



Bacteriological Study of Ventilator-Associated Pneumonia (VAP) in a Medical Critical Care Unit

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ABSTRACT

Introduction: Ventilator associated pneumoniae is one of the most common hospital-acquired infections and is a major device-associated complication encountered in critical patients receiving intensive care. Knowledge of VAP rates the common etiological agents in the critical areas of health care institutions and can help to plan empirical antimicrobial treatment.

Aim: To study the etiology and antimicrobial resistance of bacteria responsible for VAP.

Objectives:

- (1) To estimate VAP rate / 1000 ventilator days.
- (2) To study the bacteriology of Ventilator Associated Pneumonia (VAP).
- (3) To identify bacterial isolates up to species level.
- (4) To study anti-microbial susceptibility in the bacterial isolates.

Methods: The study was conducted in the Department of Microbiology of an urban tertiary care teaching hospital in Western India. The patients were admitted to the MICU during the study period who received mechanical ventilation (MV) for >48 hours and developed pneumonia, diagnosed on clinical and radiological findings were the study population to calculate the VAP rate and find out the etiological agents. Antimicrobial Susceptibilities were performed on the bacterial isolates recovered from VAP cases.

Results: A total of 125 patients developed clinical VAP proven by radiological and clinical findings out of 271 patients on mechanical ventilation studied. The VAP rate was calculated as 35.7 in 1000 ventilator days. The incidence rate of VAP was 46.12%. Late on-set VAP accounted for 66% of cases. All the clinically suspected 125 VAP cases were culture positive with 77% positive predictive value for culture-positive samples and 100% negative predictive value for culture-negative samples. The majority of the isolates of VAP comprised multi drug resistant gram-negative organisms like *K. pneumoniae*, *A. baumannii*, and *P. aeruginosa*.

Conclusion: VAP is a major cause of morbidity and mortality in critically ill patients admitted to the critical care unit. Multidrug-resistant bacteria are frequently involved in the causation of VAP. Hence, microbiological information could be used for planning antibiotic therapy and should not be limited only to making a diagnosis.

Key Words: Ventilator Associated Pneumonia, Bacteriological analysis, Medical critical care unit, Multidrug resistant, Microbiological Information, *Acinetobacter baumannii*, and *Pseudomonas aeruginosa*

INTRODUCTION

Ventilator-associated pneumonia (VAP) is a complication that occurs 48 hours after intubation and mechanical ventilation. It is one of the common device-associated complications encountered in critical patients receiving intensive care. Nearly 8-38% of patients who undergo mechanical ventilation develop VAP.¹ The mortality of VAP has been reported to be 24-76%, which is higher than that of other

hospital-acquired infections.² The clinical course of VAP is governed by a number of variables, including host immune system status, underlying diseases related, appropriate antibiotic treatment, accurate and rapid clinical and laboratory diagnosis, type of microorganism and virulence of the pathogen, and its antimicrobial susceptibility.³ The present study was conducted to investigate the VAP rate in a tertiary care hospital along with the etiology and characterization of etiological agents.

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MATERIALS AND METHODS

The present study was a prospective, descriptive type of study conducted in the Department of Microbiology of an urban tertiary care teaching hospital in Western India.

Inclusion criteria: All the patients admitted to the MICU during the study period who received mechanical ventilation (MV) for >48 hours and developed pneumonia and diagnosed according to clinical and radiological findings.

Exclusion criteria: Patients who received mechanical ventilation presenting with pneumonia before 48 hours of endotracheal intubation. In addition, patients with acute pulmonary diseases such as Acute Respiratory Distress Syndrome (ARDS), fulminant pneumonia, and pulmonary edema were excluded from the study.

A total of 590 patients were mechanically ventilated for more than 48 hours in the critical care unit during the study period. Out of these, 271 patients were included in the study as they fulfilled the inclusion criteria i.e. mechanical ventilation for >48 hours with no respiratory symptoms before ventilation. Patients on mechanical ventilation for more than 48 hours who clinically and radiologically developed pneumonia were followed up prospectively. Demographic data of each patient was recorded along with the duration of mechanical ventilation, body temperature, CBC counts, and X-ray chest. The underlying condition, indication for mechanical ventilation, antimicrobial treatment being received, and any other associated morbidity were also recorded in each patient.

Endotracheal aspirates were collected from 271 patients on mechanical ventilation using a sterile extractor under aseptic precautions. Patients were nebulized if the secretions were scanty or thick for fifteen minutes before the collection of specimens.

