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Research Article

A STUDY ON CLINICAL PROFILE OF VENTILATOR ASSOCIATED PNEUMONIA (VAP) AND ANTIBIOTIC SENSITIVITY PATTERN AT A TERTIARY CARE HOSPITAL

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Ventilator associated pneumonia; Intensive care unit; Hospital acquired infection; Clinical pulmonary infection scoring system.

A B S T R A C T

Background and objectives :Ventilator associated pneumonia(VAP) is a hospital acquired infection(HAI) seen among critically ill patients on mechanical ventilation due to various causes in intensive care units(ICUs). It is associated with increased morbidity and mortality which increases the cost of health care. The objective of our study was to determine the clinical profile, organisms isolated and antibiotic susceptibility pattern in VAP patients in a tertiary care hospital.

Materials and methods: In this cross sectional prospective study,40 patients who developed features of ventilator associated pneumonia on a platform of mechanical ventilator for >48 hrs in ICU were included in the study.VAP was then diagnosed based on clinical pulmonary infection scoring system(CPIS) with a score of >=6.

Results: The incidence density rate of VAP was 21.875 per 1,000 ventilator days. Most of the patients had late onset VAP (60.7%) with average number of days of onset, of around 8 days.

Pseudomonas spp. and Acinetobacter, whereas Enterobacteriacea and, Staphylococcus aureus were commonly isolated organisms. Polymicrobial infections were not detected. Antibiotics like colistin, tigecycline and beta-lactamases were the most commonly effective antibiotics. Prior antibiotic therapy ($P < 0.0001$), hospitalization for 5 days or more ($P < 0.0001$), MV for 5 days or more ($P < 0.0001$), supine head position ($P < 0.0001$), reintubation ($P = 0.0012$) and impaired consciousness ($P = 0.0191$) were significant risk factors for VAP.

Conclusion : Ventilator associated pneumonia is associated with a significant increase in length of stay in ICU, time of mechanical ventilation, different complications and certain risk factors which further worsens the prognosis.

INTRODUCTION

Ventilator associated pneumonia (VAP) refers to pneumonia that develops in patients who have been mechanically ventilated for a duration of more than 48 hrs. It is the most common nosocomial infection that occurs in the ICU , which is a major cause of hospital morbidity and mortality, despite recent advances in diagnosis and management. On any given day in the ICU, an average of 10% of patients will have pneumonia-VAP is the overwhelming majority of cases[1].The incidence ranges from 6 to 52% and can reach upto 76% in some specific settings[2]. Some of the risk factors believed to be associated with VAP are duration of ventilator support, reintubation, supine position, advanced age and altered level of consciousness. Three factors that are critical in the pathogenesis of VAP are: colonization of the oropharynx with pathogenic microorganisms, aspiration of these organisms from the oropharynx into the lower respiratory tract and compromise of the normal host defense mechanisms.[3]

The most common organisms to be isolated are- Pseudomonas, Klebsiella, Acinetobacter and Methicillin resistant Staphylococcus aureus species[4]. It has been found that delay in the early diagnosis and treatment is one of the major reasons for increased mortality associated with VAP. Also, lack of gold standard for diagnosis is another major reason for high mortality associated with VAP[5] .The incidence of VAP increases with the duration of mechanical ventilation.3% per day for first 5 days, 2% per day for 6-10 days and 1% per day after day 10 and the crude mortality rate of VAP is 27-76% especially with organisms like Pseudomonas or Acinetobacter[6].

Early onset VAP usually occurs within 4 days of admission and are often associated with drug sensitive organisms. Late-onset VAP occurs after 5 or more days of admission and are associated with multi-drug resistant organisms and thus carry poor prognosis.

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Objectives of the Study

1. To study the clinical profile of VAP.
2. To determine the antibiotic sensitivity pattern in VAP.

METHODS

This is a prospective cross-sectional study in patients with VAP, admitted to the medical ICU for various causes in the hospital attached to BMCRI, Bangalore, India. Study was conducted for a period of 1 year from Aug 2018 to Aug 2019. Institutional ethics committe permission was obtained from BMCRI, Bangalore. A written informed consent was obtained from each patient's atttenders since the patients were intubated.

40 patients diagnosed to have ventilator associated pneumonia based on the clinical pulmonary infection scoring system, were involved in the study, after satisfying inclusion and exclusion criteria.

