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Original Research Paper

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VENTILATOR ASSOCIATED PNEUMONIA IN INTENSIVE CARE UNIT OF A TERTIARY LEVEL HOSPITAL

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ABSTRACT

Background: Ventilator associated pneumonia (VAP) is the most common nosocomial infection diagnosed in the intensive care units (ICUs). Hence the present study was undertaken to study the incidence, risk factors, case fatality rate of ventilator associated events (VAE) and VAP in ICU of a tertiary level hospital. **Method:** Total 100 patient of either sex, having the age of >18 years and who was received mechanical ventilation more than 48 hrs for any indication over a period of 12-18 months in an ICU of a tertiary level hospital were studied. **Results:** The incidence of VAP was 38.0% and VAP rate was 59.6/1000 ventilator days. Post op status (71%) and trauma (22%) were the most common risk factors which lead to VAP and VAE. *Acinetobacter spp* (19%) and *Klebsiella spp* (12%) were the two most common microorganisms causing VAP. Mortality or case fatality rate was 42.10%. In ventilator associated events, 45% patients developed VAC (Ventilator associated condition), 44% patients developed IVAC (Infection related Ventilator associated condition) and 38% patients developed possible VAP. **Conclusion:** VAP is a serious problem in the ICU leading to longer hospital stay higher treatment costs and increased mortality and morbidity. Prolonged mechanical ventilation is an important risk factor.

KEYWORDS : Ventilator, Pneumonia, Intensive care unit, Trauma, Acinetobacter spp, Klebsiella spp, Mortality/fatality

INTRODUCTION

Ventilator associated pneumonia (VAP) is defined as pneumonia that occurs 48 hrs or more after endotracheal intubation or tracheostomy, caused by infectious agents not present or incubating at the time mechanical ventilation was started. It can be of two types: (i) early onset VAP which is defined as VAP that occurs within the first 4 days of ventilation, and (ii) late onset VAP which is defined as VAP that occurs more than 4 days after initiation of mechanical ventilation [1]. The incidence rates calculated using 1,000 ventilator days as denominator reflect more accurately VAP risks rates. VAP rates ranged from 4 - 14/1000 ventilator days in United States and 10 - 52.7/1000 days in developing countries [2].

However, VAP is a major cause of hospital morbidity and mortality despite recent advances in diagnosis and accuracy of management. VAP requires rapid diagnosis and initiation of the appropriate antibiotic treatment, since studies have shown that the delayed administration of appropriate antibiotic therapy in patients with VAP has been associated with excess hospital mortality [3]. The presence of VAP increases hospital stay by an average of 7–9 days per patient [4, 5]. It also imposes an extra financial burden to the hospital. The risk of VAP is highest early in the course of hospital stay, and is estimated to be 3%/day during the first 5 days of ventilation, 2%/day during days 5–10 of ventilation and 1%/day after this [6].

The VAE surveillance definition algorithm developed by CDC and implemented in the NHSN in January 2013 is based on objective, streamlined, and potentially automatable criteria that identify a broad range of conditions and complications occurring in mechanically-ventilated adult patients. There are three definition tiers within the VAE algorithm: 1) Ventilator-Associated Condition (VAC); 2) Infection-related Ventilator-Associated Complication (IVAC); and 3) Possible VAP (PVAP)

VAC- Daily min FiO_2 increase ≥0.20 (20 points) for 2 days or Daily min PEEP increase ≥ 3 cm H2O for ≥ 2 days after 2+ days of stable or decreasing daily minimum values
IVAC- Temperature >38*C or ≥36*C or white cell count ≥ 12,000 or ≤ 4,000 cells/cmm and a new antimicrobial agent is started and is continued for ≥ 4 days

Possible VAP- Purulent respiratory secretions OR one of the following

- Positive culture of sputum
- Positive culture of endotracheal aspirate
- Positive culture of bronchoalveolar lavage
- Positive culture of lung tissue
- Positive culture of protected specimen brushing

Probable VAP- Purulent respiratory secretions AND one of the following

- Positive culture of endotracheal aspirate
- Positive culture of bronchoalveolar lavage
- Positive culture of lung tissue
- Positive culture of protected specimen brushing

OR one of the following results without requirement of purulent respiratory secretions

