

NON-FERMENTING BACTERIA AS AN EMERGING CAUSE IN DEVELOPING VENTILATOR ASSOCIATED PNEUMONIA IN AN INTENSIVE CARE UNIT OF A TERTIARY CARE HOSPITAL

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Abstract

Background: Hospital-acquired pneumonia (HAP) and Ventilator associated pneumonia (VAP) are considered to be the most serious hospital acquired infections because of their relatively high associated morbidity and mortality. This study aims to determine bacteriological profile of VAP with respect to isolation of non-fermenting bacteria and its antibiotic susceptibility pattern for the optimal treatment of patients and to control the spread of resistance. **Materials and Methods:** A prospective study was performed in the ICU setting of a tertiary care hospital over a period of 1 year. Endotracheal aspirate (ETA) culture of 68 patients with a clinical suspicion of VAP were analyzed by standard microbiological procedures. **Result:** The present study showed Non fermenting GNB(52.5%) as the most common organisms isolated. Pseudomonas sp(24.6%), Acenitobactersp (12.3%), former being predominant in early onset variety and the latter in the late onset of the VAP. Most of these organisms showed resistance to 3rd generation cephalosporins and aminoglycosides. All of them were sensitive to carbapenems. **Conclusion:** Non-fermenting bacteria are becoming the most important pathogens causing pneumonia in patients on mechanical ventilation for prolonged period. Routine ETA quantitative cultures with antibiotic susceptibility with de-escalation therapy can help in prevention of VAP. Multidrug-resistant bacteria were isolated from the most of ETA samples of VAP patients.

INTRODUCTION

Ventilator-associated pneumonia (VAP) is defined as pneumonia occurring in a mechanically ventilated patient after 48 hours of endotracheal intubation.^[1] 8-28% of patients receiving mechanical ventilation can present with complications in due course of time after developing VAP. The mortality rate associated with VAP ranges from 24-50% and can escalate up to 76% based on host-pathogen relationship.^[2] Microorganisms responsible for VAP may differ according to the population of patients, the durations of hospital and ICU stays, and the specific diagnostic methods used. Non fermenting Gram negative bacilli were considered to be contaminants in past, now emerge as an important health care pathogens. Non-fermenting bacteria may differ in their pathogenic potential and transmissibility and many are multidrug resistant.^[3] The diagnostic challenge to differentiate between organisms responsible for infection and colonization may guide for better treatment and prevent further development of antimicrobial resistance.^[4] Routine endotracheal aspirate cultures of a patient on mechanical

ventilation may help to identify the appropriate antibiotic regimen against pathogens responsible for VAP.^[5] This study aimed to isolate the non-fermenting GNB causing VAP and its antibiotic susceptibility pattern to provide an empirical therapy in a tertiary care hospital to control the spread of drug resistance.

MATERIALS AND METHODS

A prospective study was carried out enrolling patients from an intensive care unit (ICU) in Vijayanagar Institute of Medical Sciences (VIMS), Bellary, for a period of one year from January 2015 to January 2016. Intubated patients (>18 years of age) who are mechanically ventilated for more than 48 hours, with a clinical suspicion of ventilator-associated pneumonia, patients with two of the following criteria: Fever ≥ 38 °C, Purulent Bronchial Secretions, and WBC more than 10,000/mm³ or <3000/mm³ were included in the study. Patients with pneumonia or any pre-existing lower respiratory tract infections at the time of admission or first 48hrs of mechanical ventilation were

excluded in this study. Clinically diagnosed Ventilator associated pneumonia cases were observed and data such as name, age, gender, date of admission into intensive care unit, chief complaints, risk factors involved and duration of mechanical ventilation were obtained. Data related to general physical examination, radiological and haematological investigations were also collected. Endotracheal aspirate (ETA) was collected under aseptic precautions. The samples were transported to the laboratory immediately for processing.

Collected ETA samples were subjected to Gram's stain (Microscopy). The specimen was further diluted using sterile saline (1 in 100) and the dilution factor was noted and the specimen was then inoculated for quantitative culture using standard techniques onto MacConkey agar, Blood agar and Chocolate agar plates using a 4mm sterile nichrome loop (0.01 ml), and then incubated at 37°C. The plates were examined for growth at 24 hrs, and if there was no growth, it was further incubated for another 24hrs.

