. Development of VAP posed increased risk of mortality. Klebsiella pneumoniae was the most common organism isolated from in our set up, so we have to treat using appropriate antibiotics coverage.

Diabetes mellitus carries an important risk factor in the causation of VAP. Risk of developing VAP was more in patients with serious comorbid illness. VAP was commonly seen in the 46 to 55 years age group and a majority of them developed late onset VAP. Also the male sex had higher incidence of VAP probably because the number of males admitted in the ICU was significantly higher. Late onset VAP was more severe and had higher mortality compared to early onset VAP.

The major aims of VAP management are early, appropriate antibiotics in adequate doses followed by de-escalation based on microbiological culture results and clinical response of the patient. Thus improving survival of patients, preventing emergence of multidrug resistant organisms and saving costs.

Antimicrobial stewardship programs involving pharmacists, physicians and other healthcare providers optimize antibiotic selection, dose, and duration to increase efficacy in targeting causative pathogens and allow the best clinical outcome.

VAP is a prevalent illness that is costly to treat and difficult to precisely diagnose. Its development lengthens a patient's stay in the ICU and is linked to high rates of morbidity and mortality. Valid diagnostic and therapeutic approaches were developed during the last 20 years in an attempt to enhance the result. Early diagnosis and timely intervention and appropriate antimicrobial stewardship can save lives.

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