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STUDY OF VENTILATOR-ASSOCIATED PNEUMONIA IN A TERTIARY CARE HOSPITAL IN INDIA: INCIDENCE AND RISK FACTORS

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KEYWORDS :

Introduction:
Ventilator-associated pneumonia (VAP) is defined as nosocomial pneumonia in a patient on mechanical ventilator support (by endotracheal tube or tracheostomy) for >48 hours. (1) Mechanical ventilation is an essential, life-saving therapy for patients with critical illness and respiratory failure. Despite major advances in techniques in caring for patients whose respiratory tracts are instrumented and the routine use of efficient disinfection procedures for the respiratory equipment, nosocomial bacterial pneumonia continues to complicate the course. (2&3)

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. (4&5). 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) & prevent complications like ARDS & failure of therapy. (6)

For many years, VAP has been diagnosed by the clinical criteria published by Johanson et al. in 1972, which include the appearance of a new or progressive pulmonary infiltrate, fever, leukocytosis, and purulent tracheobronchial secretions (7); however, these criteria are nonspecific. VAP can be accurately diagnosed by any one of several standard criteria: histopathologic examination of lung tissue obtained by open lung biopsy, rapid cavitation of a pulmonary infiltrate in the absence of cancer or tuberculosis, positive pleural fluid culture, same species with same antibiogram isolated from blood and respiratory secretions without another identifiable source of bacteremia, and histopathologic examination of lung tissue at autopsy (6). However, these criteria are based on invasive procedures for obtaining lung tissue or on uncommon manifestations or complications of VAP so another approach is needed for the definitive diagnosis of VAP. In the absence of gold standard criteria for the diagnosis of VAP, The Clinical Pulmonary Infection Scoring (CPIS) system originally proposed by Pugin and others helps in diagnosing VAP with better sensitivity (72%) and specificity (80%). (8)

Several risk factors may predispose patients to either colonization of the respiratory tract with pathogenic microorganisms and/or aspiration of contaminated secretions (9-11).

Knowledge of the incidence of VAP in our hospital and the associated risk factors are imperative for development and use of more effective preventive measures.

Aims and objective:
The aim of the study is to know the incidence, risk factors, spectrum of organisms and sensitivity patterns, and the outcome in patients with Ventilator-associated pneumonia (VAP) in our hospital setting.

Inclusion criteria: All the patients on mechanical ventilation (MV) for more than 48 hours in the Medical Intensive Care Unit will be included in this study.

Exclusion Criteria: Patients with pneumonia prior to mechanical ventilation or within 48 hours of MV & patients suffering from ARDS will be excluded.

Type & duration of Study: Prospective, cross-sectional.
Sample Size: All patients admitted in the MICU of our institute for the period of Jan 2014 to Dec 2015.

Methodology:
This prospective, observational, cross-sectional cohort study was undertaken after obtaining approval from Institution Ethics Committee. After taking informed consent from each patient's next of kin, data was collected & recorded in the case record form. (Appendix-1). Endotracheal aspirate (ETA) was collected from all patients who were clinically suspected of VAP, admitted in the ICU requiring mechanical ventilation for more than 48 hrs. Samples were transported to the laboratory immediately. Gram stain preparations were made from all 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 (×100objective) (12). The relative number of micro-organisms and their morphologies were recorded. The presence or absence of the potential risk factors for the development of VAP was also recorded. The study patients were monitored every third day for the development of VAP using clinical and microbiological criteria until either discharge or death.

Criteria for diagnosing VAP
The patients fulfilling both the clinical and microbiological criteria were diagnosed to be suffering from VAP. Clinical criteria included was modified clinical pulmonary infection score (CPIS) > 6 (Table 1) [8] and microbiological criteria included was positive Gram stain (> 10 polymorphonuclear cells/low power field and ≥ 1 bacteria/oil immersion field with or without the presence of intracellular bacteria) and semi quantitative endotracheal aspirate culture showing, moderate to heavy growth / ≥ 105 CFU/ ml [13-17].