Bacterial growth with > 10⁶ CFU/ml was given significance as a pathogen and was further identified using appropriate bio-chemical tests. The antibiotic susceptibility testing was performed according to CLSI guidelines.^[6] Following antibiotics were used Cotrimoxazole (25µg), Gentamycin (10µg), Amikacin (30µg), Ceftazidime (30µg), Ceftriaxone (30µg), Amoxicillin/Clavulanic acid (20/10µg), Ciprofloxacin (5µg), Piperacillin/Tazobactam (100/10µg), Imipenem (10µg), Meropenem (10µg).

RESULTS

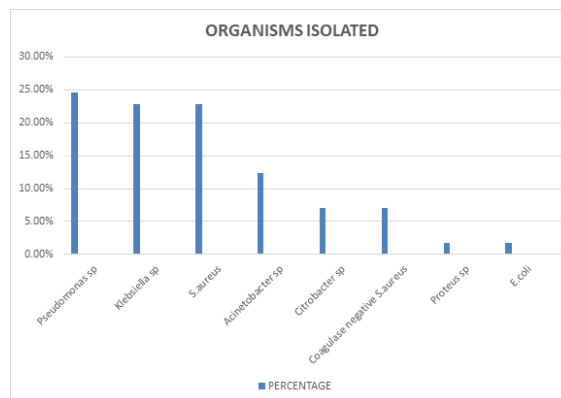
A prospective study was done enrolling 68 patients out of 240 patients on mechanical ventilation as per the inclusion criteria, and the following results were obtained. Of the total 68 patients suspected to have VAP, 52 (76.5%) developed true VAP as per the diagnostic criteria. Incidence rate of VAP in our study was 21.7%. The significant peak of incidence was seen in 25-45yrs of age group. Among them 46 (67.6%) were males and 22 (32.4%) were females. . Among them 46 (67.6%) were males and 22 (32.4%) were females. In our study late onset pneumonia was more frequent (i.e. 59.6%) than early onset pneumonia (40.4%)(Table 1). Among the organisms isolated 70.2% of them were Gram negative bacteria and 29.8% were Gram positive bacteria. The predominant GNB isolated in our study was *Pseudomonas sp* (24.6%), followed by *Klebsiellasp* (22.8%), *Acenitobactersp* (12.3%), *Citrobactersp* (7.2%), *E.coli* (1.7%), and *Proteus sp* (1.7%)(Graph 1). Among the isolates of GNB, 52.5% of them were non-fermenting GNB and remaining 47.5% were fermenting GNB(Graph 2).

NFGNB showed multidrug resistant to most of the antibiotics like, Amoxicillin/Clavulanic acid (100%), ceftazidime (93%), amikacin (74%),

cotrimoxazole (73%), but showed sensitivity to carbapenems like meropenem (78%) and imipenem (60%). Other Enterobacteraiceae isolates indicated sensitive to aminoglycosides and carbapenems.

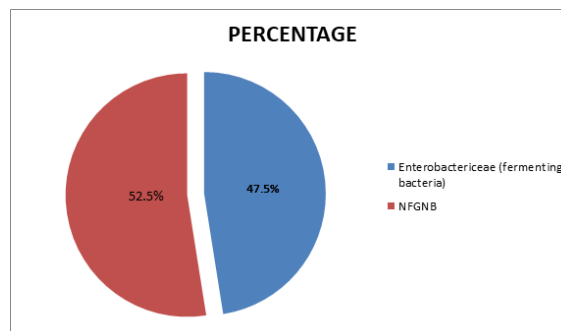
Table 1: Time of onset of Ventilator associated pneumonia

ONSET	VAP N=52(%)	NON-VAP N=16(%)	TOTAL
EARLY	21(40.4%)	7(43.8%)	28(41.2%)
LATE	31(59.6%)	9(56.2%)	40(58.8%)



Graph 1: Bacteria isolated from the endotracheal aspirate samples from ventilator associated pneumonia patients.

Pseudomonas (24.6%) was the most common isolate that was identified. The other significant Gram negative isolates implicated were, *Klebsiella sp*, *Acenitobacter baumannii*, *E.coli*, *Proteus sp*. Among the Gram positive isolates *Staphylococcus aureus* (22.8%) was most frequently found.