Detailed history of patients which involves past respiratory infections, antibiotic use and co-morbid conditions like hypertension and type 2 DM were included. All patients were evaluated by thorough clinical examination, routine investigations and specific laboratory and radiological investigations. All patients received protocol line of treatment with empirical antibiotics regimen and later changed after obtaining the culture and sensitivity report. Co-morbid conditions and other complications due to VAP were managed aggressively. Regular blood culture and ET tube sample for c/s were done. Non-responders were identified and were re-evaluated with fresh investigations. All patients were then followed up till discharge/death.

RESULTS

40 culture positive VAP patients were systematically studied regarding the clinical profile and antibiotic sensitivity pattern. All patients were analysed in terms of age, gender, need for mechanical ventilation, organisms isolated, antibiotic sensitivity and effectiveness. All patients were treated with standard care and the empirical antibiotics used were- Inj.ceftriaxone, Inj.meropenem, Inj.piperacillin-tazobactam.

All culture positive ET tube samplings were assessed for main biological parameters. Early VAP was noted in 42.5% of patients &late VAP was noted in 57.5% of patients.

The baseline demographic characteristics of study population are given in table 1.

Baseline Characteristics of Study Population **Table 1**

Age, in years	42.67±14.9
Gender (M/F)	28/12
No of patients	40
Died	20
Survived	20
Length of ICU stay	9.68±4.79
Mortality	50%

The gender distribution of study population-(FIGURE 1)

Age distribution of study population with the mean age of patients being 42.67+_14.9 years (FIGURE 2)

Mean Age Distribution of Subjects Based on Outcome **Table 2**

Outcome	N	Minimum (years)	Maximum (years)	Mean	Std. Deviation	Mean diff	P value
Death	20	22	87	49.85	18.446	14.35	0.005*
Survival	20	18	55	35.50	11.283		

Mean age was higher in those who died (49.8518.446) as compared to those survived (35.50 11.283).T test showed significant statistical difference between the mean age of died and survival (p=0.005).

Baseline Diagnosis of the Study Patients **Table 3**

Diagnosis	Number of patients
Acute alcohol Intoxication	2
COPD	6
Assault with bowel injury	2
CAP	2
DKA	3
Diabetic foot	1
Viral fever	4
CVA	3
Hollow viscus perforation	3
IHD in failure	2
Poisoning	12

Of the 40 patients admitted in ICU for mechanical ventilation, 42.5%, had H/O of poisoning,25% had metabolic complications, 20% had sepsis and remaining included polytrauma and cerebrovascular accident.

Cross-Tabulation of Et Culture and Outcome **Table 4**

Tracheal Secretions	Outcome		Total
	Death	Survival	
Acinetobacter baumanni	3	5	8
Escherichia coli	4	4	8
Klebsiella pneumoniae	6	4	10
Pseudomonas aeruginosa	7	6	13
Streptococcus pneumoniae	0	1	1
Total	20	20	40
Chi-square value- 1.97 p value- 0.74			

Table 4-shows cross-tabulation of ET culture and outcome. Out of 40 subjects, majority i.e., 13 of them had pseudomonas aeruginosa, followed by klebsiella pneumoniae among 10, 8 each of them had escherichia coli and acinetobacter baumanni and only one had streptococcus pneumoniae.

Among 20 who died, ET culture of majority i.e 7 of them had pseudomonas aeruginosa, 6 of them had klebsiella pneumonia, 4 of them had escherichia coli and 3 of them had acinetobacter baumanni Chi-square test showed no significant association between ET culture and outcome (2= 1.97, p=0.74).

Endotracheal tube culture and outcome **Figure 3**

Cross-Tabulation of Antibiotic Sensitivity and Outcome **Table-5**

		Outcome		Total	Chi-square value	P value
		Died	Survival			
Cephalosporins	Positive	0	3	3	3.24	0.07
Flouroquinolones	Positive	0	0	0		
Aminoglycosides	Positive	3	3	6	0.00	1.00
Tetracyclines	Positive	11	12	23	0.10	0.74
Betalactamases	Positive	6	8	14	0.44	0.50
Colistin	Positive	12	9	21	0.90	0.34

Regarding the susceptibility profiles of the etiological agents of VAP colistin was found to be most effective antibiotic

followed by tigecycline and the beta-lactamases like-imipenem, piperacillin/tazobactam and flouroquinolones were least effective drugs. But none of the antibiotics significantly altered the mortality

Antibiotic Sensitivity and Outcome-(Figure-4)

Comparison of VAP Onset and Outcome **Table-6**

Gender	Outcome		Total
	Died	Survival	
Early	11	6	17
Late	9	14	23
Total	20	20	40

The incidence of late onset VAP (23/40,57.75%)) was slightly more than early onset VAP(17/40,42.5%)) and death was significantly higher in early onset VAP(11/17,64.7%) than in late onset VAP(9/23,39.1%).

