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Original Article

Frequency and Outcome of Ventilator Associated Pneumonia in an Intensive Care Unit of a Tertiary Care Hospital in Dhaka

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Abstract:

Background: *Intubation and mechanical ventilation are integral parts of critical care management. Though a lifesaving intervention, invasive mechanical ventilation imposes a great risk of nosocomial pneumonia to the patient. Ventilator associated pneumonia rates in an ICU is a predictor of successful infection control strategy.*

Objectives: *objective of the current study was to study the frequency of ventilator associated pneumonia and its outcome in the critical care setting.*

Methods: *This prospective observational cross-sectional study was done in department of critical care medicine of BIRDEM General Hospital for the period of 1st July, 2017 to 30th June, 2018. All consecutive patients who were intubated and mechanically ventilated for a period of at least 48 hours within the study period were evaluated for the selection criteria of the study. The included study participants were followed up daily for signs of development of VAP. Once VAP was suspected pertinent investigations were sent to confirm the diagnosis. Study participants were observed regularly to identify signs of pulmonary infection. The microbiological tests were done in the Department of Microbiology of BIRDEM. Quantitative culture was done (expressed as CFU/ml) and antibiotic sensitivity was done by standard disc diffusion method. A cutoff value of 10^5 CFU/ml was taken as a positive culture. CPIS score was calculated to diagnose VAP .The study participants were followed up to transfer to step down unit/ward or death to see the outcome. Data were collected in preformed data collection sheet and analyzed by the statistical packages for social sciences (SPSS) software version 22.*

Results: *In this study total 92 patients out of 625 intubated patients during the study period after fulfilling the inclusion criteria were selected as study participants. The mean age of the the participants who developed VAP was 65.05±14.79 years with a range of 27 to 101 years. 62.9% (n=22) were female and 37.1% (n=13) were male. In this study DM, HTN & Renal disease were the most common co-morbidities. Among the 35 VAP positive participants 51.4% (n=18) developed early onset VAP and 48.6% (n=17) developed late onset VAP. Among the VAP positive participants 31.4% were survivors and 68.6% were non-survivors and among the VAP negative participants 68.4% were survivors and 31.6% were non survivors (p=0.001).*

Conclusion: *Frequency of VAP was 5.6% in the study. It was associated with significantly prolonged length of mechanical ventilation and length of ICU stay and high mortality.*

Key words: *Ventilator Associated Pneumonia (VAP), Clinical Pulmonary Infection Score (CPIS), American Thoracic Society/Infectious Disease Society America (ATS/IDSA), ARDS (Adult Respiratory Distress Syndrome).*

Introduction

ICU admission imposes great risk of nosocomial infections on the patients due to various invasive interventions.[1] Patients who undergo invasive procedures such as endotracheal intubation and mechanical ventilation (MV) which predispose to a nosocomial pneumonia of a special entity named as 'Ventilator Associated Pneumonia' (VAP). Almost half of all the cases of hospital acquired pneumonia are due to VAP and about half of all antibiotic administrations in ICU are for treatment of VAP.[2] American Thoracic Society/Infectious Diseases Society of America (ATS/IDSA) guidelines, 2005 on management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia suggested that a diagnosis of VAP may be considered when pneumonia develop in patients who have been receiving mechanical ventilation for at least 48 hours, characterized by the presence of a new or progressive infiltrate in CXR, signs of systemic infection (fever, altered white blood cell count), changes in sputum characteristics, and detection of a causative agent in respiratory secretion.[3] VAP may be further categorized into early-onset VAP (within 4 days) and late-onset VAP (beyond 4 days)[3]

VAP results in high morbidity and mortality, prolonged lengths and increased cost of hospitalization. This excess morbidity results in estimated costs per case of nearly US$15,000.[4] VAP rates range from 1.2 to 8.5 per 1,000

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ventilator days and are reliant on the definition used for diagnosis.[1]

