Ventilator associated pneumonia in a ICU of a tertiary care Hospital in India

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Abstract

Ventilator Associated Pneumonia (VAP) refers to a type of pneumonia that occurs more than 48–72 hours after endotracheal intubation. Risk factors include prolonged mechanical ventilation, reintubation after extubation. Our aim was to find the incidence of VAP, total days of mechanical ventilation, days of ICU and hospital stay at our institution, proportion of various bacterial pathogens isolated from tracheal aspirate of patients with VAP and their antibiotic sensitivity pattern.

Material &Methods: A prospective cohort study was conducted on 100 patients who were admitted to medical intensive care unit of SCB Medical college and on ventilatory support for two or more days and were not suffering from pneumonia prior to putting them on ventilator. Endotracheal aspirates were obtained under strict aseptic precautions using a 22-inch Romson's 12F suction catheter with a mucus extractor. Gram staining and biochemical tests for identification and antimicrobial susceptibility test were performed. The patients were classified into four groups named VAP, NON VAP, SURVIVORS and NON SURVIVORS. All the data collected were compiled and tabulated.

Observation: The incidence of VAP in this study was 30%. The association between genders (p value-0.372), age (p value-0.929) and VAP infection was not found to be significant. There was no significant correlation between the primary disease and development of VAP (p value =0.24). Most common organism isolated was *P. aeruginosa*, (9 isolates) followed by MRSA (7 isolates) and most of them were resistant to commonly used antibiotics.

Conclusion: VAP patients have higher mortality rate, longer duration of mechanical ventilation and duration of hospital stay than NON VAP patients. Early diagnosis of VAP and initiation of appropriate antibiotic treatment is vital to prevent the adverse outcomes.

Key Words: Ventilator, Pneumonia, Endotracheal

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Introduction

Hospital acquired pneumonia also known as nosocomial pneumonia, is defined as the onset of pneumonia symptoms more than 48 hrs. after admission to the hospital. Ventilator associated pneumonia (VAP) is a type of nosocomial pneumonia that occurs more than 48–72 hours after endotracheal intubation and receiving mechanical ventilation in ICU. VAP occurs in 9–27% of all intubated patients[1].Risk factors include prolonged mechanical ventilation, reintubation after extubation. If the infection occurs within 48 -72 hrs of intubation then it is called early onset type and after 72 hrs of intubation it is called late onset type VAP respectively.

Delay in initiating appropriate antibiotic therapy can increase the mortality associated with VAP, and thus therapy should not be postponed for the purpose of performing diagnosis. This initial empirical antimicrobial therapy can be modified based on the knowledge of local microbiological data, patient characteristics, and sensitivity pattern of expected pathogens at the institution.

There is currently no gold standard for diagnosis of VAP. The CDC criteria for diagnosis are as follows:

1. mechanical ventilation for greater than 48 hrs,
2. new or persistent or progressive radiographic infiltrates
3. fever greater than 38.5 c
4. leukocytosis or leukopenia
5. positive culture for endotracheal aspirate

The aim of the study was to find the incidence of VAP, whether any risk factor was there that predispose to VAP development and mortality associated with VAP and secondary outcomes like total days of mechanical ventilation, days of ICU and hospital stay at our institution, proportion of various bacterial pathogens isolated from tracheal aspirate of patients with VAP, and their antibiotic sensitivity pattern.

Material & Methods

A prospective cohort study was conducted on 100 patients who were admitted to medical intensive care unit of SCB Medical College and on ventilatory support for two or more days and were not suffering from pneumonia prior to putting them on ventilator. After getting the informed consent from the patient relatives,

the study was done. Elective tracheostomy was done in some of the patients who were thought to stay for a long period on mechanical ventilation to avoid re intubation. Patients, who died or developed pneumonia within 48 hrs. or those who were admitted with pneumonia at the time of admission and patients of ARDS (Acute Respiratory Distress Syndrome) were excluded from the study.

The baseline evaluations like age, any concomitant diseases, the severity of illness based on APACHE II score during first 24 hours of admission were noted. The diagnosis of VAP was established using clinical pulmonary infection score (CPIS),[3,4] which was evaluated on a daily basis until the patient was on ventilator support. CPIS of greater than six was used as diagnostic criteria for VAP. Early-onset VAP was defined as VAP occurring within the first 72 hours and late-onset VAP was defined as VAP occurring after 72 hours after patients put on mechanical ventilation respectively. Endotracheal aspirate was preferred over protected specimen brush (PSB) sampling and broncho-alveolar lavage (BAL), as these techniques are more invasive and studies have shown no mortality benefit of using these over endotracheal aspirate.