- Positive pleural fluid culture
- Positive lung histopathology
- Positive diagnostic test for legionella spp
- Positive diagnostic test for viral pathogens [7]

Lack of a gold standard for diagnosis is the major culprit of poor outcome of VAP. There are number of factors have been suspected or identified to increase the risk of VAP in various studies [4]. VAP causing pathogens also vary among different settings [8]. VAP is a well preventable disease and a proper approach decreases the hospital stay, cost, morbidity and mortality. Therefore, knowledge of the incidence of VAP, associated risk factors and common pathogens causing VAP can help in development of effective preventive measures, which in turn will decrease the mortality and morbidity, duration of treatment and hospital stay associated with VAP. There is lack of data on VAE and various aspects of VAP in the ICUs of tertiary care hospitals. Hence, a prospective observational study was undertaken to critically review the incidence and outcome, identify various risk factors and conclude specific measures that should be undertaken to prevent VAE and VAP.

MATERIALS AND METHODS

The present prospective observational study was conducted in 100 patient of either sex, having the age of >18 years and who was received mechanical ventilation more than 48 hrs for any indication over a period of 12-18 months in an ICU of a tertiary level hospital. Patient who were already on ventilation before admission to the ICU, patients admitted with pneumonia at the time of admission, patients of ARDS (Acute Respiratory Distress Syndrome) and patient who died or developed pneumonia within 48 hrs were excluded from the study.

A proforma was prepared and each patients were screened according to the pre-defined criteria including name, age, sex, date of admission to ICU, date of initiating mechanical ventilation and type of airway, i.e. orotracheal or tracheostomy. Indication of mechanical ventilation, ventilator mode and settings and any change in setting was recorded daily. Other parameters were vital signs and underlying clinical condition, general and physical examination, oxygen saturation, any history of previous antibiotic intake, the treatment being administered in the ICU and position of the patient. During the initial stage of ventilation, patients were adequately sedated and all necessary measures were taken for prevention of hospital acquired infections. VAP rate was defined as the number of VAPs/1,000 ventilator days.

A range of routine investigations were performed as per ICU protocol. Specialized investigations, like culture of tracheal tube aspirate, blood and urine was also performed. Sputum from the patients was collected from the tip of the suction catheter and transported to the laboratory in a sterile tube. Endotracheal aspirate (ETA) samples was collected on 2nd,4th and 7th day from all patients admitted in the ICU requiring mechanical ventilation for more than 48 hrs. Gram stain preparations was made from all ETA samples and examined first under low power (×10 objectives) to determine the presence and type of cells in the specimen and then observed under oil immersion field (×100 objective). The relative number of microorganisms and their morphologies was also recorded. All the samples was inoculated on blood agar, MacConkey agar and chocolate agar for semi quantitative cultures(10) Growth10^5 CFU/ml was taken as the cut-off threshold for ETAs while samples showing growth less than these thresholds were assumed to be due to colonization or contamination. In case of significant growth, the isolated colonies were subjected to gram stain and biochemical tests for identification.

Table 1: Clinical Pulmonary Infection Scoring System

CPIS points	0	1	2
Tracheal secretions	**Rare**	**Abundant**	**Purulent**
Leukocyte count (mm3)	>4,000 and <11,000	<4,000 and >11,000	<4,000 or >11,000 + band forms
Temperature (°C)	>36.5 and <38.4	>38.5 and <38.9	>39 or <36
PaO2/FIO2 ratio (mmHg)	>240 or ARDS	-	≤240 and no ARDS
Chest radiograph	No infiltrate	Diffuse infiltrate	Localized infiltrate
Culture of tracheal aspirate	**Negative**	-	**Positive**

Patients were monitored from the date of inclusion in the study to the final outcome in the ICU. VAP was diagnosed on clinical grounds based on the modified CPIS system [Table 1]. The diagnosis was confirmed when significant growth was obtained in the samples. Once the clinical suspicion was established, empirical antibiotic therapy was initiated based on guidelines prescribed by the American Thoracic Society. All patients were routinely screened by arterial blood gas (ABG) analysis every 12 hourly and appropriate steps was taken to correct any change.

A three-tiered approach simplifies VAE identification. Tier 1 focuses on respiratory status; tier 2 infection and inflammation; and tier3 VAP.