VAP Onset and Outcome-(FIGURE-5)

Analysis of Risk Factors of Ventilator Associated Pneumonia (VAP) By Chi Square (Fisher's Exact) Test- **Table-7**

Risk factors	***P*-value**
Hospitalization for 5 days or more	<0.0001
Mechanical ventilation for 5 days or	<0.0001
Emergency intubation	0.1721
Reintubation	0.0012
Intravenous sedatives	0.6704
Prior antibiotic therapy	<0.0001
Impaired consciousness	0.0191
Tracheostomy	0.5269
Steroid therapy	0.5754
Supine head position	<0.0001
Surgical causes	1.0000
Neurological disorders	0.5167

DISCUSSION

VAP is an important nosocomial infection among the critically ill patients, receiving MV for different etiologies.VAP carry high morbidity and mortality with increased costs of treatment. Many factors are responsible for poor prognosis in VAP patients. Many scoring systems include APACHE 2, SOFA and CPIS scoring systems are available to predict the outcome in these patients. With all modern technology and latest antibiotics, VAP still carry high mortality, if not recognized early.

40 VAP patients were systematically studied for the poor prognostic markers in this study. The commonest organisms to be isolated were Klebsiella pneumonia (25%), Pseudomonas aeruginosa(32.5%) and proportionate deaths include (60%)in Klebsiella and(53.8%) in Pseudomonas which is on par with study done by Kanafani Z.*et al*[8](2003) and Dey A.*et al*[9] (2007).

A few biochemical markers are associated with poor prognosis like -elevated WBC counts (15478.50 7884.3) (p= 0.034) were associated with poorer prognosis compared to low WBC counts(10913.70 4846.5).Mean urea levels was statistically higher among dead patients (77.00 73.84) as compared to survived patients (33.45 15.60), p=0.014.Creatinine levels showed a statistically significant higher mean among dead (1.90 1.83) compared to survived patients (0.910 .42), p= 0.024.

In a similar study by J Inchai *et al*[10],also found that prognosis was poorer in patients with elevated total count and dearanged RFT.

Regarding the susceptibility profiles of the etiological agents of VAP-colistin was found to be most effective antibiotic followed by tigecycline and the beta-lactamases like-imipenem, piperacillin/tazobactam and flouroquinolones were least effective drugs. But none of the antibiotics significantly altered the mortality.

In a similar study by Michal Walaszek *et al*[11], also found that colistin as the most effective antibiotic followed by beta-lactamases, aminoglycosides and third generation cephalosporins.

In our study we found that presence of co-morbidities like diabetes mellitus(p=0.028),hypertension(p=0.047),severe sepsis(p=0.002) were associated with poorer prognosis as compared to others.

In a similar study by Li chang *et al*[12], found that in patients who had developed VAP -the poor prognostic factors were age >65 years, smoking, coronary heart disease, DM, hypertension, COPD, Icu & Hospital stay and days of mechanical ventilation.

The incidence of late onset VAP(23/40,57.75%) was slightly more than early onset VAP(17/40,42.5%)however death was significantly higher in early onset VAP(11/17,64.7%) than in late onset VAP(9/23,39.1%).In a similar study by Reham M *et al*[13], incidence of late onset VAP(60.36%) was found to be more than early onset VAP(39.6%).

In a study by J Chastre *et al*[14], also found that mortality was significantly higher among early onset VAP patients than late onset VAP patients.

In the present study we found that-prior antibiotic therapy, hospitalization of 5 days or more, supine head position, re-intubation were the other significant risk factors associated with poor prognosis in VAP.

In a similar study by Udayan M *et al*[4], also found that prior antibiotic therapy, supine head position and mechanical ventilation for more than 5 days as significant risk factors for developing VAP.

CONCLUSION

Ventilator associated pneumonia is a common and serious ICU complication, that is associated with a longer duration of mechanical ventilation, ICU/hospital stay, and increases in-hospital morbidity and mortality which may lead to higher treatment costs.

To conclude, awareness of independent risk factors documented in this study may be helpful in identifying patients who are at higher risk for developing VAP and also those who are likely to have poorer prognosis. This can help in implementing appropriate preventive measures, including proper positioning and patient care and modulating intervention measures during management.

Limitations

Sample size was small only 40 patients were included in the study.

Declarations

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by institutional ethical committee**.**

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