A Clinical Study of 50 Cases of Ventilator Associated Pneumonia

Dr. Ghanshyam B. Borisagar[1], Dr. Jayant B. Chauhan[2], Dr. R. N. Solanki[3]

Abstract

Ventilator Associated Pneumonia (VAP) is a major threat to the recovery of patients receiving Mechanical Ventilation (MV) and is one of the most common ICU-acquired infection in mechanically ventilated patients.VAP is a common complication in Intensive Care Units (ICUs); occurring in 8-28% of patients mechanically ventilated for longer than 48 hours. **Objectives**: To study the incidence and crude mortality rate, to evaluate and study the clinical profile of the patients having VAP and to study the role of modified baseline CPIS in the diagnosis of VAP. **Methodology:** The present study was carried out in a teaching tertiary care hospital. All patients above 15 year age, receiving MV for more than 48 hours at ICU with clinical suspicion of VAP were evaluated. **Results**-In the present study, out of 50 patients, maximum no. of patients were in 4^{th} to 6^{th} decades of life (62%). The youngest patient was of 16 years, while the eldest one was of 72 years. Patients belonging to pediatric age group were excluded in the present study. Majority (74%) of the patients were males. 26% of the patients were females. In the present study, Incidence of VAP is 21% and crude mortality rate is 42%.Mortality in late onset VAP (50%) was found to be twice as compared to mortality in early onset VAP (25%).Mortality in inappropriately treated patients (61.11%) was significantly higher than that of appropriately treated patients (31.25%).

Key Words: Intensive Care Unit (ICU), Infection, Mechanical Ventilation, Ventilator Associated Pneumonia

[1]Associate Professor, Department of T.B. and Chest Diseases, P.D.U. Government Medical College, Rajkot, Gujarat,India. [2]Associate Professor, Department of T.B. and Chest Diseases, GMERS Medical College,Sola, Ahmedabad,Gujarat,India. [3]Addi. Professor, Dept. of TB & Chest Diseases, B. J. Medical College, New Civil Hospital, Asarva, Ahmedabad, Gujarat, India.

Corresponding author email: gbborisagar@yahoo.co.in

Introduction: VAP is a major threat to the recovery of patients receiving MV and is one of the most common ICU-acquired infection in mechanically ventilated patients.VAP is a common complication in ICUs; occurring in 8-28% of patients mechanically ventilated for longer than 48 hours. Because of this large disease burden and the resultant attributable morbidity and mortality, there is great interest in accurately diagnosing, treating, and preventing this complication. More severely ill patients tend to develop VAP, and there are patient related, infection control related and intervention related risk factors for VAP. Most episodes of VAP are thought to develop from the aspiration of oropharyngeal secretions containing potentially pathogenic organisms. Aspiration of gastric secretions may also contribute to a lesser degree.

VAP is classified into early onset and late onset VAP depending on the duration of MV at the time of onset of VAP and commonly isolated microorganisms in these two groups are distinct. The detection of the causative organisms is imperative for guiding an appropriate therapy as there is strong evidence of the adverse effect of inadequate empirical treatment on outcome.

The early and accurate diagnosis of VAP is difficult, but because of the increasing problem of multi-resistant pathogens in many ICUs, it constitutes an urgent challenge as well as rational basis for an optimal antibiotic treatment.

The efficacy of diagnostic and preventive strategies is somewhat controversial. Diagnosis by invasive methods requires a considerable commitment of resources but can potentially reduce cost of care; however mortality benefit from this approach has not been demonstrated. Prompt administration of appropriate antibiotics seems to be the only intervention that alter outcome once the diagnosis is established.

Today there is no standard test for the diagnosis of VAP and no standard method to exclude pulmonary infections in mechanically ventilated patients with fever and multi-organ dysfunction syndrome or

multiorgan failure. Even the postmortem histological diagnosis of VAP is uncertain.

The bronchoscopic methods BAL and PSB are well standardized and widely accepted invasive diagnostic techniques for identifying the etiological pathogen of VAP. In the past the impracticability of bronchoscopic methods in ICUs and also their cost, has led to other strategies in clinical use such as non bronchoscopic techniques with catheters or mini-lavage.