Table-1

CPIS points	0	1	2
Temperature (°C)	≥ 36.5and ≤ 38.4	≥ 38.5 and ≤ 38.9	≥ 39 or ≤ 36
Leucocyte count (per mm3)	4,000 - 11,000	< 4,000 or > 11,000	< 4,000 or > 11,000 + band forms ≥ 500
Tracheal secretions	Rare	Abundant	Abundant + Purulent
PaO2/ FiO2 mm Hg	> 240 or ARDS	-	≤ 240 and no ARDS
Chest radiograph	No infiltrate	Diffuse infiltrate	Localized infiltrate
Culture of tracheal aspirate	Light growth or no growth	Moderate or heavy growth of pathogenic bacteria	Moderate or heavy growth of pathogenic bacteria and presence of the same bacteria in Gram stai

Identification of VAP pathogens
Semi-quantitative culture of endotracheal aspirate (EA) was performed for identification of VAP pathogens. EA was inoculated on

5% sheep blood agar. After incubation at 37°C in a 5% CO2 incubator for 24 hours, a colony count was done and expressed as number of colony forming units per ml (CFU/ml). The microorganisms isolated at a concentration of more than 10^5 CFU/ ml was considered as VAP pathogens [13-17] and were identified based on standard bacteriological procedures including Gram's stain, colony morphology on blood agar and Mac Conkey agar, and biochemical reactions [18]. Sensitivity testing was done as per CLSI guideline. [19]

Statistical analysis:
Test of proportion and Chi square tests were used for data analysis.

Results
During the study period 3517 patients were admitted to MICU, of which 592 patients required Mechanical Ventilation. Among these, 439 patients required mechanical ventilation for more than 48 hours.

(Study group)
Of the 439 patients, 83 patients developed VAP during their ICU stay. The incidence of VAP/1000 ventilator days was 48.06. (Table-2). Eighty two percent cases developed VAP after 72 hours of mechanical ventilation (Late onset VAP) (Table-3). All the patients were followed consecutively till patient were either extubated, tracheotomized, expired, or lost in follow-up.

Demographic Characteristics: Fifty one percent patients were in the age group of 51 to 70 years, Out of 83 patients Sixty seven were males & 16 females. (Table -4)

The indication for mechanical ventilation among these patients was different, common indications being Trauma (15), respiratory failure (12), neurological disease (28), Poisoning (17), Septicemia (5) and Others (5). (Table-4)

Microbial Etiology: In 68 cases VAP was of monobacterial origin while polymicrobial in 15 patients (18.0%).(Table-5)

Most cases of VAP were caused by Gram-negative bacteria, which accounted for 89.5% of causative organisms. Klebsiella (48.8%), Pseudomonas aeruginosa (20.9%) and Acinetobacter baumannii (19.7%) were the most common Gram-negative bacteria associated with VAP and Staphylococcus aureus (10.4%) was the most common Gram-positive bacteria among patients with VAP. MRSA accounted for 50.0% of the VAP due to Staphylococcus aureus. The sensitivity pattern of those GNB by Kirby Bauer disc diffusion method showed maximum sensitivity for Meropenam (98%) followed by Pipracillin tazobactum (63%). Maximum resistance was seen for Ciprofloxacin & Cephalosporins [Table-7] Presence of ESBL was seen in 91.8% gram negative isolates. Fifty percent of Staphylococcus strains were Methicillin resistant.

Risk factors: Risk factors for VAP in our study were, use of nasogastric tube, prolonged mechanical ventilation(>5 days),, intense sedation, altered level of consciousness, re-intubation, and tracheostomy.(Table-8)

Discussion:
Nosocomial infections are a significant problem in the delivery of intensive care services. VAP is an important nosocomial infection among ICU patients receiving Mechanical Ventillation.

In the study of our set up, males predominated (80%). The mean age group in our study was 50.41+/- 13.16 years. As most of the cases were of Neurological disorders & respiratory failure mean age was on higher side.

Ventilator-associated pneumonia (VAP) is the most frequent intensive-care-unit (ICU)-acquired infection, with an incidence ranging from 6 to 52%. (20). The incidence of VAP is varied among different studies, depending on the definition, the type of hospital or ICU, the population studied and the level of antibiotic exposure. The incidence of VAP in present study was 48.06/1000 ventilator days. In the present study, 18.07 % of cases were early-onset VAP, The incidence of early onset VAP was low in our study as compared to other studies which show early onset VAP to be between 27 to 40 %.

According to Odds Ratio & chi Square test, most significant risk factor in our study was Re-intubation/ emergency intubation & tracheostomy followed by duration of ventilation. Patients with neurological disorders were significantly predisposed for the development of VAP due to impaired consciousness and inadequate cough reflexes. In a study involving four multidisciplinary ICUs in Athens, univariate analysis indicated that tracheostomy, bronchoscopy, enteral feeding, duration of mechanical ventilation ≥5 days, mean duration of central vein catheterization, APACHE II score ≥18 on admission, and acute physiology score ≥10 on admission were significantly associated with VAP (21).

