



DIVERSITY OF MICROBIAL FLORA IN VENTILATOR ASSOCIATED PNEUMONIA (VAP) AND THEIR SUSCEPTIBILITY PATTERNS

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ABSTRACT

VAP is one of the serious complications that occur at ICU. As its causative pathogens are antibiotic resistant in many cases, it is difficult to select appropriate antibiotics. The causative pathogens of VAP may vary depending on country, region, and hospital. Therefore, the diversity of the microbial flora in VAP & knowing their susceptibility pattern is very important in the prevention of VAP. 96 patients who were under mechanical ventilation for more than 48 hours by endotracheal tube or tracheostomy were evaluated. Endotracheal sampling was cultured, and pathogens were isolated. It was also observed that the mortality rate was 20.83% (20 out of 96 patients). 108 pathogens were isolated, and it was found that 12 patients had co infection with 2 organisms. Out of 108 isolates, 28(25.92%) were *Pseudomonas aeruginosa*, 21(19.44%) were *Klebsiella pneumoniae*, 17(15.74%) were *Staphylococcus aureus*, 8(7.4%) were *Acinetobacter* species, 7(6.48%) were Coagulase negative *Staphylococcus*, 6 (5.55%) were *Proteus mirabilis*, 5 (4.62%) *Escherichia coli*, 5 (4.62%) were *Candida* species and 5 (4.62%) was *Enterobacter* sp. Almost all the *Pseudomonas aeruginosa*, *Acinetobacter* sp & *Klebsiella pneumoniae* were multidrug resistant and all the *Staphylococcus aureus* and CoNS were Methicillin resistant. Prompt and early diagnosis of pneumonias would be the mainstay in bringing down mortality rate in Ventilator associated Pneumonia.

Keywords :- VAP, Ventilator associated pneumonia

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INTRODUCTION

Ventilator associated pneumonia (VAP) manifests after 48 hours of endotracheal intubation and Artificial mechanical ventilation. It is one of the commonest infectious disease found in an intensive care unit (ICU), ranging from 8~38%.[1] Ventilator-associated pneumonia (VAP) results from the incursion of the lower respiratory tract and lung parenchyma, by microorganisms such as bacteria, fungi, virus, etc. Common causative pathogens of VAP include *Pseudomonas aeruginosa*, *Escherichia coli*, *Klebsiella*

pneumoniae, *Acinetobacter* species and *Staphylococcus aureus*. Intubation compromises the integrity of oropharynx and trachea and allows oral and gastric secretions to enter the lower airways.

Diagnosing VAP entails a high clinical suspicion, along with bedside examination, radiographic examination, and microbiologic analysis of respiratory secretions. Judicious antibiotic usage is indispensable, as resistant organisms continue to spate intensive care units and critically ill patients.

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Simple nursing and respiratory therapy interventions for prevention should be adopted. Over the past several decades our understanding of VAP has grown significantly with regard to pathogenesis, risk factors, diagnostic testing, therapies, and prevention by modifying risk factors. Therefore, the diversity of the microbial flora in VAP & knowing their susceptibility pattern is very important in the prevention of VAP.

Lung functions are deranged because of damage to lung tissues induced by oxidants and inflammation. This derangement reduces oxygen intake leading to tissue hypoxia causing hyperuricemia. Hyperuricemia is defined as serum uric acid (UA) levels $>7.1\text{mg/dL}$ in males or $>6.1\text{mg/dL}$ in females. In comparison to normal individuals, hyperuricemics have more inflammation and oxidative stress injuries. Proinflammatory effect of UA is more profound in those with high serum UA levels. Our study aim is to assess whether the presence of higher values of serum UA is associated with changes in clinical and functional characteristics in patients with chronic obstructive pulmonary disease (COPD).

MATERIALS & METHODS

This is a prospective study which was done in Sri Lakshmi Narayana Institute of Medical Sciences, Puducherry, India, from May 2018 and April 2019 (one year). Clearance from the Institutional ethical committee was obtained. 96 patients who were under mechanical ventilation for more than 48 hours by endotracheal tube or tracheostomy were evaluated for the development of ventilator associated pneumonia. Demographic details like age, sex, etc was obtained. In addition to that, reason for artificial ventilation, underlying diseases (Cardiothoracic), Co morbid conditions, duration of mechanical ventilation, radiographic findings, treatment given, and follow up was also recorded.

The criteria used for diagnosis of VAP are not standardized, but tends to be a combination of several of the following radiographic, clinical sign, and laboratory evidence: Temperature greater than 38°C or less than 36°C ; White blood cell count greater than $12,000/\text{mm}^3$ or less than $4,000/\text{mm}^3$; Purulent secretions, increased secretions, or change in secretions; Positive tracheal cultures or broncho alveolar lavage cultures; Some sign of respiratory distress, such as shortness of breath, rapid breathing, abnormal breathing sounds when listening with stethoscope; Increased need for oxygen on the ventilator; Chest X-Rays: at least two serial X rays showing sustained or worsening shadowing (infiltrates or consolidations). In our study, to diagnose VAP, we considered one clinical symptom such as shortness of breath, one clinical sign such as fever, plus evidence on chest X-ray and in tracheal cultures.