In the future, it will be possible to diagnose VAP accurately and rapidly and to reduce mortality by initial appropriate antibiotic therapy. Identification of risk factors associated with VAP will help to reduce the incidence of VAP in future by avoiding the risk factors.

Aim and Objectives:

1. To study the incidence and crude mortality rate.
2. To evaluate and study the clinical profile of the patients having VAP.
3. To study the role of modified baseline CPIS in the diagnosis of VAP.
4. To study the relationship between the duration of MV and time of onset of VAP.
5. To study the microbiological organism profile in early and late onset VAP.
6. To study the mortality in early and late onset VAP and mortality in relation to appropriateness of antibiotic therapy in VAP.

Materials and Method: The present study was carried out in a teaching tertiary care hospital. All patients above 15 year age, receiving MV for more than 48 hours at ICU with clinical suspicion of VAP were evaluated. All patients had no evidence of pneumonia on admission.

The particulars of the patients like, age, sex, admission diagnosis, indication for MV, details of clinical examination and investigations including x-ray chest, hemogram, and serum biochemistry were noted. Modified baseline CPIS score was calculated in each patient. ABG was done whenever possible.

Patients were monitored for the development of VAP. Clinically suspected pneumonia was defined as the presence of new and/or progressive infiltrate in the chest radiograph with no other obvious cause and the presence of any two of the following.

1. Temperature $\geq 38^0$ C or $\leq 36^0$ C
2. White blood cell count : $\geq 11 \times 10^9$ / L or $\leq 4 \times 10^9$ / L
3. Purulent tracheal secretion or change in character of tracheal secretions.

All patients who had clinically suspected pneumonia were to undergo FOB with collection of BAL to diagnose VAP. Clinically suspected cases of VAP in which BAL culture were positive (threshold value for BAL culture was 10^4 cfu/ml) were included in the present study. Study patients were followed until they were successfully treated and discharged from the hospital or until death.ET intubation was done to initiate MV and tracheostomy was carried out when a prolonged period of MV was anticipated. Patients were managed on SERVO ventilator 900 c (siemens-elema, Sweden). There are 5 such ventilators in the ICU. They can provide MV by different modes including volume control, SIMV, pressure control, PS, CPAP etc. They also have a numbers of alarms, which protect the patients by altering ICU personnel to any malfunctions. Respiratory physiotherapy was given by a trained physiotherapist during the routine hours.

Once the vital parameters had normalized, respiratory drive had improved, patients were conscious and there was control of infection, the patients were weaned from artificial MV. Three modes SIMV, pressure support and T piece were used for weaning.

Observation and Results: In the present study 50 patients were include. The ages of the patients in the present study ranged from 16 to 72 years. Maximum no. of patients was in 4^{th}, 5^{th} and 6^{th} decades of life. (31 patients 62%), (10 patients 20%) were of geriatric age group and 3 patients (6%) were below 20 years.

In the present study 50 patients were included. Out of which 37 patients (74%) were male and 13 patients (26%) were females. So, in the present study, males outnumbered the females.

Neurological conditions (44%) including GBS, CVA, meningitis, snakebite etc. were the most common conditions for mechanical ventilation. Tropical problems (40%) like fulminant tetanus, OP poisoning and cerebral malaria were the second most common indication. The number of patients requiring mechanical ventilation due to respiratory disorders including acute exacerbation of COPD, military TB and Brconchial Asthma was minimum out of the three groups (8 patients 16%).The duration of MV at a time of onset of VAP ranged from 3 days to 38 days.

In 38 patients (76%) VAP developed within 15 days of initiation of MV. In 12

patients (24%) VAP developed between 16 to 38 days of initiation of MV. So, the onset of VAP was most common during the first 2 weeks of initiation of MV.

Purulent trachea secretions were present in 35 patients (70%), Fever was present in 33 patients (66%) and Leukocytosis in 32 patients (64%). Rales or dullness to percussion on chest examination was present in 10 patients (20%), Leucopenia was present in 2 patients (4%) and Hypothermia in only 1 patients (2%).So, purulent tracheal secretions, Fever and Leukocytosis were commonly found in patients with VAP.