Material and Methods

This cross-sectional study was carried out in the Intensive Care Unit of Department of Critical Care Medicine (ICU) of BIRDEM General Hospital, Dhaka., over a period of 12 months in 2017-18. All intubated and mechanically ventilated patients aged above 18 years who were kept intubated for a duration of more than 48 hours were included as study participants by consecutive sampling. Those who were suspected or confirmed as having community-acquired pneumonia, nosocomial pneumonia or ARDS on admission were excluded. Patients intubated in other ICUs prior to admission, patients intubated for less than 48 hours and patients developing pneumonia within 48 hours of intubation were also excluded from the study. The included participants had initial diagnoses other than pneumonia which included neurological, cardiac, renal, pulmonary, infectious pathologies. The indication for intubation and M/V were respiratory failure, cardiac arrest, air way protection. The endotracheal tube used in the ICU were not antibiotic coated and two types of tubes were used (conventional and tube with subglottic suction lumen).Informed written consent was taken from participants' first degree relatives as the participants were unable to communicate properly due to presence of endotracheal tubes and sedations provided during mechanical ventilation. Study participants were observed regularly to identify signs of pulmonary infection. Once VAP was suspected clinically, complete blood count, portable CXR was advised and tracheal aspirate was collected using conventional specimen trap and aseptic endotracheal suctioning technique and sent for Gram staining, Acid Fast Bacilii (AFB) staining, culture and sensitivity testing. Quantitative culture was done (expressed as CFU/ml) and antibiotic sensitivity was done by standard disc diffusion method. A cutoff value of 10^5 CFU/ml was taken as a positive culture. CPIS [6] score was calculated to diagnose VAP. Serial complete blood count, portable CXR was done for further follow up. When a participant required inotropes to maintain blood pressure, serum lactate level was sent to confirm septic shock. Participants were further followed to assess outcome up to transfer out or death. Participants who were readmitted to the ICU after initial improvement, only the first admission was included in the study.

VAP rates were described in accordance with the standard established by the National Control System of Nosocomial Infection of the Centers for Disease Control and Prevention (rate = number of VAP cases/1000 mechanical ventilator days).[7] The primary outcome studied was ICU mortality and the secondary outcome parameters studied were length of M/V and length of ICU stay. Those who were transferred were classified as survivors and those who were dead were categorized as non-survivors.

Appropriate data was collected by using a preformed data sheet.

Necessary data including patients' particulars, age, gender, primary diagnosis on admission, co-morbidities, indication for intubation and ventilation, date of intubation, physical examination findings and laboratory investigations on admission and on diagnosis of VAP was documented from history sheet and investigation papers. Prior to this study, written permission was obtained from institutional review board.

Collected data was processed and analyzed by using Statistical Package for Social Sciences (SPSS) software version 22. All the descriptive data were expressed by frequency and percentage (%). All the quantitative data were expressed in mean ± SD. Unpaired t test and chi-square tests were performed to assess significance of association between the variables. The level of significance was accepted as <0.05 P value.

Ethical approval from the Institutional Review Board of BIRDEM was obtained prior to the commencement of the study. Informed written consent was taken from the participants family members after explaining all the facts. As the procedure involved in the study were of minimal risk, no further potential ethical issue was to be raised. The participants were assured of confidentiality.

Results

The aim of this study was to observe the frequency and outcome of patients developing ventilator associated pneumonia. All results were presented as mean ± SD or frequency as applicable.

During the study period a total of 1563 patients were admitted into the ICU and 625 patients were intubated. 92 patients had fulfilled the inclusion criteria and were selected as study participants

Table I shows distribution of study participants according to association of age with development of VAP.

Table 1

	VAP		
Age (years)	**Positive (n,%) (n=35)**	**Negative (n,%) (n=57)**	**p-value**
≤40	2 (5.7)	2 (3.5)	
41 - 60	12 (34.3)	24 (42.1)	
61 - 80	16 (45.7)	24 (42.1)	
>80	5 (14.3)	7 (12.3)	
Total	**35 (100.0)**	**57 (100.0)**	
Mean±SD	**65.05±14.79**	**62.56±13.62**	0.411

Table II shows co-morbidities of the study participants.

