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Research Article

Incidence and risk factors associated with development of ventilator-associated pneumonia from a tertiary care center of northern India

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ABSTRACT

Background: The incidence of VAP varies among different studies, depending on the definition, the type of hospital or ICU, the population studied, and the level of antibiotic exposure. This study was planned to ascertain and analyse the incidence and risk factors associated with development of ventilator-associated pneumonia from a tertiary care center.

Methods: In this retrospective study, all the adult patients on mechanical ventilation (MV) for more than 48 hours in the Medicine Intensive Care Unit (MICU) and the Critical Care Unit (CCU) during September 2015 to February 2016 were included in the current study. Patients diagnosed with pneumonia prior to MV or within 48 hours of MV were excluded from the study. Patients' records served as study tools. Medical records department (MRD) was approached and data was collected on all patients who received mechanical ventilation during the study period. The relevant data were recorded from medical records, bedside flow sheets, radiographic reports, and reports of microbiological studies of the patients. The chi-square (χ^2) test or Fisher's exact test was used to compare different groups. Univariate and multivariate logistic regression analysis was performed to identify risk factors associated with development of ventilator-associated pneumonia.

Results: Overall incidence of VAP was 23.54 per 1,000 ventilator days. The incidence of VAP in MICU and CCU were 31.77 and 16.47 per 1,000 ventilator days respectively. 60% of the cases were late-onset VAP, while 40% were early-onset VAP. The most common organism isolated was Pseudomonas aeruginosa followed by Methicillin-resistant Staphylococcus aureus (MRSA). Impaired consciousness, tracheostomy, re-intubation, emergency intubation, and nasogastric tube were significantly associated with VAP. On multivariate analysis, impaired consciousness, emergency intubation and tracheostomy were independent risk factor for VAP among study subjects.

Conclusions: Data thus generated can be used to plan and modulate the potential intervention measures while managing VAP. Knowledge of the important risk factors predisposing to VAP may prove to be useful in implementing effective preventive measures.

Keywords: Incidence, Risk factors, Ventilator-associated pneumonia, ICU

INTRODUCTION

Ventilator Associated Pneumonia (VAP) refers to a type of pneumonia that occurs more than 48-72 hours after endotracheal intubation, and is one of the most common nosocomial infections in patients receiving mechanical ventilation.[1,2] VAP occurs in 9-27% of all intubated patients.[3] 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 diagnostic studies.[4]

The initial empirical therapy can be modified based on the knowledge of local microbiological data, patient characteristics, and sensitivity pattern of expected pathogens at the institution. One of the consequences of increasing antimicrobial resistance is an increased probability of inappropriate initial empiric antimicrobial treatment of infections.[5] Several risk factors may predispose patients to either colonization of the respiratory tract with pathogenic microorganisms and/or aspiration of contaminated secretions.

The incidence of VAP varies among different studies, depending on the definition, the type of hospital or ICU, the population studied, and the level of antibiotic exposure.[6,7] Knowledge of the incidence of VAP and their associated risk factors are imperative for development and use of more effective preventive measures. Therefore the present study was planned to ascertain and analyze the incidence and risk factors associated with development of ventilator-associated pneumonia from a tertiary care center of northern India.

METHODS

The present study was planned and executed by the Department of Anesthesiology in collaboration and consultation with the Departments of Microbiology and Critical Care Medicine of a tertiary care teaching institution of northern India. In this retrospective study, all the adult patients on mechanical ventilation (MV) for more than 48 hours in the Medicine Intensive Care Unit (MICU) and the Critical Care Unit (CCU) during September 2015 to February 2016 were included in the current study. Patients diagnosed with pneumonia prior to MV or within 48 hours of MV were excluded from the study.

Patients' records served as study tools. Medical records department (MRD) was approached and data was collected on all patients who received mechanical ventilation during the study period. The relevant data were recorded from medical records, bedside flow sheets, radiographic reports, and reports of microbiological studies of the patients. Other relevant details were also captured viz. name, age, gender, IPD number, primary diagnosis, date of admission in hospital and ICU. The presence or absence of the potential risk factors for the development of VAP was also recorded. The study patients were monitored at every third day for the development of VAP using clinical and microbiological criteria until either discharge or death.