The clinical pulmonary infection score (CPIS) developed in 1991 based on 6 variables. Temperature, Leucocyte count, Tracheal secretions, Chest x-ray infiltrates, Oxygenation, (Pao_2 / FIo_2 mmHg) and microbiological culture of tracheal aspirates. The modified baseline CPIS was calculated from the first five variables.Modified baseline CPIS ≥ 6 was present in 43 patients (86%). In 7 patients (14%) modified baseline CPIS was < 6.Lowest modified baseline CPIS was 4 found in 3 patients (6%) and highest modified baseline CPIS was 9 found in 2 patients (4%).

Among gram negative bacilli pseudomonas aeruginosa (13 cases, 23.2%), Hemophilus influenza (6 cases, 10.7%), Enterobacter (5 cases, 8.9%) were the leading etiological microorganisms. Other gram negative bacilli isolated were Escherichia coli (2 cases, 3.6%), Klebsiella pneumoniae (3 cases, 5.3%), Serratia, Proteus, Acinetobacter each (2 cases, 3.6%).Among gram-positive cocci, staphylococcus aureus (14 cases, 25%) was the leading etiological microorganism. Streptococcus pneumoniae was isolated in 2 cases (3.6%).

In present study, out of 50 cases of VAP, in 44 patients (88%) single microorganism was isolated and in 6 patients (12%) two microorganisms were isolated.So, Monomicrobial VAP was present in 44 patients (88%), Polymicrobial VAP in 6 patients (12%) and 56 microorganisms were isolated in 50 cases of VAP.

In present study, out of 16 cases of early onset VAP, Hemophilus influenzae (5 cases, 8.93%), MSSA (5 cases, 8.93%), S. Pneumoniae (2 case, 3.57%) were the leading etiological agents.

Out of 40 microorganisms isolated in late onset VAP, Pseudomonas (11 cases,

19.64%), MRSA (8 cases, 14.29%), Enterobacter (4 cases, 7.14%), Klebsiella pneumoniae (3 cases, 5.36%) were the leading etiological agents.(1) Coagulase negative staphylococcus aureus (2) Citrobacter (3) Stenotrophomonas maltophilia (4) Streptococcus species (5) Moraxella Catarrhalis

In present study, out of 16 patients of early onset VAP, 4 patients expired so mortality of early onset VAP was 25%.Out of 34 patients of late onset VAP, 17 patients expired, so mortality of late onset VAP was 50%.So, in present study, mortality of late onset VAP (50%) was significantly higher than that of early onset VAP (25%).

In present study, out of 32 appropriately treated patients, 10 patients expired. So, mortality in appropriately treated patients was 31.25%.Out of 18 inappropriately treated patients, 11 patients expired. So, mortality in inappropriately treated patients was 61.11%.So, in present study, mortality in inappropriately treated patients (61.11%) was significantly higher than that of appropriately treated patients (31.25%).

Appropriate treatment is defined as administration of antibiotic drugs that are active against all lower respiratory isolates or those isolated in significant concentration by invasive methods.

In 22 cases MV was indicated due to neurological conditions. Out of these 22 patients, 10 patients (45.45%) expired. In 20 cases MV was indicated due to tropical problems including OP poisoning fulminant tetanus, cerebral malaria. Out of these 20 patients, 7 patients (35%) expired. Out of 8 patients requiring MV due to respiratory disorders, 4 patients (50%) expired. So, mortality was high in patients requiring MV due to neurological conditions or respiratory disorders, and low in patients requiring MV due to tropical problems.

Discussion: VAP is a common complication in mechanically ventilated patients. Due to large disease burden and morbidity and mortality attributed to VAP, there is great interest in accurately diagnosing, treating, and preventing this complication. The bronchoscopy methods BAL & PSB are well standardized and widely accepted invasive diagnostic techniques for identifying the etiological pathogen for VAP.

In the present study, the incidence of VAP is 21%. Incidence of VAP depends on hospital setting, diagnostic criteria used to

confirm pneumonia, mean duration of MV and underlying medical conditions.

The incidence of VAP in present study (21%) is comparable with other studies like Torres et al[1] (24%), Timsit et al[2] (15%), Fagon et al[3] (28%), Tejada Artigas et al[4] (22%), Cook et al[5] (18%). In all these studies BAL or PSB was used as diagnostic criteria for VAP. The high incidence of VAP in study by Kerver et al[6] (67%) is due to use of only clinical criteria to diagnose VAP.All necessary preventive measures must be taken to reduce the incidence of VAP in ICU.