STATISTICAL ANALYSIS

Data analysis was done with the help of SPSS software version 20.0. Quantitative data was presented with the help of mean and standard deviation. Qualitative data was presented with the help of frequency, percentage. Analysis or their significance was done by using the p values obtained through Chi-square test and Fisher's exact test. Chi-square test/Fisher's exact tests were applied when to compare two or more set of variables were compared. For statistical comparison, the difference was considered significant when the p-value was found to be less than 0.05.

RESULTS

A total of 100 patients were enrolled, of them 38 patients fulfilled the clinical and microbiological criteria for the diagnosis of VAP. Thus the incidence of VAP in our study was 38.0% and the incidence density of VAP was 59.6/1000 ventilator days. In relation to gender the incidence of VAP was more among males 30(78.94%) than females 8(21.05%) and in different age groups the incidence of VAP was highest in patients between 31 to 40 years of age (26.31%) as shown in table 2.

Table 2: Age group and sex distribution Vs occurrence of VAP

Parameters		VAP		Total (n=100)	P value
		Present (n=38)	Absent (n=62)		
Age group (Years)	≤30	01 (2.63%)	06 (9.67%)	07 (7%)	0.560
	31-40	10 (26.31%)	08 (12.90%)	18 (18%)	
	41-50	05 (13.15%)	08 (12.90%)	13 (13%)	
	51-60	09 (23.68%)	16 (25.80%)	25 (25%)	
	61-70	07 (18.42%)	13 (20.96%)	20 (20%)	
	>70	06 (15.78%)	11 (17.74%)	17 (17%)	
Gender	Male	30 (78.94%)	45 (72.58%)	75 (75%)	0.635
	Female	08 (21.05%)	17 (27.41%)	25 (25%)	

Patients admitted to the ICU after post op status and trauma were at the highest risk of developing VAP with 71% and 22% of patients developing pneumonia. The incidence of VAP increased in patients who were on mechanical ventilation for >4 days (late onset) (60.52%) as compared to those who were ventilated for less than ≤4 (early onset) (15; 39.47%). Out of the 38 patients who developed VAP 12 (20%) were on a broad spectrum antibiotics in the preceding 7 days as compared to 5 (11.2%) from non VAP group. There was a total agreement in bacteriology between semi-quantitative ETAs in our study.

Patients intubated with endotracheal tube (ETT) developed VAP of 31(81.57%) and tracheostomised 26(68.42%). Co-morbidity observed in 58 patients, among them 19 (50%) patients developed VAP as shown in table 3.

Table 3: Type of airway and co-morbidity Vs Occurrence of VAP

Type of airway		VAP		Total (n=100)	P value
		Present (n=38)	Absent (n=62)		
ETT	Present	31 (81.57%)	51 (82.25%)	82 (82%)	0.999
	Absent	07 (18.42%)	11 (17.74%)	18 (18%)	
Tracheostomy tube	Present	26 (68.42%)	22 (35.48%)	48 (48%)	0.002
	Absent	12 (31.57%)	40 (64.51%)	52 (52%)	
Co-morbidities	Present	19 (50%)	39 (62.90%)	58 (58%)	0.218
	Absent	19 (50%)	23 (37.09%)	42 (42%)	

The majority, i.e. 72.22% of bacterial isolates were found to be Gram-negative bacilli Acinetobacter spp. accounted for 19% of VAP cases followed by kleibsiella pneumonae which was responsible for 12% cases. Other Gram-negative bacilli isolated were pseudomonas aeruginosa, Citrobacter freundii, Enterobacter spp., and candida, (Figure 1). Out of the total 43 isolates only 4 isolates were Gram-positive bacteria of which 3 were Staphylococcus aureus and 1 was Enterococcus spp. Among the total 38 episodes of VAP reported, 10 episodes of VAP were polymicrobial and 28 episodes were monomicrobial. In the monomicrobial episodes, Gram-

negative isolates accounted for 96% and even in polymicrobial episodes of VAP Gram-negative isolates were predominant accounting for 90%.

