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Original Research Article

A study on poor prognostic factors associated with ventilator associated pneumonia at a tertiary care hospital

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ABSTRACT

Background: 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 aim of this study was to determine the poor prognostic factors associated with VAP.
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. All patients were evaluated and correlated with different parameters for the treatment and outcome.
Results: Most of the patients had late onset VAP (60.7%) with average number of days being around 8 days. *Pseudomonas*, *Acinetobacter*, *Enterobacteriacea*, *Staphylococcus aureus* were commonly isolated organisms. Polymicrobial infections were not detected. Antibiotics like colistin, tigecycline and beta-lactamases are the most commonly effective antibiotics. Of the 40 VAP patients,20 patients survived and 20 died with protocol line of treatment. Following poor prognostic factors were identified-Early onset VAP (42.5%), elderly patients (>65 years) (90%), Type 2 DM (80%), hypertension (70%), prior antibiotic therapy (65%), prolonged supine position (68%) and re-intubation (75%).
Conclusions: Ventilator associated pneumonia is associated with a significant increase in length of stay in ICU, time of mechanical ventilation and different complications and certain risk factors further worsens the prognosis.

Keywords: Clinical pulmonary infection scoring system, Hospital acquired infection, Intensive care unit, Ventilator associated pneumonia

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 to occur in ICU and 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 up to 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, acteinobacter and Methicillin resistant *staphylococcus aureus* species.[4] It has been found that delay in early diagnosis and treatment is one of the major reasons for increased mortality associated with VAP. Also, lack of gold standard for diagnosis is one of the major reasons 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.

A number of poor prognostic factors are associated with increased morbidity and mortality in Ventilator associated pneumonia in spite of appropriate treatment, like Age, h/o antibiotic use, other existing co-morbidities-DM, hypertension, poor immunity of the individual, late onset VAP are associated with high degree of morbidity and mortality.[7]

Objective of this study was to assess the treatment outcome in VAP patients. To identify the poor prognostic factors.

METHODS

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

Among 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 involving past respiratory infections, antibiotic use and co-morbid conditions like hypertension, type 2 DM were included. All patients were evaluated with thorough clinical examination, routine investigations, specific laboratory and radiological investigations. All patients received protocol line of treatment with empirical antibiotics regimen and was later changed after obtaining the culture and sensitivity report.

Co-morbid conditions and other complications due to VAP were managed aggressively. Regular blood culture, 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

Among 40 culture positive VAP patients were systematically studied for the treatment outcome and later for the factors which contributed to the morbidity and mortality. Out of 40, 24 patients had history of antibiotic exposure and 8 of them were in antibiotic abuse category wherein antibiotics were used for >5 occasions in past 6 months. Of 24 patients who misused antibiotics only 6 completed the full course of prescribed antibiotics in last 6 months. Important co-morbid conditions like hypertension, type 2 DM, COPD, alcohol intake, obesity, malnutrition were taken into consideration.

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 and late VAP was noted in 57.5% of patients. All poor responders were thoroughly investigated with special investigations like blood culture, HRCT, fibreoptic bronchoscopy.

The baseline demographic characteristics of study population is given in Table 1.

Table 1: Baseline characteristics of study population.

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%

Table 2: Mean age distribution of subjects based on outcome.

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

Table 3: Baseline diagnosis of the study patients.

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

Mean age was higher in died (49.85±18.446) as compared to those survived (35.50±11.283). T test showed statistically significant difference between the mean age of died and survival (p=0.005) (Table 2).

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, cerebrovascular accident (Table 3).

Table 4 comparison of the mean distribution of various parameters of the subjects based on outcome using independent sample t. Mean urea levels was statistically significantly higher among dead (77.00±73.84) as compared to survival (33.45±15.60), p=0.014.

Table 4: Comparison of the mean distribution of the subjects based on important parameters.

	Survival	N	Minimum	Maximum	Mean	Std. Deviation	Mean diff	p value
WBC	Died	20	6400	41200	15478.50	7884.3	4564.8	0.034*
	Survival	20	2060	20800	10913.70	4846.5		
Urea	Died	20	10	270	77.00	73.84	43.55	0.014*
	Survival	20	10	70	33.45	15.60		
Creatinine	Died	20	0.40	8.60	1.90	1.83	0.99	0.024*
	Survival	20	0.20	1.80	0.91	0.42		

Table 5: Cross-tabulation of et culture and outcome.