The etiological agent varies according to patient population, unit, hospital or country. Multidrug resistant and ESBL producers were chiefly responsible for late onset VAP whereas early onset VAP was caused mainly by Staphylococcus aureus. In our study high rate of ESBL-producing bacteria was seen among all Gram negative bacteria (91.8%) .A multicentric study done in India has shown a rate between 73 and 79%.[22]

In the present study polymicrobial etiology was seen in 18% cases. In two Indian studies, by Mukhopadhyay C et al. & Singhal R. et al. 12.3% and 16.3% of VAP cases were polymicrobial.(23 & 24)

Early-onset VAP is often caused by Staphylococcus aureus, Streptococcus pneumoniae, Haemophilus influenzae,while late-onset VAP is more frequently caused by multidrugresistant Pseudomonas aeruginosa, Acinetobacter or Enterobacter spp., or methicillin-resistant S. aureus (MRSA)(2) . In present study Eighty nine percent cases of VAP were due to gram negative bacteria, Klebsiella (49%), followed by Pseudomonas (21%) & Acinetobacter (20%) were most commonly isolated gram negative bacilli associated with VAP study. Staphylococcus aureus was etiological factor in 10% cases out of which 5% cases were due to MRSA

In case of gram negative bacteria Carbapenam (Meropenam & Imepenam) were found to be most effective antibiotic followed by Pipracillin- tazobactum. Least sensitive were third generation cephalosporins (Ceftriaxone & Ceftazadime) & ciprofloxacin. MSSA & MRSA showed 100% susceptibility to Vancomycin. Incidence of MDR pathogen was very high (89.5%), indicating need for appropriate antimicrobial therapy against MDR pathogens.

Conclusions: Knowledge of incidence of VAP & risk factors may be useful in implementing simple and effective preventive measures. The most common pathogens causing VAP in our study were Klebsiella spp. and *Pseudomonas* aeruginosa and were associated with a high fatality rate.

Tables

Table-2 Vap Incidence/1,000 Ventilator Days

Year	Total No of DAYS of Patients on Mechanical Ventilation	Patients acquiring VAP	Incidence/1,000 ventilator days
2014	693	44	63.49
2015	1034	39	30.94
TOTAL	1727	83	48.06

Table-3 Early Onset V/s Late Onset

	TOTAL	Early Onset:	Late Onset:
2014	44	7	37
2015	39	8	31
Total	83 (100%)	15 (18.07%)	68(81.92%)

Table 4: Demographic Characteristics.

AGE	Number of cases
LESS THAN 30	**6**
31-40	**15**
41-50	**16**
51-60	**23**
61-70	**22**
MORE THAN 70	**1**
Male	67
Female	16

Table-5 Primary Diagnosis On Admission

Admission Diagnosis	Number
Trauma	12
Respiratory failure	16
Neurological disease (Meningitis, Encepalitis, GBS, Stroke)	28
Poisoning	14
Septicemia	6
Others	7
Total	83

Table-6. Etiological Agents

Etiological agents	Number of cases
Monobacterial	68 (81.92%)
Polymicrobial	15 (18.07%)
Total	

Table-7 Resistance Pattern Of Gram Negative Bacilli

Organism	AK	LE	PT	CIP	I	CIS	CTR	CAZ	MER
Pseudomonas (18)	9	13	4	17	2	16	18	13	0
Acinetobacter (17)	11	12	10	17	2	17	17	17	1
Klebsiella (42)	20	25	14	37	0	39	40	40	0
E.Coli (6)	2	1	0	5	0	4	4	4	0
Non-fermenter (3)	2	2	2	3	2	3	3	3	1
TOTAL 86(89.58)	44(51.1)	53(61.6)	30(34.8)	79(91.8)	6 (6.9)	79(91.8)	82(95.3)	77(89.5)	2(2.3)

TABLE-8 RISK FACTORS FOR VAP

Risk Factors	Non VAP (n=356)	VAP (n=83)	Chi-square X^2	Odds Ratio	*P* Value
Stress ulcer prophylaxis	331 (93%)	83 (100%)	-	-	-
Nasogastric tube	167 (47%)	52 (63%)	6.7	1.89 (1.16-3.10)	0.0098
Duration of Ventillation > 5d	235 (66%)	70 (84%)	10.6	2.77 (1.47-5.21)	0.001
Altered level of Unconciousness	75(21%)	35 (42%)	15.9	2.73 (1.65-4.53	0.00007
Reintubation /emergency intubation/ Tracheostomy	106(30%)	60(72%)	51.73	6.15 (3.62-10.47)	0.00001