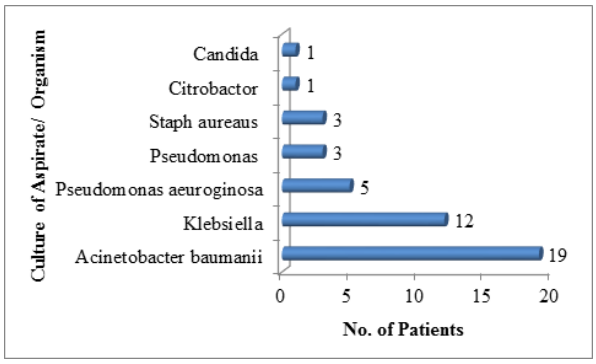

Figure 1: Patterns of the various bacterial pathogens causing VAP in the ICU

Positive End Expiratory Pressure (PEEP) was >5 cm in 34 (100%) patients among the total 38 episodes of VAP reported, FiO2 was >50% in maximum number of patients i.e. 37 and TLC was abnormal in 36 patients out of 38 cases of VAP as shown in table 4.

Table 4: PEEP, FiO2 and TLC Vs Occurrence of VAP

Parameters		VAP		Total	P value
		Present	Absent		
PEEP	≤5 cm	00	40	40	<0.001
	>5 cm	34	14	48	
	Total	34	54	88	
FiO2	10-50%	01	28	29	<0.001
	>50%	37	34	71	
	Total	38	62	100	
TLC	Normal	02	24	26	<0.001
	Abnormal	36	38	74	
	Total	38	62	100	

The overall mortality associated with VAP was observed to be 42.10% (16 cases) as depicted in figure 2. Mortality in non VAP group was not significant. As these two groups were not similar in other aspects, so the excess mortality could not be attributed entirely to VAP. Severity adjusted mortality could not be calculated. We noted that the mortality associated with VAP was highest in the age group of 31-40 years (55.6%), followed by 51-60 years (36.0%), 61-70 years (35%), >70 years (35.3%) , 41-50 years (38.5%) and <30 years(14.3) respectively. In Ventilator associated events, 45% patients developed VAC, 44% patients developed IVAC and 38% patients developed possible VAP.

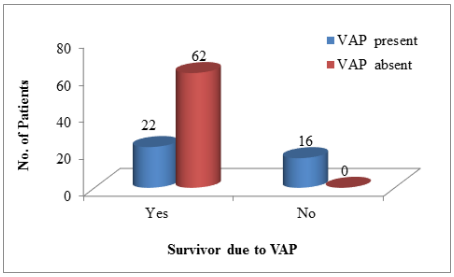

Figure 2: Survive due to VAP vs. Occurrence of VAP

DISCUSSION

In present study, the overall incidence of VAP was 38.0% which is comparable with the study conducted by Dominic et al [9] where the overall incidence of VAP was 38.56%. This was marginally higher than the incidence of 37% reported by Gadani et al [10]. The incidence density of VAP in present study was 59.6/1000 ventilator days which is high but comparable to ICUs in other developing countries [2]. The lower incidence of VAP in our study can be attributed to the fact that the total number of cases in the study and the study duration are less as compared to other study done by Sachdeva et al, showing higher incidence of VAP (70%) and the VAP rate calculated in the study was 25.11 per 1000 ventilator days, [11]. One more reason for this low incidence can be due to adequacy of nursing staff (nurse to patient ratio should ideally be 1:1 as compared to 1:4 in our institute) which may have benefitted the quality of care given to patients.

Out of the 38 cases, 15 (39.47%) were categorized under early onset group and 23 (60.52%) under the late onset group. This finding is comparable with the study done by Khan et al where they found early onset VAP was 47.5% and late onset VAP was 52.5% [12]. In present study two pathogens were responsible for 38% VAP cases. *Acinetobacter spp*. accounted for the highest number of cases followed by *Kleibsiella pneumoniae*. Similarly, in Kanafani et al study the gram-negative bacilli accounted for 83% of all isolates. The most commonly identified organism was *Acinetobacter anitratus*, followed by *Pseudomonas aeruginosa* [13] Also in Diamantis et al study *Acinetobacter baumannii* (66; 77%) was the most common pathogen, followed by *Klebsiella pneumoniae* (12; 14%) and *Pseudomonas aeruginosa* (8; 9.3%) [14] Airway intubation is associated with increased frequency of Gram-negative bacterial colonization of upper and lower respiratory tract with subsequent overgrowth and pneumonia. Non fermenters such as *Pseudomonas spp*. and *Acinetobacter spp*. were significantly associated with late onset VAP as observed by other workers but in our study even in patients with early onset VAP, *Acinetobacter* was the most common pathogen and late onset VAP *acinetobacter, pseudomonas, kleibsiella* [10, 12, and 15].