Endotracheal aspirates were obtained under strict aseptic precautions using a 22-inch Romson's 12F suction catheter with a mucus extractor, which was gently introduced through the endotracheal tube for a distance of approximately 25 cm. Gentle aspiration was then performed without instilling saline, and the catheter was withdrawn from the endotracheal tube. After this, 4 ml of 0.9% saline was injected in the endotracheal tube with a sterile syringe to flush the exudates into a sterile container for collection. The samples were immediately taken to the laboratory for processing. Care was taken during the procedure to avoid injury to the tracheal mucosa and hypoxia development.

Gram stain preparations were made from all aspirate samples within the first hour. Samples were inoculated onto 5% blood agar, Mac Conkey agar. Isolated colonies were subjected to Gram staining and biochemical tests for identification. Antimicrobial susceptibility test was performed using Mueller-Hinton agar plates by Kirby-Bauer disc diffusion method, according to the Clinical Laboratory Standards Institute (CLSI) guidelines. The patients diagnosed with VAP were started on initial empirical antibiotic therapy, which was guided by the fact whether a multi-drug resistant pathogen was expected. Later on, based on culture sensitivity reports the treatment was modified.

The primary outcome measure assessed was mortality. Other measures assessed included the incidence of VAP, frequency of different pathogens isolated, their antibiotic sensitivity pattern, duration of mechanical ventilation and duration of hospital stay. The results were also analysed to find out any association between patient characteristics, severity of underlying illness as assessed by APACHE II score, factors related to course of care like re-intubation with the incidence and rate of mortality in VAP.

The patients were classified into four groups named VAP, NON VAP, SURVIVORS and NON SURVIVORS. All the data collected were compiled and tabulated. The statistical analysis were done by chi-square test, fisher test and paired t test. The p value was calculated and <0.05 was considered significant.

Observation

Table 1: Gender Distribution

Sex	Non VAP(%)	VAP(%)	Total	P-Value-0.372
Male	45(64%)	16(53%)	61	
Female	25(36%)	14(47%)	39	

It showed that the disease had no predilection for gender as nearly same percentage of males and females are affected and not significant (p value=0.372)

Table 2: Age Distribution

Age	Non VAP	%	VAP	%	Total	
15-20	9	13	6	20	15	**P – Value- 0.929**
21-30	21	30	6	20	27	
31-40	7	10	4	13	11	**CHI –Square-1.90**
41-50	10	14	4	13	14	
51-60	12	17	6	20	18	
61-70	8	12	3	10	11	
>70	3	4	1	4	4	

Age did not affect the development of VAP (p- value= 0.929) which was not significant.

Table 3: Comparison of diseases with VAP, Non VAP, Survivor, Non Survivor

Disorder	No. of PTS	VAP(%)	Non-VAP(%)	CHI Square Test-13.87	Survivors (%)	Non Survivors(%)	CHI-Square Test- 14.69
Meningitis	10	3(30)	7(70)		9(90)	1(10)	
GBS	6	3(50)	3(50)		5(83)	1(17)	
Snake Bite	17	3(18)	14(82)	P Value-0.24	16(94)	1(6)	
Cerebral Vascular Accident	20	4(20)	16(80)		10(50)	10(50)	P-Value-O.2
Cardiogenic Shock	10	1(10)	9(90)		6(60)	4(40)	
Sepsis	12	7(58)	5(42)		7(58)	5(42)	
Metabolic(ARF/CRF/DKA)	6	2(33)	4(67)		4(67)	2(33)	
Malaria	4	2(50)	2(50)		3(75)	1(25)	
Dengue Shock Syndrome	3	0	3(100)		2(67)	1(33)	
Poisoning	6	2(33)	4(67)		3(50)	3(50)	
Pancreatitis	3	2(67)	1(33)		1(33)	2(66)	
Hepatic Encephalopathy	3	1(33)	2(67)		2(67)	1(33)	
Total	100	30	70		68	32	

Most no. of cases were CVA followed by snake bite, sepsis, meningitis, cardiogenic shock etc. Sepsis contributed most to VAP (58%). CVApatients contributed most to the mortality followed by sepsis. But there was no association between clinical disease and development of VAP and also for mortality.

Table 4: Causative Organisms in VAP- Frequency, Type of VAP, and Associated Mortality

Organism	Total No. of Isolates	% of Isolates	Early VAP	Late VAP	Survivors (%)	Non Survivors (%)
Pseudomonas Aeruginosa	9	30	0	9	6(66.6)	3(33.3)
MRSA	7	23	2	5	5(71)	2(29)
K. Pneumonia	6	20	2	4	2(33.3)	4(66.6)
A. Baumannii	5	17	2	3	1(20)	4(80)
Enterococii	1	3.3	0	1	1(100)	0
S.Pneumoniae	1	3.3	1	0	1(100)	0
Candida	1	3.3	0	1	1(100)	0
Total	30		7	23	17	13

Out of total 30 VAP patients, most no. of isolates were pseudomonas aerugenosa spp. (30%) followed by methicillin resistant staphylococcus aureus(MRSA). Pseudomonas caused late VAP in all the isolates. All other organisms caused both early and late VAP. Mortality rate was highest in patients infected by acenatobacter baumanii and Klebsiella pneumonie.