Sample collection

Lower respiratory secretions were collected by endotracheal sampling technique. Rubber catheter was inserted into the endotracheal tube after disconnecting Breathing circuit/oxygen. Sterile Saline in small aliquots was infused using the rubber catheter and aspirated after infusion to collect sample. The total volume of saline infused should not exceed $\sim 2\text{ml/kg}$. The volume of sample retrieved was often a much smaller volume than that infused. Wash sample was stored in a sterile container and sent to laboratory for culture and sensitivity. After the sample was collected, patient was connected to ventilator circuit immediately.

Processing of samples

When the Samples were received in the microbiology laboratory, endotracheal samples should be mechanically homogenized using glass beads and vortexed for 1 min. For Qualitative culture, these specimens were considered like sputum samples and immediately inoculated in Blood agar, MacConkey agar, Mannitol Salt agar, Chocolate agar and were incubated at 37°C for 24 - 48 hours. They were also inoculated in Sabouraud's Dextrose agar and were incubated in BOD incubator at 28°C for 24 - 48 hrs. Smears from the sample were made for Gram staining and acid fast staining.

In this culture, the potential pathogens were considered significant, only if they grow as the predominant organism. Pathogens like *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Haemophilus influenzae*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Proteus* species, *Aspergillus* species, and *Candida* species were isolated & identified using standard microbiological methods. Antibiotic sensitivity of the organisms isolated was performed by "Kirby Bauer disc diffusion method", according to CLSI guidelines.

For quantitative culture, Serial dilutions (0.1, 0.01, and 0.001) of each sample were prepared in sterile normal saline. One hundred milliliters of each dilution of endotracheal sample was inoculated into 5% sheep blood, chocolate, MacConkey and Sabouraud's dextrose Agar. All cultures were incubated at 37°C in CO_2 -enriched atmosphere. Cultures were evaluated for growth 24 and 48 h later. All microorganisms isolated were identified by standard laboratory methods. Results were expressed as $\text{cfu/ml} = \text{number of colonies} \times \text{dilution factor} \times \text{inoculation factor}$. The diagnostic thresholds for ETA were taken as 10^5cfu/ml . Growth below the threshold was assumed to be due to colonization or contamination.

RESULTS

In the study period of one year, there were a total of 156 patients were admitted for respiratory

intensive care unit. 124 (79.48%) patients were mechanically ventilated and 96 patients (77.41%) among the ventilated patients were ventilated for more than 48 hours & had signs & symptoms of VAP. Only these 96 patients were included in this study.

The Sex and age distribution of these cases were studied, and it was found that, out of 96 patients, 67 (69.79%) patients were males and 29 (30.20%) were females. It was found that infection rate in Ventilator Associated Pneumonia was more common in males than in females and the Predominant age group was 21 – 40 years, in both males and females.

They were further analyzed according to the clinical diagnosis and it was found that 33 (34.37%) were poisoning cases with hypoxia, 19(19.79%) with sepsis with septic shock, 12(12.5%) with burns, 10 (10.41%) with Aspiration pneumonitis, 7(7.29%) had history of bronchial asthma with severe hypoxia, 9 (9.37%) had head injury, 1 (1.04%) were suffering from Severe pulmonary edema, 1 (1.04%) Bronchogenic carcinoma, 2 (2.08%) COPD, 2 (2.08%) ARDS. It was observed that incidence of Ventilator Associated Pneumonia was more in poisoning cases followed by sepsis, burns & aspiration pneumonitis.

The 108 pathogens were isolated, and it was found that 12 patients had co infection with 2 organisms. Out of 108 isolates, 28(25.92%) were *Pseudomonas aeruginosa*, 21(19.44%) were *Klebsiella pneumoniae*, 17(15.74%) were *Staphylococcus aureus*, 8(7.4%) were *Acinetobacter* species, 7(6.48%) were Coagulase negative *Staphylococcus*, 6 (5.55%) were *Proteus mirabilis*, 5 (4.62%) *Escherichia coli*, 5 (4.62%) were *Candida* species and 5 (4.62%) was *Enterobacter* sp.

Quantitative analysis of 108 positive isolates showed that, colony counts of $>10^5$ cfu/ml were present in 87(80.55%) isolates, colony count between 10^4 and 10^5 were seen in 14 (12.96%) isolates and colony count between 10^3 and 10^4 cfu/ml were seen in 7(6.48%) isolates. It was observed that 80.55% of positive isolates showed colony count $>10^5$ cfu/ml, which is a diagnostic threshold for endotracheal aspirates.

Almost all the *Pseudomonas aeruginosa*, *Acinetobacter* sp & *Klebsiella pneumoniae* were multidrug resistant and all the *Staphylococcus aureus* and CoNS were Methicillin resistant.