In the present study, out of 94 clinically suspected VAP cases, bacteriological confirmation was present in only 53% cases (50 cases). Bacteriological confirmation of clinically suspected VAP cases in the present study (53%) is also comparable with other studies like Luna et al[7] (49%), Bonten et al[8] (52%), Kollef et al[9] (46%), Ruiz et al[10] (55%) etc.

Clinical suspicion of VAP is based on presence of fever, leucocytosis, purulent secretion and persistent radiological infiltrates. Not all the patients with clinical suspicion of VAP have VAP. So, to reduce the over diagnosis of VAP, cost of treatment and antibiotics resistance, bacteriological confirmation of VAP must be done by quantitative culture of PSB or BAL samples collected by bronchoscopic techniques.

In the present study, the duration of MV at a time of onset of VAP ranged from 3 days to 38 days. Out of 50 patients, in 38 patients (76%) VAP developed within 15 days of initiation of MV and in 12 patients (24%). VAP developed between 16 to 38 days of initiation of MV.

In the study by Leonides Gregorakos et al[11] out of 56 patients, 50 patients (89.28%) developed VAP within 15 days of initiation of MV. In the study by Emad H. Ibrahim et al[12] out of 132 patients, 101 patients (76.51%) developed VAP during the first 15 days of initiations of MV. So, from the above studies, it is evident that the onset of VAP is most common during the first 15 days of initiation of MV.

In the present study, purulent tracheal secretions were present in 35 patients (70%), Fever in 33 patients (66%), Leucocytosis in 32 patients (64%), Rales or dullness to percussion on chest examination in 10 patients (20%), Leucopenia in 2 patients (4%) and Hypothermia in only 1 patients (2%).In the study by Camargo et al[13], purulent tracheal secretions were present in

22 patients (57.8%), Fever in 24 patients (63.1%), Leucocytosis in 26 patients (68.4%) and Rales or dullness to percussion on chest examination in 9 patients (23.6%).So, presence of purulent tracheal secretions, fever, leucocytosis or rales or dullness on chest examination in mechanically ventilated patients should raise the suspicion of VAP and further investigations should be done to diagnose VAP as early as possible and to reduce the mortality by appropriate antibiotic treatment.

In the present study, CPIS ≥ 6 was present in 43 patients (86%).In the studies by Schurink CA et al[14], Luyt CE et al[63] and Muriel Fartoukh et al[15], CPIS ≥ 6 was present in 83%, 89%, 84% patients respectively.So, In a mechanically ventilated patients, if CPIS is ≥ 6 chances of VAP is high. CPIS < 6 does not rule out VAP because in present study 7 patients (14%) had CPIS < 6. So, Routine monitoring of CPIS of mechanically ventilated patients should be done to diagnose VAP as early as possible.

The total number of organisms is more than the number of patients because some patients had more than one isolate. In the present study, among gram negative bacilli, pseudomonas (23.2%), Hemophilus influenzae (10.7%), Enterobacter (8.9%) were the leading etiological agents. Among gram positive cocci, staphylococcus aureus (25%) was the leading etiological agents.

The micro organisms profile in present study is comparable with other studies by Robert Fowler et al[16], Fagon et al[17].Pseudomonas aeruginosa and S. aureus are the most common organisms that have become more frequent and more antibiotic resistant.Type of microorganisms in VAP depends on underlying disease condition, duration of MV before onset of VAP and prior antibiotic exposure.

In the present study, 56 microorganisms were isolated in 50 cases of VAP. Polymicrobial VAP was present in 6 patients (12%).In the studies by, Fagon et al[17], Ritu Singhal et al[18],and Josep-Maria Sirvent et al[19], Polymicrobial VAP was present in 27.78%, 12.28%, 10.77% patients respectively.Presence of polymicrobial VAP requires combination of antibiotics to cover all the microorganisms isolated. Polymicrobial infection is usually a combination of aerobic gram negative bacilli

along with S. aureus or other gram positive cocci.