References

1. Davis KA. Ventilator-associated pneumonia: a review. J Intensive Care Med 2006 ;21:211–26.
2. Rello J, Ollendorf DA, Oster G, et al. Epidemiology and outcomes of ventilator associated pneumonia in a large US database. Chest 2002;122:2115–21.
3. Chastre J, Fagon JY. Ventilator-associated pneumonia. Am J Respir Crit Care Med 2002;165:867–903.
4. 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
5. Joseph NM, Sistla S, Dutta TM et al,. Ventilator-associated pneumonia in a tertiary care hospital in India: incidence and risk factors. J Infect Dev Ctries 2009; 3(10):771-777.
6. C. Glen Mayhall. Ventilator-Associated Pneumonia or Not? Contemporary Diagnosis. Emerging Infectious Diseases . Vol. 7, No. 2, March–April 2001:200-04
7. Johanson WG Jr, Pierce AK, Sanford JP, Thomas GD. Nosocomial respiratory infections with gram-negative bacilli. The significance of colonization of the respiratory tract. Ann Intern Med 1972;77:701-6.
8. Pugin J, Auckenthaler R, Mili N, Janssens JP, Lew PD, Suter PM (1991) Diagnosis of ventilator-associated pneumonia by bacteriologic analysis of bronchoscopic and nonbronchoscopic "blind" bronchoalveolar lavage fluid. Am Rev Respir Dis 143: 1121-1129.
9. Ibrahim EH, Tracy L, Hill C, Fraser VJ, Kollef MH (2001) The occurrence of ventilator-associated pneumonia in a community hospital: risk factors and clinical outcomes. Chest 120: 555-561.
10. Afdar N, Crnich CJ, Maki DG (2005) The pathogenesis of ventilator-associated pneumonia: its relevance to developing effective strategies for prevention. Respir Care 50: 725-739.
11. Erbay RH, Yalcin AN, Zencir M, Serin S, Atalay H (2004) Costs and risk factors for ventilator-associated pneumonia in a Turkish university hospital's intensive care unit: a case-control study. BMC Pulm Med 4: 3
12. Duguid JP. Staining methods. In: Collee JG, Fraser AG, Marimion BP, Simmons A, editors. Mackie and McCartney Practical Medical Microbiology: 14th ed. New York: Churchill Livingstone; 1996; p. 793- 812
13. Jourdain B, Novara A, Joly-Guillou M-L, Dombret M-C, Calvat S,Trouillet J-L, et al. Role of quantitative cultures of endotracheal aspirates in the diagnosis of nosocomial pneumonia. Am J Respir Crit Care Med 1995;152:241-6.
14. Porzecanski I and Bowton DL (2006) Diagnosis and treatment of ventilator-associated pneumonia. Chest 130: 597-604.
15. Wu CL, Yang DI, Wang NY, Kuo HT, Chen PZ (2002) Quantitative culture of endotracheal aspirates in the diagnosis of ventilator-associated pneumonia in patients with treatment failure. Chest 122: 662-668.
16. Koenig SM and Truwit JD (2006) Ventilator-associated pneumonia: diagnosis, treatment, and prevention. Clin Microbiol Rev 19: 637-657.
17. Marquette CH, Georges H, Wallet F, Ramon P, Saulnier F, Neviere R,et al. Diagnostic efficiency of endotracheal aspirates with quantitative bacterial cultures in intubated patients with suspected pneumonia.Comparison with the protected specimen brush. Am Rev Respir Dis 1993;148:138-44
18. Collee JG, Miles RB, Watt B. Test for identification of bacteria. In:Collee JG, Fraser AG, Marimion BP, Simmons A, editors. Mackie and McCartney Practical Medical Microbiology. 14th ed. New York: ChurchillLivingstone; 1996. p. 131-49.
19. Clinical and Laboratory Standards Institute. Performance Standards for Antimicrobial Susceptibility Testing; 17th informational supplement. CLSI document M100-S17(ISBN 1- 56238-625-5).Clinical and Laboratory Standards Institute USA, 2007.
20. Koenig SM, Truwit JD. Ventilator-associated pneumonia: diagnosis, treatment, and prevention. Clin Microbiol Rev 2006;19:637–57.
21. Apostolopoulou E, Bakakos P, Katostaras T, Gregorakos L. Incidence and risk factors for ventilator-associated pneumonia in 4 multidisciplinary intensive care units in Athens, Greece. Respir Care 2003;48:681–8.
22. Chaudhuri BN, Rodrigues C, Balaji V, et al. Incidence of ESBL producers amongst Gram-negative bacilli isolated from intra-abdominal infections across India (based on SMART study, 2007 data). J Assoc Physicians India. 2011 May;59:287-92.
23. Mukhopadhyay C, Bhargava A, Ayyagari A. Role of mechanical ventilation & development of multidrug resistant organisms in hospital acquired pneumonia.Indian J Med Res 2003;118:229–35.
24. Singhal R, Mohanty S, Sood S, Das B, Kapil A. Profile of bacterial isolates from patients with ventilator associated pneumonias in a tertiary care hospital in India.Indian J Med Res 2005;121:63–4.