It was also observed that the mortality rate was 20.83% (20 out of 96 patients). Mortality was seen in patients with prolonged artificial ventilation, prolonged ICU stay, Bronchogenic carcinoma & also in drug resistant pathogens.

DISCUSSION

VAP is one of the serious complications that occur at ICU. As its causative pathogens are antibiotic resistant in many cases, it is

difficult to select appropriate antibiotics. The causative pathogens of VAP may vary depending on country, region, and hospital. If information on the causative pathogens of VAP is available, it could increase the possibility of appropriate antibiotic therapy, thereby reducing the mortality and improving the prognosis. Hence this study was attempted to know the diversity of the causative organisms in Ventilator associated Pneumonia and their sensitivity pattern.

In the present study it was found that 67 (69.79%) patients were males and 29 (30.20%) were females. It was found to be more common in males than in females. Male predominance in VAP is also seen in other studies ranging from 56% to 62%^{2,3}. In the present study, age group commonly involved in Ventilator Associated Pneumonia was between 21- 40 years, and the important clinical condition involved in mechanical ventilation was poisoning cases 33 (34.37%) especially suicidal poisonings. Panwar et al concluded in their study that 30-40 years as the common age group in VAP associated with Poisoning⁴. As in our study, 45.6% of the poisoning cases in mechanical ventilation developed Ventilator Associated Pneumonia in some other studies⁵. Most of the poisoning cases were subjected to gastric lavage prior to admission. These patients had signs of severe respiratory disease and increased need for mechanical ventilation; hence increase in Ventilator Associated Pneumonias. The pulmonary symptoms might be due to aspiration because of induced vomiting and lavage.

In the current study, the predominant isolates were gram negative bacilli like *Pseudomonas aeruginosa*, *Klebsiella pneumoniae* and other organisms. Similar study by Rajesh chawla et al⁶ also found that 87% of patients with Ventilator Associated Pneumonia were infected with Gram negative bacilli, most commonly *Pseudomonas aeruginosa* and *Klebsiella pneumoniae*, which are in support of this study. It has been known for decades that the microbial flora of hospitalized and critically ill patients becomes drastically altered within days after admission. In these patients, usual low virulent mixed flora of oropharynx and anaerobic flora of the colon become overgrown by endogenous aerobic gram negative bacilli, which can then colonize the airway and lead to lung infection. This may be the reason for increased incidence of gram negative organisms in this study also.

In this study, it was shown that an overall rate of 95% *Pseudomonas aeruginosa* were multidrug resistant. *Pseudomonas aeruginosa* was resistant to Gentamicin (71.9%), Ceftriaxone (78.6%), Ciprofloxacin (57.5%), Ofloxacin (56.9%), Amikacin (24%), Piperacillin tazobactam (47.3%), Cefipime (64.6%) and Carbenicillin (77.8%), and 100% resistant to Ampicillin, Cefotaxime, Cotrimoxazole, and Doxycycline. Similar study Arindam et al⁷ also showed 48% of *Pseudomonas aeruginosa* were

multidrug resistant. This correlates with present study. Increased resistance might be due to various factors like prolonged usage of antibiotics, prolonged hospital stay or by the liberation of either IMP- type metalloenzymes or carapenemases by *Pseudomonas*.

In present study, *Klebsiella pneumoniae* also played a major role in producing resistance (77%) for many antibiotics, as *Klebsiella* can produce ESBL, which are typically plasmid mediated, and Clavulanate susceptible enzymes that hydrolyze penicillins, expanded spectrum Cephalosporins and Aztreonam.

All the isolates of *Staphylococcus aureus* were resistance for methicillin (100%), showing that MRSA was the most frequent causative agent for Ventilator Associated Pneumonia. Arindam et al⁷ showed more isolates of MRSA in their study, and explained that these resistance pathogens always varied in different set up. Occurrence of resistance for multiple drugs in these patients might be one of the major reasons for Ventilator Associated Pneumonia.

In present study it was found that the mortality rate was 20.83%. Similar study by Chastre J Fagon JY et

al⁸ who proved the mortality rates to be 25% is in great support of this study. It was seen that the mortality was significantly high in patients with multidrug resistant *Pseudomonas*. Mortality was predominately related to underlying diseases, duration of hospital stay, patients with prolonged intubation. Similar study by Panwar Rakshit et al⁹ also demonstrated that mortality was significantly high in co morbid illness colonized with *Pseudomonas*.

CONCLUSION

Ventilator associated pneumonia is considered, a serious infective hospital acquired condition related to high mortality rate, hence it needs a prompt diagnosis and proper Antibiotic therapy. The pathogens isolated could have possibly been present in the hospital environment. Hence multifaceted strategies to bring down incidence of Ventilator Associated Pneumonia should be implemented & executed. However, prompt, and early diagnosis of pneumonias would be the mainstay in bringing down mortality.

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