A 103 dilution of homogenized endotracheal aspirate was prepared by adding 0.1 mL of sample to 100 mL of normal saline. From this 1 µl was inoculated onto each of the three culture media viz. Blood Agar, Chocolate Agar, and McConkey Agar. Plates were incubated aerobically at 37°C. Chocolate Agar plates were incubated in the presence of 5% CO₂ at 35°C.

The number of bacteria per mL in the original specimen was calculated by counting the Colony Forming Units (CFU) on the Blood Agar Plate. Bacterial growth of 10⁵ CFU per mL was considered significant for the causation of VAP.²

All the isolates were identified using either standard conventional methods² or the automated identification system Vitek 2.

All the bacterial isolates were subjected to Antimicrobial Susceptibility Testing.⁴

Data entry and analysis were performed using Microsoft Office 2010-Excel spreadsheet software. All P<0.05 were considered statistically significant.

RESULTS

During the study period of 1.5 years, a total of 590 patients were intubated and were on mechanical ventilation. Out of 590 patients, 271 patients were included in the study as they fulfilled the inclusion criteria i.e., mechanical ventilation for >48 hours with no respiratory symptoms before ventilation. A total of 125 patients developed clinical VAP proven by radiological and clinical findings. The total ventilator days for the study period were counted to calculate the VAP rate. During this period the total ventilator days were calculated as 3494 and therefore the VAP rate was calculated as 35.7 in 1000 ventilator days. The incidence rate of VAP was 46.12%. There was a male preponderance of 67.2% compared to the female population (32.8%). The mean age of patients with VAP was 42.16 years. Of the endotracheal secretions from 271 patients, 109 were culture-negative whereas 162 were culture-positive. All the clinically suspected 125 VAP cases were culture positive and yielded 166 isolates. In 146 cases without clinical or radiologically, suspected VAP 37 specimens yielded significant growth with 77% positive predictive value for culture-positive samples and 100% negative predictive value for culture-negative samples. Out of 125 VAP cases, early onset VAP was seen in 43 (34%) patients and late onset VAP in 82 (66%) patients. Out of 166 isolates from VAP cases, there was a predominance of Gram-negative organisms (93%). The organisms isolated were predominantly GNB like *Klebsiella spp* 49 (30%), *Acinetobacter spp* 48 (29%), *Pseudomonas aeruginosa* 35 (21%), and *E. coli* 08 (5%) and Gram-positive were 12% with 5% MRSA and 3% MRCONS. Among VAP cases, a single type of bacterial isolate was recovered from 87 specimens (mono-microbial) whereas in 38 specimens more than one type was isolated.

Out of 166 bacterial isolates from VAP cases, 50 were from the early onset, and 166 were from late-onset VAP. The majority of the isolates of late-onset VAP comprised of gram-negative organisms like *K pneumoniae* (25.6%), *A baumannii* (26.4%), and *P aeruginosa* (25%), which were also among the top MDR pathogens of 77%, 92%, and 43% strains respectively. Among the gram-negative organisms, all were sensitive to colistin except four isolates of *A baumannii* and one isolate of *Acinetobacter spp*. All the MRSA isolates (3) were sensitive to vancomycin and linezolid antibiotics.

A total of 28 deaths were recorded among the 125 VAP diagnosed patients. The deaths were associated with different clinical conditions, but most of them were associated with central nervous system manifestations. VAP-associated mortality was highest above fifty years of age.

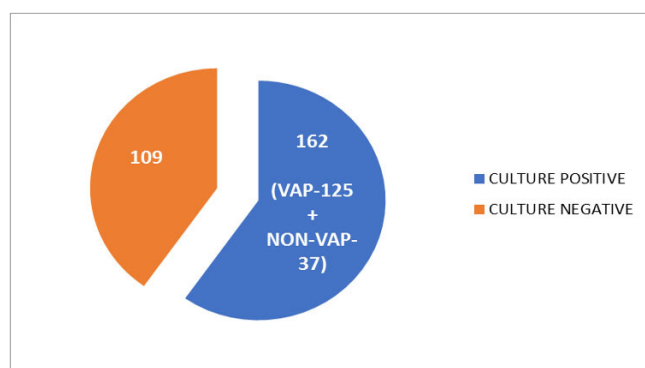


Figure 1: Distribution of culture positive and culture negative isolates.