Tracheal secretions	Outcome		Total
	Died	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

Creatinine levels showed a statistically significant higher mean among dead (1.90±1.83) compared to survival (0.91±0.42), p= 0.024.

Table 5 cross-tabulation of ET culture and outcome, out of 40 subjects' majority 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 ($\chi 2$= 1.97, p=0.74).

Out of 40 only 10 of them had diabetes mellitus, among died 12 of them did not have DM and 8 of them had DM, whereas among survival 18 of them did not have DM and only 2 had DM. Chi-square test showed significant association between DM and outcome ($\chi 2$= 4.8, p=0.028).

Table 6: Cross tabulation of systemic diseases and habits and outcome.

Outcome			Total	Chi-square value	p value
	Died	Survival			
DM	8	2	10	4.8	0.028*
HTN	10	4	14	3.95	0.047*
Sepsis	8	0	8	10.0	0.002*
Prior antibiotic exposure	16	8	24	3.63	0.05
Prolonged supine	15	8	23	5.012	0.025
Re-intubation	10	4	14	3.956	0.046
Early onset vap	11	6	17	2.55	0.01

Among 14 out of 40 had HTN, among died 10 of them had HTN and 4 of them did not have HTN, in survival 16 did not have and only 4 of them have HTN. Chi-square

test showed significant association between DM and outcome (χ2= 3.95, p=0.047).

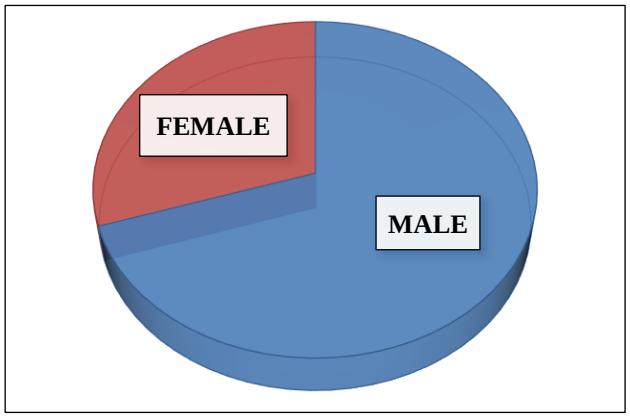

Figure 1: The gender distribution of study population.

Figure 1 shows that 70% i.e majority of patients were males (28/40) and 30% of patients were females (12/40).

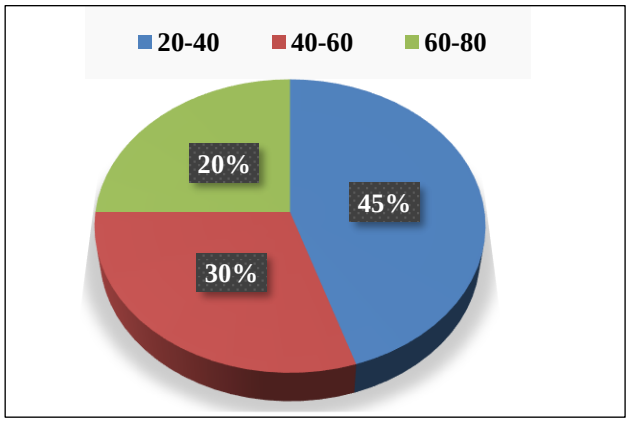

Figure 2: Age distribution of study population.

Figure 2 shows that majority of patients are in younger age group i.e <40 years (45%), 30% in middle age group and only 20% in elderly age group.