A total of 10 out of 100 patients required reintubation while receiving mechanical ventilation. Out of the 10 patients 8 developed VAP i.e.80%. (p value =0.0009) which was highly significant. Elective tracheostomy was done in 10 patients and 4 of them developed VAP and 6 did not (p value =0.4814).13 patients(3 Early VAP and 10 Late VAP) out 30 in VAP category had died where as in non VAP category 19 patients out of 70 had died (p value = 0.15). So there was no strong correlation of VAP and mortality.

Table 5: Comparison of Apache II Score and Outcome from Ventilator

Category	VAP	Non VAP	P Value	Survivor	Non Survivor	P Value
Apache II Score	21 ±7.02	15.88 ±5.57	<0.0002	14.11 ±3.49	24.43 ±5.56	0.001
Duration of Mechanical Ventilation (Days)	12.66 ± 3.69	5.72 ± 2.58	<0.0001	7.25±3.54	9.0 ±5.57	0.06
Duration of Hospital Stay(Days)	16.1± +/- 3.81	8.7± 3.73	<0.0001	11.20±4.42	10.31 ± 6.24	0.414

The mean APACHE II score, mean duration of mechanical ventilation and mean duration of hospital stay in VAP group was significantly higher than non VAP group (p value <0.05). Mean APACHE II score was significantly higher in non-survivor but mean duration of mechanical ventilation and mean duration of hospital stay had no effect on mortality.

Table 6: Antibiogram of the Isolates

Organism Isolated	Highly Sensitive	Intermediate	Resistant
Pseudomonas Aerugenosa(9)	Polymyxin, colistin, meropenem, imipenem	Piperacilin +tazobactam, gatifloxacin	Levofloxacin, ceftazidime, cefoperazone+sulbactam
MRSA(7)	Vancomycin, linezolid	Clindamycin, levofloxacin, gatifloxacin	Oxacillin, methicillin, amoxicillin+clavulanate, erythromycin
Klebsiella Pneumonea(6)	Polymyxin b, colistin,	Imipenem, meropenem, gatifloxacin	Ceftriaxone, ceftazidime, cefotaxime
Acenatobacter Baumannii(5)	Polymyxin b, colistin,	Imipenem, meropenem	Levofloxacin, cefoperazone+sulbactam, piperacilin+tazobactam
Streptococcus Pneumonia(1)	Vancomycin, imipenem, meropenem	Penicillin, ceftriaxone, ceftazidime	Erythromycin, tetracyclines, ofloxacin, chloramphenicol
Candida Spp.(1)			
Enterococii (1)	Vancomycin, linezolid	Penicillins, cephalosporin	Ofloxacin, gentamycin

Discussion

The incidence of VAP in this study was 30%. Gupta et al[1] found it to be 28%. The association between genders(p value-0.372), age (p value-0.929) and VAP infection was not found to be significant which was similar to study done by Gupta et al.[1]

Different types of clinical cases were included in our study like CVA, snake bite, cardiogenic shock, meningitis, acute pancreatitis, hepatic encephalopathy and dengue shock syndrome etc. (Table 3). Patients who needed more days of mechanical ventilation developed VAP more often. So cases of septicemic shock, guillain-barrie syndrome, meningitis, complicated malaria required prolong mechanical ventilation and developed more VAP because of prolong mechanical ventilation. At the same time cases requiring less ventilation like snake bite, cardiogenic shock developed less number of VAP. There was no significant correlation between the primary disease and development of VAP (p value =0.24). This was supported by the study of Gupta et al[1] and Awasthi S et al[2]. CVA patients contributed most to the mortality in our study second being sepsis but the relation between diseases and mortality was not significant (p value= 0.2)

CPIS scoring system was used as a diagnostic tool for VAP identification. Patients with a score >6 were considered to be affected by pneumonia. Luytet al[3] and Croce et al[4] found CPIS scoring system a highly sensitive tool to diagnose VAP.