Table 1: Modified clinical pulmonary infection score (CPIS)-criteria for diagnosing VAP.

CPIS points	0	1	2
Temperature (oC)	≥ 36.5and ≤ 38.4	≥ 38.5 and ≤ 38.9	≥ 39 or ≤ 36
Leucocyte count (per mm^3)	4,000 - 11,000	< 4,000 or > 11,000	< 4,000 or > 11,000 + band forms ≥ 500
Tracheal secretions	Rare	Abundant	Abundant + Purulent
PaO_2/ FiO_2 mmHg	>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 stain

For the purpose of this study, patients fulfilling both the clinical and microbiological criteria were considered to be suffering from VAP. Clinical criteria included modified clinical pulmonary infection score (CPIS)>6 (Table 1)[8] and microbiological criteria included positive Gram stain (>10 polymorphonuclear cells/low power field and ≥1 bacteria/oil immersion field with or without the presence of intracellular bacteria) and quantitative endotracheal aspirate culture showing ≥105 CFU/ ml.[9]

Endotracheal aspirates (EA) were cultured for identification of VAP pathogens. EA was serially diluted in sterile normal saline as 1/10, 1/100, 1/1,000, and 0.01 ml of 1/1,000 dilution was inoculated on 5% sheep blood

agar. After incubation at 37oC in a 5% CO_2 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 105 CFU/ml were considered as VAP pathogens and were identified based on standard microbiological procedures including Gram's stain, colony morphology on blood agar and Mac Conkey agar, and biochemical reactions.[10]

Non-glucose fermenting, motile, oxidase positive, nitrate reducing, Gram-negative bacilli, with a characteristic sweet grape-like odour and distinctive blue-green pigment were identified as *Pseudomonas aeruginosa*. Non- glucose fermenting, non-motile, oxidase negative, nitrate non-reducing, gram-negative *coccobacilli*, producing acid from glucose oxidatively, were identified as *Acinetobacter baumannii*. Oxidase-negative, catalase positive, nitrate reducing, non-spore forming, gram-negative bacilli, fermenting comparisons. Catalase-positive, mannitol fermenting, coagulase producing, Gram-positive cocci in clusters, with characteristic golden yellow pigment and hemolysis, were identified as *Staphylococcus aureus*. Methicillin-resistant *Staphylococcus aureus* (MRSA) were identified based on their ability to grow on oxacillin screen agar with 6 µg/ml oxacillin and 4% NaCl.

The study adhered to the tenets of the declaration of Helsinki for research in humans. Informed consent was obtained from study subject's next of kin after discussing advantages and risks. Permission of Institutional ethics committee (IEC) was sought before the commencement of the study. All the questionnaires along with other relevant data were manually checked and were then coded for computer entry. After compilation of the collected data, analysis was done using Statistical Package for Social Sciences (SPSS), version 20 (IBM, Chicago, USA). The results were expressed using appropriate statistical methods. The chi- square (χ^2) test or Fisher's exact test was used to compare different groups. Univariate and Multivariate logistic regression analysis were performed to ascertain risk factors for VAP among study subjects. A two tailed $p<0.05$ was considered statistically significant.

RESULTS

In this study during the study period 442 and 181 consecutive patients admitted to MICU and CCU respectively were retrospectively evaluated. Of these patients, 302 (68.3%) in MICU and 50 (27.6%) in CCU were not intubated, as there were no indications for MV. Among those requiring MV, 90 (20.4%) and 80 (44.2%) patients were mechanically ventilated for less than 48 hours in MICU and CCU respectively. Fifty patients (11.3%) from MICU and fifty-one patients (28.2%) from CCU received MV for more than 48 hours and therefore data of these patients was included in the study.

Of the 101 patients, 20 (19.8%) developed VAP during their ICU stay. The overall incidence of VAP was 23.54 per 1,000 ventilator days. The incidence of VAP in MICU and CCU were 31.77 and 16.47 per 1,000 ventilator days respectively. There was no statistically significant difference in the incidence of VAP among MICU and CCU patients.

Table 2: Baseline characteristics of patients with and without VAP (Ventilator-associated pneumonia).