Table II

Co-morbidities	VAP Positive (n=35)	Negative (n=57)	p-value
Diabetes mellitus	30 (85.7)	46 (80.7)	0.538
Hypertension	29 (82.9)	43 (75.4)	0.402
IHD	15 (42.9)	22 (38.6)	0.686
CKD	18 (51.4)	23 (40.4)	0.299
CVD	8 (22.9)	5 (8.8)	0.072
COPD/Bronchial asthma	3 (8.6)	8 (14.0)	0.433

IHD: Ischaemic heart disease, CKD: Chronic renal disease, CVD: Cerebrovascular disease, COPD: Chronic obstructive airway disease

Table III shows frequency and Incidence of VAP (per 1000 ventilator days).

Table III

Total Intubated Patients	VAP	Frequency	Incidence per 1000 ventilator days
625	35	5.6	3.64

Table IV shows frequency of Early and Late VAP (n=35).

Table IV

Type of VAP	Frequency (n)	Percentage (%)
Early VAP	18	51.4
Late VAP	17	48.6
Total	**35**	**100.0**

Table V shows mortality in VAP positive and VAP negative participants (N=92).

Table V

Outcome	VAP Positive (n=35)	Negative (n=57)	p-value
Survivor	11	39	**0.001**
Non survivor	24	18	
Total	**35**	**57**	

Table VI shows association of co-morbidities with mortality.

Table VI

Co-morbidities	Survivor (n=50)	Non survivor (n=42)	p-value
Diabetes mellitus	38 (76.0)	42 (90.5)	0.098
Hypertension	41 (82.0)	31 (73.8)	0.343
IHD	18 (36.0)	19 (45.2)	0.368
CKD	18 (36.0)	23 (54.8)	0.071
CVD	8 (16.0)	5 (11.9)	0.574
COPD/Bronchial asthma	7 (14.0)	4 (9.5)	0.510

Multiple responses

IHD: Ischaemic heart disease, CKD: Chronic renal disease, CVD: Cerebrovascular disease, COPD: Chronic obstructive airway disease

Table VIII shows length of ICU stay of the study participants.

Table VIII

	VAP Positive (n=35)	Negative (n=57)	p-value
Length of ICU stay (days)	17.17 ± 9.68	11.98 ± 6.16	0.002

Table IX shows length of M/V of the study participants.

Table IX

	VAP Positive (n=35)	Negative (n=57)	p-value
Length of MV (days)	14.25 ± 9.76	8.22 ± 5.42	<0.001

Discussion

In our study, the mean age of the participants who developed VAP was 65.05 ±14.79 years with a range of 27 to 101 years. Commonest age range were 41-60 years (34.3%) and 61-80 years (45.7%). The mean age of the participants who did not develop VAP was 62.56±13.62 years. There was no statistically significant difference in terms of age in the two groups and increased age was not significantly associated with development of VAP.

Commonest co-morbidity was Diabetes mellitus (85.7% in VAP positive vs 80.7% in VAP negative) followed by Hypertension (82.9% in VAP positive vs 75.4% in VAP negative). Comparison of other co-morbidities among VAP positive and VAP negative patients were respectively as follows, Chronic renal disease (51.4% vs 40.4%), CVD

(22.9% vs 8.8%), Ischemic Heart disease (42.9% vs 38.6%), COPD/Bronchial asthma (8.6% vs 14%). Most of the patient had multiple co-morbidities. There was no significant difference in terms of co-morbidities among VAP positive and VAP negative patients .In a study done by Karatas in Turkey, they found that Diabetes mellitus significantly increased risk of VAP (p=.003) and COPD increased risk of VAP by 4.19 times (p<0.001). [1]Agarwal et al reported association of Chronic kidney disease with development of VAP. But in this study co-morbidities were not related to VAP which may be due to the fact that the study was performed in a tertiary care hospital specialized in treating diabetic patients where most of the patients were diabetic and had pre-existing multiple co-morbidities. So almost all patients in both VAP positive and negative group had diabetes and it's complications like CKD,IHD,CVD. COPD could not be related to VAP as most of the COPD patients admitted had infectious exacerbation and pre-existing infection was an exclusion criteria for this study. So only few COPD patients were included in the study who did not have pre-existing pneumonia and the sample size was not enough to draw a conclusion.