Out of the 10 patients, who were reintubated, 8 developed VAP (p value = 0.0009). It showed that reintubation was a definite risk factor for VAP development. Similar results also found by Gupta et al[1], Panwar et al[5], Rit et al[6]. This might be because of invasive procedure of intubation was repeated and also duration of ventilation was increased. Another hypothesis for this was that the patient who required re-intubation would have been vulnerable to aspiration in the interval between extubation and re-intubation. Although the incidence of VAP was found to be lower in patients who underwent early tracheostomy (4 out of 10), but was not found to be statistically significant (*P* - 0.4816).

The most common organism isolated was *P. aeruginosa*, (9 isolates). All were from patients with late-onset VAP. The next most common organism isolated was MRSA (seven isolates, of which five were isolated from patients with late onset VAP) but there was no specific correlation between infecting organism and type of VAP (p value = 0.373). Other common organisms isolated were *K. Pneumoniae*(6 isolates) and *A. baumannii*(5 isolates). Rit et al[6] found the same result.

Antibiotic sensitivity pattern of organisms (table-6) suggested that most strains of *P. Aeruginosa* were resistant to the commonly used beta-lactam antibiotics with 5 (55.56%) isolates being resistant to ceftazidime, cefepime, cefoperazone+sulbactam but they were highly sensitive to antibiotics like polymyxin B, colistin, meropenem, imipenem. All isolated strains of *S. aureus*were MRSA and sensitive to linezolid and vancomycin but resistant to methicillin, oxacillin, amoxicillin+ clavulanic acid, erythromycin etc. Most isolates of *K. Pneumonia* were ESBL producing. One isolate of *K. Pneumonia* was resistant to both the carbapenems used but were sensitive to polymyxin and colistin and resistant to commonly used cephalosporins like ceftriaxone, cefotaxime, ceftazidime

Carbapenem resistance was noted still higher with *A. baumannii*, with 50% isolates resistant to carbapenems but they were sensitive to higher antibiotics like polymyxin b and colistin. The overall picture suggests that number of drug-resistant strains of various organisms was rising and an important cause of VAP in our setting. Ijaj et al[7], Krishnamurthy et al[8], Gupta et al[1]got same antibiogram profile of VAP patients in their studies.

In our study the overall mortality was 32%. Out of that mortality in VAP group was 43.33%, while in non-VAP group, it was 27.14% and the difference was not statistically significant (*P value*-0.15). Although VAP was not independently associated with mortality, mortality rate was higher in patients with VAP. In other studies mortality varied from 30% to 50%. The mortality in VAP patients was significantly higher than NON VAP patients. Gupta et al[1] and Panwar et al[5], found same type of result.

Naved et al[9] and Gupta et al[1] took APACHE II score to evaluate the condition of patient at admission and they found that patients with high scores had higher mortality rate thus supporting our study. Mortality was also influenced by the type of organism isolated being highest for infections caused by *A. baumannii*(80%) and *K. pneumoniae*(66.6%).

The mean duration of mechanical ventilation was higher in VAP patients that in NON VAP patients (p value <0.0001). This showed that there was a highly significant difference between VAP and NON VAP patients regarding duration of mechanical ventilation. Gupta et al[1] found that longer duration of ventilation was required in VAP patients than NON VAP patients. Awasthi et al[2] mentioned same result in VAP patients of age 1 to 12 yrs. But there was no significant difference in days of mechanical ventilation between survivors and non survivors (p value = 0.06).

The VAP patients had a longer duration of hospital stay than non VAP (p value < 0 .0001). Dubey et al[10], Gupta et al[1] found that VAP patients had a longer duration of hospital stay but there was no significant difference between survivors and non survivors regarding total duration of hospital stay(p value = 0.414).

The mean duration of ICU stay was significantly higher in VAP patients than in NON VAP patients (p value < 0.0001). It increased the cost of treatment which was a very important aspect for patient family in Indian setup.

Conclusion

Demographic profiles like age, gender did not affect the development of VAP neither did the underlying primary disorders of the patients. Patients with high APACHE II score were found to be more vulnerable to VAP. Patients who were reintubated for a number of times were seen to develop VAP more frequently. Most frequent species of bacteria isolated were pseudomonas spp and MRSA. Most of the isolated organisms were resistant to commonly used antibiotics like penicillins, cephalosporins but sensitive to higher and newer antibiotics like polymyxin, colistin, linezolid, vancomycin. Patients with high APACHE II score had more adverse outcome in terms of mortality, duration of mechanical ventilation, ICU stay and hospital stay.

VAP patients have higher mortality rate, longer duration of mechanical ventilation and duration of hospital stay than NON VAP patients. Early diagnosis of VAP and initiation of appropriate antibiotic treatment is vital to prevent the adverse outcomes. Proper hand hygiene and other sterile techniques will prevent spread of infection. Regular fumigation of ICUs and sterilization of ventilators will definitely decrease the incidence of VAP.

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