In the present study, the crude mortality rate of VAP is 42%.In the studies by Torres et al[1], Timsit et al[2], Cook et al[3], Fagon et al[5] and Tejada Artigas et al[4], the crude mortality rate was 33%, 57%, 24%, 53% and 44% respectively.VAP increases the mortality in mechanically ventilated patients.

In the present study, mortality was 61.11% in inappropriately treated patients and 31.25% in appropriately treated patients.In the studies by Celis et al[20] and Rello et al[21], mortality in inappropriately treated patients was 92%, 57%, 82%, 63% respectively.So, mortality in inappropriately treated patients is significantly higher than that of appropriately treated patients.So, treatment of VAP must be started promptly with adequate and appropriate antibiotics to reduce the mortality.

In the present study, mortality in early and late onset VAP was 25% and 50% respectively. In the studies by Mauricio Ruiz et al[22] and Daren Heyland et al[23], mortality in early onset VAP was 20% and 23.9% respectively and in late onset VAP mortality was 47.54% and 23.6% respectively. So, mortality is high in late onset VAP (VAP developing > 7 days after initiation of MV) and low in early onset VAP (VAP developing ≤ 7 days after initiation of MV).

The difference of mortality in early and late onset VAP may be due to difference of microorganisms commonly isolated in early and late onset VAP and their susceptibility to antibiotics. Hemophilus influenzae, MSSA, S. pneumoniae are commonly isolated in early onset VAP and these organisms are usually susceptible to many antibiotics.MRSA, psuedomonas aeruginosa and other gram-negative bacilli are commonly isolated in late onset VAP and these organisms may be resistant to antibiotics commonly used.

Conclusion: In the present study, out of 50 patients, maximum no. of patients was in 4th to 6th decades of life (62%). The youngest patient was of 16 years, while the eldest one was of 72 years. Patients belonging to paediatric age group were excluded in the present study. Majority (74%) of the patients were males. 26% of the patients were females. Male: Female ratio was around 3:1.The indications for mechanical ventilation in 44% patients were neurological conditions in the form of CVA,

GBS, Snake bite, meningitis and others. The next common indications were tropical conditions (40%) including fulminant tetanus, OP poisoning and cerebral malaria. The remaining (16%) were due to respiratory conditions like acute exacerbation of COPD, Bronchial Asthma and military TB.In 76% patients VAP developed within 15 days of initiation of MV. So, the onset of VAP was most common during the first 15 days of initiation of MV.Commonest clinical feature was purulent tracheal secretions present in 70% patients followed by fever in 66% patients and leucocytosis in 64% patients. Modified baseline CPIS ≥ 6 was present in 86% patients. In 14% patients modified baseline CPIS was < 6. So, in mechanically ventilated patients, if CPIS is ≥ 6 chances of VAP is high but CPIS < 6 does not rule out VAP.Monomicrobial VAP was present in 88% patients and polymicrobial VAP in 12% patients. 56 microorganism were isolated in 50 cases of VAP.Out of 16 cases of early onset VAP, MSSA (31.25%), Hemophilus influenzae (31.25%), S. Pneumonia (12.5%), were the leading etiological agents.Out of 40 microorganism isolated in late onset VAP, pseudomonas (27.5%), MRSA (20%), Enterobacter (10%) and Klebsiella (7.5%) were the leading etiological agents.In the present study, Incidence of VAP is 21% and crude mortality rate is 42%.Mortality in late onset VAP (50%) was found to be twice as compared to mortality in early onset VAP (25%).Mortality in inappropriately treated patients (61.11%) was significantly higher than that of appropriately treated patients (31.25%).

References

1. Torres A, Aznar R, Gatell JM, Jimenez P, Gonzalez J, Ferrer A, Celis R, Rodriguez-Roisin R. Incidence, risk, and prognosis factors of nosocomial pneumonia inmechanically ventilated patients. Am Rev Respir Dis 1990; 142: 523-528.
2. Timsit JF, Chevret S, Valcke J, Misset B, Renaud B, Goldstein FW, Vaury P, Carlet J. Mortality of nosocomial pneumonia in ventilated patients: influence of diagnostic tools. Am J Respir Crit Care Med 1996; 154: 116-123.
3. Fagon JY, Chastre J, Vuagnat A, Trouillet JL, Novara A, Gibert C. Nosocomial pneumonia and mortality

among patients in intensive care units. JAMA 1996; 275: 866-869.