In our study, 35 out of total of 92 participants included in the study developed VAP with a rate of 5.6%. Incidence per 1000 ventilator days was 3.64/1000 ventilator days. Due to the lack of a gold standard for it's diagnosis, comparison of VAP frequency, rate and incidence between various studies is difficult. Mallick et al conducted a study in the same ICU and he found a VAP incidence of 20.2% (35.73 per 1000 ventilator days) which was higher than the current study.[9] Patil et al conducted a study in India where incidence of VAP was 27.71% and VAP rate was 39.59/1000 ventilator days, which was higher in comparison to our study.[10] Whereas VAP rates were reported to be 8.8 per 1000 ventilator days in European and South American ICUs. [11] The lower frequency of VAP in this study may be due to improved infection prevention strategies, use of endotracheal tubes with subglottic suction port and closed suction catheter routinely in the ICU. VAP rate in an ICU is indicator of effectiveness of infection control strategies. It is associated with increased cost, adverse outcome and increased requirement for nursing care. So, specific preventive steps should be an integral part of standard ICU care.

In our study, among the 35 VAP patients, 18 (51.4%) developed early VAP and 17 (48.6%) developed late VAP. The mean time interval between intubation and development of VAP was 5.65 ± 3.99 days. In early VAP mean interval was 2.83 ± 0.85 and in late VAP mean interval was 8.64 ± 3.82 days.

Primary outcome of our study was ICU mortality and secondary outcome studied were length of ICU stay, length of mechanical ventilation, development of sepsis or septic shock and association of mortality with early or late onset VAP. Overall mortality rate in the VAP positive participants was statistically significantly higher than the participants not developing VAP (68.6% vs 31.6%). We found no significant difference in mortality among the participants with early onset VAP and late onset VAP (66.7% vs 70.6%).In contrary to these findings Tejerina et al found no statistically significant difference in overall mortality rate among patients with or without VAP (38.1% vs 37.9%).[12] A study done by Kant et al in India concluded that VAP did not increase mortality in ICU. [13] Violan et al concluded that after controlling for the other determinants of outcome, VAP was not a major cause of mortality in mechanically ventilated patients. [14] These conflicting conclusions in different studies may be due the difference in study population, inclusion criteria, presence or absence of matching the confounding factors among the study participants.

We found no significant difference in mortality among the participants with early onset VAP and late onset VAP (66.7% vs 70.6%).Gadani et al found that, the mortality of the early-onset type was found to be 20%. [15] In case of the late-onset type, it was found to be 66.67% which was statistically significant in their study. Mallick et al found significant difference of outcome between early and late VAP.[9]

In our study length of ICU stay was significantly higher (17.17 ± 9.68 vs 11.98 ± 6.16) days in patients who developed VAP in comparison to patients who did not develop VAP (p = 0.002). Karatas et al showed the mean length of stay in the ICU in VAP patients was 26.7±16.3 days and mean length of stay in the ICU in non-VAP patients was 18.1±12.7 days. The difference was significant in his study.[1]

In this study, length of mechanical ventilation was significantly higher (14.25 ± 9.76 vs 8.22 ± 5.42) days in participants who developed VAP in comparison to participants who did not develop VAP (p <0.001). This finding was similar to findings of Karatas et al where mean length of MV was 23.5±10.8 days in VAP participants and mean length of MV was 12.6±7.4 days in non-VAP participants. [1] (p<0.001). The association of length of mechanical ventilation and ICU stay with VAP may be bidirectional. Increased duration of mechanical ventilation and ICU stay is a risk factor for developing VAP and also an effect of developing VAP.

Limitation

Like any other scientific study the present study is not without limitations. The following limitations deserve mentioning:

1. As it was an academic time bound study, sample size was small. Thus the findings derived from study cannot be generalized to reference population.
2. Study was conducted in a predominantly medical ICU with few surgical patients and no trauma patients. Moreover paediatric group of patients were excluded. So, data from these group of people were missing.
3. VAP was diagnosed clinically which was not confirmed by histopathological examination, so incidence of VAP may have been overestimated or underestimated.
4. The overall mortality of VAP was studied which may not reflect the attributable mortality due to VAP as because patients with VAP had other confounding factors for outcome.

Conclusion

This study showed that VAP significantly prolonged length of M/V and ICU stay. Overall mortality was higher in VAP positive participants than in VAP negative participants.

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