DISCUSSION

VAP is one of the most common hospital-acquired infections among critically ill patients, receiving mechanical ventilation (MV). VAP are significant public health issue with high morbidity and mortality and increased costs of treatment.³ VAP accounts for one-fourth of the bacterial infections occurring in critically ill patients and is the reason for half of antibiotic prescriptions in mechanically ventilated patient.⁵ The incidence density rate of VAP in our study was 35.7 per 1,000 ventilator days. Data from Asian countries suggest an incidence-density rate of VAP varying from 8.9 to 46 per 1,000 ventilator days.^{3,6,7} Our study showed a preponderance of male sex (67.2%) for VAP which was similar to the study by Rit et al. where male sex preponderance was also 67.85%.³ Overall male preponderance has been observed in most studies on VAP.^{8,9} In the present study, VAP rate was found to be more in 25-50 years age group.

In our study population of 271 patients, 125 patients developed VAP (46%); this translates to an incidence of 35.7 episodes of VAP per 1000 ventilator days. Joseph et al. reported the incidence of VAP to be 30.67 and 15.87 per 1000 ventilator days in the two different ICUs.¹⁰ Similarly in a study by Patil et al., the incidence of VAP was 27.71% with the rate of 39.59 per 1000 ventilator days. Late on-set infection i. e. development of VAP 4 days after the intubation accounted for 66% of cases.⁵

Joseph et al. and Combes et al. reported poly-microbial VAP in 30–70% and 48%, respectively.^{10,11} In the present study, 16% of patients had poly-microbial VAP. A total of 166 isolates were recovered from 125 clinical VAP cases. The predictive value of negative cultures was 100% indicating the usefulness of cultures of endotracheal secretions. The predictive value of positive cultures was 77% in the present study lower than the positive predictive value (PPV) observed by Leonard et al (84.5%).¹²

The majority of early and late-onset VAP comprised of gram-negative organisms like *K pneumoniae*, *A baumannii* and *P*

aeruginosa. Sarkar et al. have reported early onset cases to be caused by *Acinetobacter* spp, *Klebsiella pneumoniae* and *Staphylococcus aureus* mainly whereas *Pseudomonas* spp. and *Acinetobacter* spp. caused late-onset VAP whereas Liang YJ et al. did not observe significantly different etiologies between groups.^{7,13}

Chastre and Fagon, compiled the data from 24 published studies and found that 58% of the isolates were gram negative bacteria, of which the most common organisms were *Pseudomonas* followed by *Acinetobacter* species and *Proteus* species.¹⁴ A relatively high rate of Gram positive organisms in pneumonias were also reported in those studies, with *Staphylococcus aureus* being the most common Gram-positive organism (20% of cases). Polymicrobial infections have been a common feature in the many studies on VAP.^{5,10,11}

Out of 166 bacterial isolates, 113 were Multi Drug Resistant (MDR), *Acinetobacter baumannii* (92%) and *Klebsiella pneumoniae* (77%) being the most important. Colistin was found to be most effective antibiotic followed by piperacillin/tazobactam combination and Imipenem. Amoxycillin+clavulanate and third generation cephalosporins were the least effective drugs. MRSA strains showed 100% susceptibility to vancomycin and linezolid. The exact prevalence of MDR organisms varies between institutions and also within institutions. This emphasizes the need for the bacteriological diagnosis of VAP with appropriate antimicrobial susceptibility reports.

Risk factors like COPD, reintubation, coma, steroid treatment, intra-aortic balloon counter pulsation, enteral feedings, and tracheostomy have been reported for VAP.^{15,16} In this study, impaired consciousness, re-intubation, emergency intubation, and pre-existing co-morbidities were the significant risk factors for developing VAP. The overall mortality observed in VAP cases was 22.4%. The mortality rates among patients with VAP infections were from 20% to 76% in various studies, with higher rates reported among patients with MDR infections.¹⁷

CONCLUSION

VAP is a major cause of morbidity and mortality in critically ill patients admitted to the critical care unit. Multidrug-resistant bacteria are frequently involved in the causation of VAP. Hence, microbiological information could be used for planning antibiotic therapy and should not be limited only to making a diagnosis. The high negative predictive value has a utility to rule out the VAP and for initiation of therapy. The empirical antibiotics for suspected VAP are the potential for the misuse of antibiotics eventually responsible for the emergence of antibiotic resistance.

AUTHORS CONTRIBUTION

- Conceptualization and study design: Author 1, Author 2
- Aims and objectives formulation: Author 1, Author 3
- Materials and methods development: Author 2, Author 4
- Data collection: Author 1, Author 2, Author 4
- Data analysis and interpretation: Author 2, Author 5
- Drafting of the manuscript (Abstract, Introduction, Results): Author 1, Author 3
- Drafting of the manuscript (Discussion and Conclusion): Author 2, Author 5
- Critical revision of the manuscript for important intellectual content: All authors
- Final approval of the version to be published: All authors

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