4. Tejada Artigas A, Bello Dronda S, Chacon Valles E, Munoz Marco J, Villuendas Uson MC, Figueras P, Suarez FJ, Hernandez A. Risk factors for nosocomial pneumonia in critically ill trauma patients. Crit Care Med 2001;29:304-309.
5. Cook DJ, Walter SD, Cook RJ, Griffith LE, Guyatt GH, Leasa D, Jaeschke RZ, Brun-Buisson C. Incidence of and risk factors for ventilator-associated pneumonia in critically ill patients. Ann Intern Med 1998; 129: 433-440.
6. Kerver AJ, Rommes JH, Mevissen-Verhage EA, Hulstaert PF, Vos A, Verhoef J, Wittebol P. Colonization and infection in surgical intensive care patients: a prospective study. Intensive Care Med 1987; 13: 347-351.
7. Luna CM, Vujacich P, Niederman MS, Vay C, Gherardi C, Matera J, Jolly EC. Impact of BAL data on the therapy and outcome of ventilator-associated pneumonia. Chest 1997; 111: 676-685.
8. Bonten MJ, Bergmans DC, Stobberingh EE, van der Geest S, De Leeuw PW, van Tiel FH, Gaillard CA. Implementation of bronchoscopic techniques in the diagnosis of ventilator-associated pneumonia to reduce antibiotic use. Am J Respir Crit Care Med 1997; 156: 1820-1824.
9. Kollef MH, Bock KR, Richards RD, Hearns ML. The safety and diagnostic accuracy of minibronchoalveolar lavage in patients with suspected ventilator-associated pneumonia. Ann Intern Med 1995; 122: 743-748.
10. Ruiz M, Torres A, Ewig S, Marcos MA, Alcon A, Lledo R, Asenjo MA, Maldonaldo A. Noninvasive versus invasive microbial investigation in ventilator-associated pneumonia: evaluation of outcome. Am J Respir Crit Care Med 2000; 162: 119-125.
11. Leonides Gregorakos et al : Incidence and risk factors for VAP in 4 multidisciplinary ICU in Athens, Greece. Respir Care 2003;48(7):681-688.
12. Emad H. Ibrahim et al : The occurrence of VAP in a community hospital. Risk factors and clinical outcome. Chest 2001;120: 551-561.
13. Camargo et al : Ventilator associated pneumonia : comparison between quantitative and qualitative culture of

tracheal aspiration; Crit Care 2004;8(6):R422-R430.

14. Schurink CA et al : CPIS for VAP : accuracy and inter-observer variability. Intensive Care Med. 2004 Feb;30(2):217-24.
15. Luyt CE et al : Value of CPIS for the identification and management of VAP Intensive Care Med. 2004 May; 30(5):844-52.
16. Robert A Fowler et al : Variability in antibiotic prescribing patterns and outcomes in patients with clinically suspected VAP. Chest 2003;123:835-844.
17. Fagon et al : Invasive and non-invasive strategies for management of suspected VAP. Am Intern Med 2000;132:621-630.
18. Ritu Singhal et al : Profile of bacterial isolated from patients with VAP in tertiary care hospital in India. Indian J. Med Res 121, January 2005; pp63-64.
19. Sirvent JM, Vidour L, Gonzalez S et al: Microscopic examination of intracellular organisms in protected bronchoalveolar mini-lavage fluid for the diagnosis of ventilator associated pneumonia Chest 2003;123:518-523.
20. Celis et al : Nosocomial pneumonia : a multivariate analysis of risk and prognosis. Chest 1988;93:318-324.
21. Rello et al : The value of routine microbial investigation in VAP. Am J Respir Crit Care Med 1997;156:196-200.
22. Mauricio Ruiz et al : Non invasive versus invasive microbial investigation in VAP. Evaluation of outcome. Am J. Respir. Crit Care Med vol.162, No. 1, July 2000; 119-125.
23. Heyland DK, Cook DJ, Griffith L, Keenan SP, Brun-Buisson C. The attributable morbidity and mortality of ventilator-associated pneumonia in the critically ill patient. The Canadian Critical Trials Group. Am J Respir Crit Care Med 1999; 159: 1249-1256.