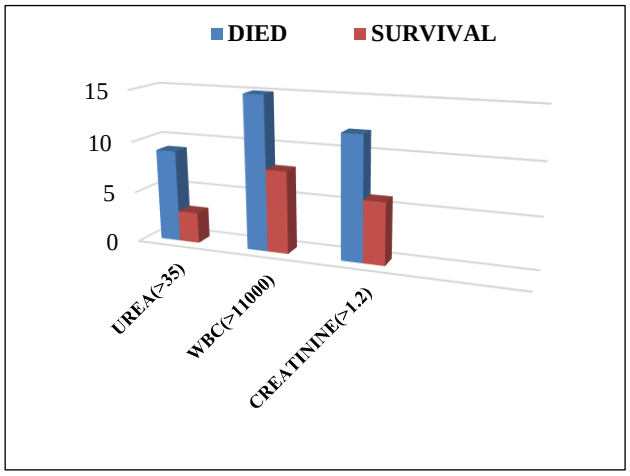

Figure 3: Important parameters and outcome.

Figure 3 represents that blood urea (>35), creatinine (>1.2) and total counts (>11000) were much elevated in dead patients than who survived.

Out of 40 i.e, 32 did not have sepsis, among died 12 of them were negative and 8 of them were positive to sepsis, in survival all 20 of them were negative to sepsis. Chi-square test showed significant association between sepsis and outcome (χ2= 10.0, p=0.002).

Out of 40, 23 of them had late onset of VAP, among died majority 11 had early onset of VAP, whereas in survival 14 of them had late onset VAP. Chi-square test showed significant association between early VAP onset and outcome (χ2= 2.55, p=0.01).

Out of 40, 18 patients had prior antibiotic exposure and among died 12 had history of antibiotic exposure where as in survival patients only 6 had prior antibiotic exposure (χ2=3.63, p=0.05).

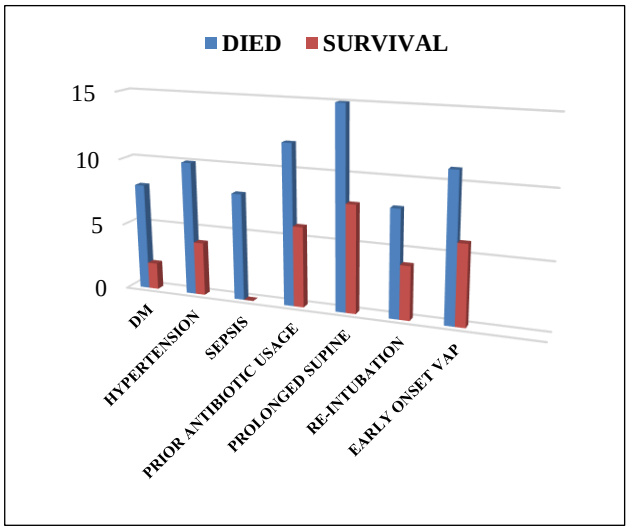

Figure 4: Prognostic factors and outcome.

Figure 4 illustrates the distribution of poor prognostic factors among dead and survived patients.

Out of 40 patients, 23 patients were in prolonged supine position, out of which 15 of them died and only 8 of them survived. (χ2=5.012, p=0.025) Out of 40 patients, 12 patients had to re-intubated, among them 8 patients died and only 4 survived (χ2= 3.956, p=0.046) (Table 6).

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.

Among 40 VAP patients were systematically studied for the poor prognostic markers in this study. The commonest organisms to be isolated were Klebsiella pneumoniae (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, and Dey A. et al.[8,9]

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 (0.91±0.42), p= 0.024. In a similar study by J Inchai et al, also found that prognosis was poorer in patients with elevated total count and dearanged RFT.[10]

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 Walaszek M et al, also found that colistin as the most effective antibiotic followed by beta-lactamases, aminoglycosides and third generation cephalosporins.[11]

In this study authors 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, found that in patients who had developed VAP -the poor prognostic factors were age >65 years, smoking, coronary heart disease, DM, hypertension, COPD, ICU and Hospital stay and days of mechanical ventilation.[12]

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, incidence of late onset VAP (60.36%) was found to be more than early onset VAP(39.6%).[13]

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

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, also found that prior antibiotic therapy, supine head position and mechanical ventilation for more than 5 days as significant risk factors for developing VAP.[4]

Limitation of this study was to Sample size was small only 40 patients were included in the study.

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.

This study gives an idea about the clinical picture of ventilator associated pneumonia in India and poor prognostic factors associated resulting in increased morbidity and mortality in VAP.

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.

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