In the present study, three samples, i.e. ETA were taken for each patient and these methods produced comparable results. In study by C. Glen Mayhall, the absence of gold standard criteria for the diagnosis of VAP, the diagnostic test of choice is quantitative culture and microscopic examination of lower respiratory tract secretions. This approach provides the most accurate diagnosis of VAP and identification of the causative microorganism(s), can predict the onset of VAP and provide the identity and susceptibility of the causative microorganism(s) at the time clinical manifestations of VAP appear, can be used to assess the cause of therapy failure, provides the most effective modality for diagnosis of VAP. The study also showed that quantitative cultures of ETAs were comparable to those using invasive bronchoscopic methods [4, 16, and 17].

VAP has been associated with mortality rates of 24-76% at a variety of institutions. Patients with VAP appear to have a 2-10 fold higher risk of death compared to ventilated patients without pneumonia [18]. The overall mortality in patients with VAP in current study was 42.10% while in the non VAP patients the mortality was not significant. This figure is comparable to that of the study done by Gupta et al et al where the mortality in VAP group was 46.67% [19]. Similarly in Ranjan et al study overall mortality associated with VAP was observed to be 48.33% [20].

There is now growing evidence that high work load and low staffing level increase the risk for negative patients' outcomes such as death and healthcare-associated infections. When considering the development of VAP in relation to the underlying condition, we observed that post op status, trauma were the most common in our study. Many studies have shown that injured patients (head injury and multiple fractures) are at increased risk for VAP relative to medical patients. Another risk factor, which was evaluated in this study, was the duration of mechanical ventilation. It is observed that the incidence of

VAP increased in patients who were on mechanical ventilation for >4 days (85.17%) as compared to those who were ventilated for less than ≤4 (50%). Thus, the incidence of VAP increases with the duration of mechanical ventilation. One more risk factor, which was evaluated in our study, was the administration of broad spectrum antibiotics in the preceding 7 days. It is observed that out of the 100 patients who developed VAP, 12 (20%) are on a broad spectrum antibiotics in preceding 7 days as compared to 5 (11.2%) in the non VAP group . Furthermore, prolonged antibiotic administration to ICU patients for primary infection is thought to favour selection and subsequent colonization with resistant pathogens responsible for super infection.

Limitation of the study:

The population in the present study sample include only surgical ICU patients were small in number which has leads to lower incidence VAP and VAE.

CONCLUSION

VAP is a serious problem in the ICU leading to longer hospital stay higher treatment costs and increased mortality and morbidity. Prolonged mechanical ventilation is an important risk factor. In addition, prior use of antibiotics increases the risk of acquiring drug resistant pathogens. Effective nursing care and adequate staffing also impact on VAP prevention. Better knowledge of local patterns of pathogens causing VAP can help facilitate treatment choices. Local data collected the similar studies can assist in making informed treatment choices

We arrive at the following conclusions:

1. The incidence of VAP and VAE is directly proportional to the duration of MV.
2. Co-morbid conditions and re-intubation contribute to development of VAP and VAE.
3. A decline in PaO2/FiO2 ratio can help in early suspicion of VAP.
4. Early and planned tracheostomy is associated with lower incidence of VAP and low mortality rates.
5. Gram-negative microbes followed by methicillin resistant Staphylococcus aureus are commonest incriminating organisms.