Variable		Non-VAP	VAP	P value
Age	Mean ± SD	37.3 ± 14.4	42.6 ± 13.1	0.244
Sex	Male	49	13	0.714
	Female	32	7	
Primary diagnosis	Poisoning#	27	5	0.475
	Neurological disorders (GBS, MND)^	4	3	0.137
	Intra-abdominal diseases	6	2	0.655
	Snake bite	5	2	0.622
	CNS infections (encephalitis/ meningitis)	1	1	0.358
	Pregnancy-related disorders	6	2	0.655
	Fracture	1	1	0.358
	Tetanus	3	1	0.592
	Cardiovascular disease	4	0	-
	Subdural/ extradural hemorrhage	2	2	0.174
	Neuromuscular disorders	4	1	0.676
	Leptospirosis	0	1	-
	Miscellaneous*	17	0	-

#Includes organophosphorous, yellow oleander poisoning; ^GBS – Guillain Barre syndrome; MND – Motor neuron Disease; *cerebrovascular accident, multiple injury, sepsis, chronic obstructive pulmonary disease with cardiac failure, diabetes mellitus with hypertension, diabetic nephropathy, severe anaemia, chronic or acute renal failure.

The onset of VAP was more likely to occur during the first two weeks of MV as 96% cases occurred during this period. In this study, 60% of the cases were late-onset VAP, while 40% were early-onset VAP.

Of the 101 study patients, 62 were male (61.4%) and remaining 39 (38.6%) were female. Mean age of VAP and Non-VAP subjects was 37.3 ± 14.4 years and 42.6 ± 13.1 years respectively. There was no statistically

significant difference in the age and sex distribution of the patients in VAP and non-VAP groups. The most frequent cause of ICU admission was poisoning (Table 2).

The most common organism isolated was *Pseudomonas aeruginosa* followed by Methicillin-resistant *Staphylococcus aureus* (MRSA), *Klebsiella pneumoniae*, and *Acinetobacter baumannii* (Figure 1).

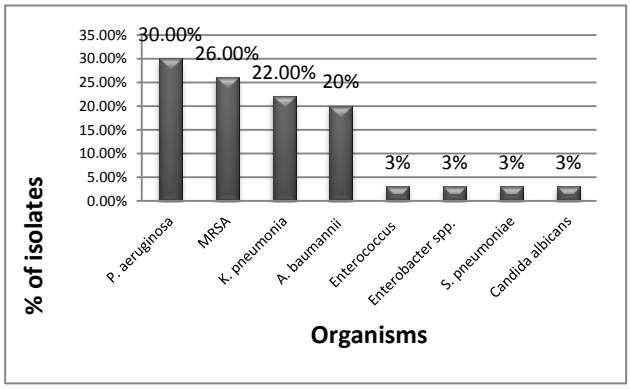

Figure 1: Bar chart showing causative organisms of VAP in study subjects

Table 3: Univariate logistic regression analysis of risk factors for VAP among study subjects.

Risk factor	Non-VAP	VAP	Relative risk (95% CI)	P value
Supine head position	4	1	0.99 (0.12-8.36)	0.676
Stress ulcer prophylaxis	74	18	1.02 (0.86-1.19)	0.567
Impaired consciousness	7	4	2.43 (1.14-3.83)	0.024*
Tracheostomy	12	5	2.59 (1.24-4.49)	0.019*
Re-intubation	5	3	2.41 (1.11-3.58)	0.031*
Emergency intubation	1	3	2.08 (1.21-3.75)	0.023*
Nasogastric tube	17	7	2.03 (1.08-3.14)	0.047*
Surgery	12	2	1.48 (0.36-6.10)	0.730
Burns	0	0	-	-
Chronic renal failure	2	1	0.49 (0.05-5.18)	0.488
Trauma	6	1	1.48 (0.19-11.68)	0.579
IV sedatives	17	4	0.63 (0.34-1.28)	0.273
Steroid therapy	15	4	1.05 (0.41-2.78)	0.596
Duration of MV ≥ 5 d	53	11	1.19 (0.78-1.82)	0.385
*p<0.05				

Univariate logistic regression analysis of risk factors for VAP among study subjects indicated that impaired consciousness, tracheostomy, re-intubation, emergency intubation, and nasogastric tube were significantly associated with VAP (Table 3).