Graph 2: Fermenting and non-fermenting gram-negative bacteria

Among isolates of GNB, 52.5% isolates were non-fermenting GNB and 47.5% were fermenting GNB.

DISCUSSION

VAP is the most prevalent nosocomial infection, leading to increased hospital stay, high cost, morbidity and mortality. The incidence of VAP was reported different; depending on the type of hospital or ICU, the population studied and the organisms prevalent; and varied from 7 to 70%. This study was conducted to assess the bacterial etiological agents with a perspective to find out the frequency of non-

fermenting bacteria which are emerging microbial cause for hospital acquired infections.

Our study showed occurrence of VAP to be 21.7%, which was in close agreement with a study conducted on nosocomial pneumonia by Vincent (2001).^[6] In a South Indian study, Rakshith et al (2005) reported the incidence of 26 per 1000 ventilator per day.^[7] The organisms responsible for VAP vary according to case, institution, prior antibiotic exposure, local resistance patterns, length of mechanical ventilation, and specific diagnostic method(s) used. Kanj et al,^[8] showed incidence of GNB of 83% which were predominant in the study. Thakuria et al study also showed high predominance of aerobic gram negative bacteria (89.29%).^[9] In our study, the incidence of aerobic gram negative bacteria was 70.2% which were similar to above mentioned studies.

In a study of Rakesh Kumar Mukhia et al, the most common gram-negative bacteria isolated were *Acinetobacter* sp, *Pseudomonas* sp, *Klebsiella* sp and *Escherichia coli*.^[10] In a study of Dr.Hina Gadani et al,^[11] the order of prevalence of organism in VAP cases was found to be *Pseudomonas* (43.2%), *Klebsiella* (18.91%), followed by MRSA, *Escherichia coli*, *Acinetobacter*, Methicillin Sensitive *Staphylococcus aureus* (MSSA) and *Streptococcus pneumoniae*. The findings of our study were similar to above mentioned studies with *Pseudomonas* sp (24.6%) as the predominant gram negative organism isolated, followed by *Klebsiella* sp (22.8%), *Acinetobacter* sp (12.3%), *Citrobacter* sp (7.2%), *E.coli* (1.7%), and *Proteus* sp (1.7%).

In our study late onset pneumonia was more frequent (i.e. 59.6%) than early onset pneumonia (40.4%). The more the number of days the patient is on a ventilator, the higher is his chances of getting pneumonia. This has been proved beyond doubt in study conducted by Sanmath K et al, 55 where 90.32% of patients who were intubated for 10 days or more had VAP compared to 34.83% of patients who were intubated for less than 10 days^[12].

The most common pathogen associated with early-onset VAP was *Pseudomonas aeruginosa* (25%) in a study by Ibrahim *et al.*^[13] and in our study also *Pseudomonas sp* (30.4%) in early onset and *Acinetobacter* sp (20.6%) in Late VAP were noted.

A number of studies showed that non-fermenting bacteria are major VAP pathogens but its incidence rate varies in different setting. In a study by Trouillet *et al.* study^[14], frequency of non-fermenting bacteria and fermenting GNB were 33.9% and 17.9%, respectively and in another study by Esperati *et al.*^[15], 28% were non-fermenting bacteria and 26% were fermenting GNB. In this study 52.5% isolates were non-fermenting GNB and 47.5% were fermenting GNB.

NFGNB displays a wide and variable spectrum of antibiotic sensitivity. In our study NFGNB showed multidrug resistance to most of the antibiotics. Data from the National Nosocomial Infection Surveillance System also showed that resistance to

imipenem of *Acinetobacter* isolates causing pneumonia in ICUs had increased from 0% to 42%.

CONCLUSION

This prospective study has addressed the incidence and microbiology of VAP with respect to non-fermenting bacteria in a tertiary care hospital.

Nonfermenting bacteria like *Pseudomonas* and *Acinetobacter* sp were most commonly isolated with former being predominant in Early VAP and latter in Late VAP. Majority of the pathogens isolated were resistant to multiple drugs. Carbapenems and aminoglycosides are more effective to initiate empirical treatment.

There is a risk of emergence of MDR pathogens with inadequate, inappropriate antibiotic treatment. An updated local antibiogram for each hospital and ICU based on local bacteriological patterns and susceptibilities is essential to guide optimally dosed initial empiric therapy.

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