REFERENCES

1. Morehead RS, Pinto SJ. Ventilator-associated pneumonia. Arch Intern Med 2000;160:1926-36.
2. Rodrigues DO, Cezário RC, Filho PP. Ventilator-associated pneumonia caused by multidrug-resistant Pseudomonas aeruginosa vs. other microorganisms at an adult clinical-surgical intensive care unit in a Brazilian University Hospital: Risk factors and outcomes. Int J Med Med Sci 2009;1:432-7.
3. Iregui M, Ward S, Sherman G, Fraser VJ, Kollef MH. Clinical importance of delays in the initiation of appropriate antibiotic treatment for ventilator-associated pneumonia. Chest 2002;122:262-8.
4. Chastre J, Fagon JY. Ventilator-associated pneumonia. Am J Respir Crit Care Med. 2002;165:867–903.
5. Rello J, Ollendorf DA, Oster G, Montserrat V, Bellm L, Redman R, et al. Epidemiology and outcomes of ventilator-associated pneumonia in a large US database. Chest. 2002;122:2121.
6. Cook DJ, Walter SD, Cook RJ, Griffith LE, Guyatt GH, Leasa D, et al. Incidence of and risk factors for ventilator-associated pneumonia in critically ill patients. Ann Intern Med. 1998;129:440.
7. National Healthcare Safety Network. Device-associated module ventilator-associated event (VAE) [Accessed February 2, 2017];*Centers for Disease Control and Prevention website*. 2017 Jan; http://www.cdc.gov/ nhsn/PDFs/pscManual/10-VAE_FINAL.pdf.
8. Michael S N, Donald E C. American Thoracic Society, Infectious Diseases Society of America. Guidelines for the management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia. Am J Respir Crit Care Med 2005;171:388-416.
9. Dominic RMS, Prashanth HV, Shenoy S, Baliga S. A clinico-microbiological study of ventilator-associated pneumonia in a tertiary care hospitalInt J Biol Med Res. 2012; 3(2):1651-1654.
10. Gadani H, Vyas A, Kar AK. A study of ventilator-associated pneumonia: Incidence, outcome, risk factors and measures to be taken for prevention. Indian J Anaesth. 2010;54(6):535-540.
11. Sachdeva D, Singh D, Loomba P, Kaur A, Tandon M, Bishnoi I. Assessment of surgical risk factors in the development of ventilator-associated pneumonia in neurosurgical intensive care unit patients: Alarming observations. Neurol India. 2017 Jul-Aug;65(4):779-784.
12. Khan, Z.H., Ceriana, P. & Donner, C.F. Ventilator associated pneumonia or ventilator induced pneumonia. Multidiscip Respir Med 2017;**12:**5:1-3.
13. Kanafani Z, Kara L, Hayek S & Kanj S. Ventilator-Associated Pneumonia at a Tertiary-Care Center in a Developing Country: Incidence, Microbiology, and Susceptibility Patterns of Isolated Microorganisms. Infection Control & Hospital Epidemiology 2003; 24(11):864-869.
14. Diamantis P. Kofteridis, Christina Alexopoulou, Antonios Valachis, Sofia Maraki,Dimitra Dimopoulou,1 Dimitrios Georgopoulos, and George SamonisAerosolized plus Intravenous Colistin versus Intravenous Colistin Alone for the Treatment of Ventilator-Associated Pneumonia: A Matched Case-Control Study2010; 51(11):1238–1244.
15. Usman SM, James PM, Rashmi M. Clinical and microbiological facets of ventilator associated pneumonia in the main stream with a practical contact. Int J Res Med Sci 2014;2:239-45.
16. Huang KT, Tseng CC, Fang WF, Lin MC. An early predictor of the outcome of patients with ventilator-associated pneumonia. Chang Gung Med J. 2010;33(3):274-82.
17. C. Glen Mayhall University of Texas Medical Branch, Galveston, Texas, USAVentilator-Associated Pneumonia or Not? Contemporary Diagnosis 2001;7(2).
18. Craven DE, Kunches LM, Kilinsky V, Lichtenberg DA, Make BJ, McCabe WR. Risk factors for pneumonia and fatality in patients receiving continuous mechanical ventilation. Am Rev Respir Dis. 1986;133:792–6.
19. Gupta A, Agrawal A, Mehrotra S, Singh A, Malik S, Khanna A. Incidence, risk stratification, antibiogram of pathogens isolated and clinical outcome of ventilator associated pneumonia. Indian J Crit Care Med. 2011;15(2):96-101.
20. Ranjan N, Chaudhary U, Chaudhry D, Ranjan KP. Ventilator-associated pneumonia in a tertiary care intensive care unit: Analysis of incidence, risk factors and mortality. Indian J Crit Care Med. 2014;18(4):200-204.