Multivariate analysis was performed to identify independent risk factor for VAP among study subjects. Selected risk factors were entered into this logistic regression model. This revealed that impaired consciousness, emergency intubation and tracheostomy were independent risk factor for VAP among study subjects (Table 4).

Table 4: Multivariate logistic regression analysis of independent risk factors for VAP among study subjects.

Variables	p-value	Odds ratio	95%CI	
			Upper	Lower
Impaired consciousness	0.015*	5.38	1.841	23.634
Tracheostomy	0.028*	2.73	0.853	6.012
Re-intubation	0.062	2.33	1.067	6.677
Emergency intubation	0.013*	4.72	0.744	11.458
Nasogastric tube	0.058	2.36	0.942	8.593
*p<0.05				

DISCUSSION

VAP continues to be a major challenge to the critical care physicians in India and is a common nosocomial infection occurring in mechanically ventilated patients. In this study we analyzed the incidence and risk factors associated with development of ventilator-associated pneumonia from a tertiary care center of northern India. In this study we observed that the overall incidence of VAP was 23.54 per 1,000 ventilator days. The incidence of VAP in MICU and CCU were 31.77 and 16.47 per 1,000 ventilator days respectively. This correlates with other similar studies in which the incidence of VAP was 15.5-47%, depending on the diagnostic criteria used.[11-12] On the other hand, in other Asian countries like Thailand and Japan, the incidence rate is relatively less, ranging from 9 to 12 per 1,000 ventilator days.[13,14]

Regarding timing of onset of VAP, in this study we observed that 60% of the cases were late-onset VAP, while 40% were early-onset VAP. The result of this study is in agreement with previous studies they observed early-onset VAP in almost half of all VAP episodes.[2,7] It was also noted that most of the VAP episodes occurred within the first two weeks of MV. The interaction of several risk factors during the initial days of MV put the patient at higher risk and also the exhaustion of most vulnerable patients during the first few weeks leads to the decline in the occurrence of VAP in later days as observed in Athens.[15]

In this study the most common organism isolated was *Pseudomonas aeruginosa* followed by Methicillin-resistant *Staphylococcus aureus* (MRSA), *Klebsiella pneumoniae*, and *Acinetobacter baumannii*. The organisms implicated in VAP were similar in other such studies.[7,11]

In the current study, multivariate analysis revealed that impaired consciousness, emergency intubation and tracheostomy were independent risk factor for VAP among study subjects. Supine head position, stress ulcer prophylaxis, surgery, burns, chronic renal failure, trauma, steroid therapy and duration of MV ≥5d were documented as independent risk factors for the development of VAP by multivariate analysis by other authors.[2,6] Understanding of the independent risk factors acknowledged in this study may assist in identifying patients at higher risk for VAP, guide implementation of appropriate preventive measures, and regulate possible intervention measures while managing them.

In this study tracheostomy was established to be another independent risk factor. There is increased tracheal colonization around the tracheostomy tube into the trachea because of leakage of pooled secretions, which leads to VAP. Administration of intravenous sedatives to patients on MV might impair their cough reflexes, increasing the risk of aspiration and subsequently predisposing them to development of VAP. Re-intubation also most often results in aspiration contributing to the development of VAP.[16]

This study has several strengths. To our knowledge, assessment of burden and risk factors associated with development of ventilator-associated pneumonia has not been extensively investigated in our setup. Very few similar studies are available in the literature. Findings of this study may assist in identifying patients at higher risk for VAP which is a very important aspect of critical care medicine now a day. The study has some limitations as well. First, some may argue that this study may not have identified all the important risk factors of VAP. I agree because underlying factors tend to vary from place to place. Second, this was a retrospective study. Third, validation of risk factors was not done.

CONCLUSION

The findings of the study highlight that in spite of the advances in the diagnosis, treatment, and prevention of VAP, it continues to be a major cause of morbidity and mortality among critically ill patients. Data thus generated can be used to plan and modulate the potential intervention measures while managing VAP. Knowledge of the important risk factors predisposing to VAP may prove to be useful in implementing effective preventive measures. Local epidemiological data need to be generated at all centres, as such information can help in guiding the initial empirical antibiotic therapy, which would be more rationale and help in decreasing mortality and morbidity.

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