“STUDY OF VENTILATOR ASSOCIATED PNEUMONIA IN SHRI B.M. PATIL MEDICAL COLLEGE HOSPITAL & RESEARCH CENTER”

By

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Dissertation submitted to BLDE University, Vijayapur

In partial fulfilment of the requirements for the award of the degree of

DOCTER OF MEDICINE

IN

GENERAL MEDICINE

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Dr. SANDIP J SINGH

LIST OF ABBREVIATIONS USED

ABG	-	Arterial blood gas analysis
APACHE	-	Acute Physiology Age Chronic Health Evaluation
APTT	–	Activated Prothrombin time
ARDS	-	Acute respiratory distress syndrome
BAL	-	Bronchial alveolar lavage
CCF	-	Congestive Cardiac Failure
CDC	-	Centers for disease control
COPD	-	Chronic obstructive pulmonary disease
CPIS	-	Clinical pulmonary infection score
CRF	-	Chronic renal failure
CXR	-	Chest x-ray
C/S	-	Culture Sensitivity
DKA	-	Diabetic ketoacidosis
ECG	-	Electrocardiogram
EPIC	-	Extended prevalence of infection in Intensive care
ESBL	-	Extended Spectrum beta lactam
ETA	-	Endotracheal aspiration
ET	-	Endotracheal Tube
Fio2	-	Fraction of Inspired Oxygen
GBS	-	Gullian Barrie syndrome
Hb	-	Haembologin
ICU	-	Intensive Care Unit

ICP	-	Intracranial pressure
IHD	-	Ischaemic heart disease
LRT	-	Lower respiratory tract
MDR	-	Multidrug Resistant
MRSA	-	Methicillin Resistant Staphylococcus Aureus
MV	-	Mechanical Ventilation
NNIS	-	National Nosocomial Infection Surveillance System
NP	-	Nosocomial pneumonia
PaO2	-	Partial Pressure of Oxygen
PAE	-	Post Antibiotic Effect
PEEP	-	Positive End Expiratory Pressure
PSB	-	Protected specimen brush
PSB	-	Protected specimen brushing
PT	-	Prothrombin Time
PUO	-	Pyrexia of unknown origin
QEA	-	Quantitative endotracheal aspirate
TA	-	Tracheal Aspirates
VAP	-	Ventilator associated pneumonia

ABSTRACT

Background and objectives:

Ventilation associated pneumonia (VAP) is a form of nosocomial pneumonia that occurs in patients receiving mechanical ventilation for more than 48 hours. This study is conducted to find incidence, common organism causing it, common culture sensitive antibiotic and clinical profile of VAP patients in Shri B.M. Patil Medical College Hospital and Research Center.

Materials and Methods:

All patients on mechanical ventilation admitted in intensive care units (MICU/ICCU) of hospitals of Shri B.M. Patil Medical College Hospital and Research Center, Vijaypur, for approximately one and half years from January 2015 to June 2016 were considered. The patients who developed VAP and who satisfied inclusion criteria were studied. Detail history, physical examination was done in patient were investigated with chest x-ray and culture of endotracheal aspirate.

Results:

Incidence of VAP was 8.16%. Totally 50 patients developed VAP. Out of which 28 developed early onset and 22 developed late onset VAP. The most common sign in early and late onset VAP was Bronchial breath sounds (82.1% & 81.8% respectively) followed by Fever and Tachycardia (75%) in early onset VAP and Crepitation's (77.3%) in late onset VAP.

Most common organism isolated in early onset VAP was Pseudomonas (60.7%) and Actinobacter 14.3%). While Staphylococcus (36.4%) and Pseudomonas (27.3%) were the common organism in late onset VAP.

Ceftizidime, Piperacillin & Tazobactum and Amikacin were the common antibiotics for which cultures were sensitive in early onset and late onset VAP.

Common risk factors in early and late onset VAP was use of Proton pump inhibitors (100%) respectively followed by Ryle's tube insertion (71.4% & 66%) respectively.

21.4% was mortality rate of early onset VAP and 50% was in late onset VAP.

Interpretation and conclusion:

The incidence of 8.16% is significant for a VAP in our study. Pseudomonas was commonest bacteria overall causing it. The mortality in late onset VAP (50%) is highly significant as compared to early onset VAP (21.4%). Only strategies which decrease the incidence of VAP are preventive measures.

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INTRODUCTION

Pneumonia:

An acute disease that is marked by inflammation of lung tissue accompanied by infiltration of alveoli and often bronchioles with white blood cells (as neutrophils) and fibrinous exudate, is characterized by fever, chills, cough, difficulty in breathing, fatigue, chest pain, reduced lung expansion and is typically caused by an infectious agent (e.g. bacteria, virus, or fungus).[1]

Introduction

Lower respiratory tract infections in mechanically ventilated patients are a frequent cause of antibiotic treatment in intensive-care units. These infections present as severe sepsis or septic shock with respiratory dysfunction in intubated patients. Purulent respiratory secretions are needed for diagnosis, but distinguishing between pneumonia and tracheobronchitis is not easy. Both presentations are associated with long lasting mechanical ventilation and extended intensive-care unit stay, providing a rationale for antibiotic treatment initiation. Differentiation of colonizer's from true pathogens is difficult, and microbiological data show Staphylococcus aureus and Pseudomonas aeruginosa to be of great concern because of clinical outcomes and therapeutic challenges. Key management issues include identification of the pathogen, choice of initial empirical antibiotic and decisions with regard to the resolution pattern.[2]

Intensive care unit plays vital role in recovery of critically ill patients. However, nosocomial infections are matter of concern in patient admitted to intensive care unit. Nosocomial infections are those which manifest after 48 hours in patient admitted to the hospital. Pneumonia is presumed to be second most common nosocomial infection

in critically ill patients admitted to I.C.U. It is leading cause of morbidity and mortality associated with hospital acquired infection. Ventilator associated pneumonia (VAP) is one of the cause for hospital acquired pneumonia. Ventilator associated pneumonia is the pneumonia that develops in patient who are on mechanical ventilator for 48 hours or more. To support critically ill patients, there has been widespread increased in the use of Tracheal intubation and mechanical ventilator and which in turn has increased the risk of nosocomial infection in the form of ventilator associated pneumonia.[3]

Critical care units increasingly use high technology medicine for patient care, hemodynamic monitoring, ventilator support, hemodialysis, parenteral nutrition, and a large battery of powerful drugs, particularly antibiotics to counter infection. It is indeed a paradox that the use of high-tech medicine has brought in its wake the dangerous and all too frequent complication of nosocomial infections.

The incidence of VAP is 5% to 67%, the average incidence is 20% to 25%, so one in four patient undergoing mechanical ventilation will acquire V.A.P.[4] V.A.P has not only increased morbidity and mortality but also has increased the cost of care.

.In the Extended Prevalence of Infection in Intensive Care II (EPIC II) study, the one which looked at 1265 intensive care units (ICUs) in 75 countries, 51% of adults admitted to ICUs were infected, and the respiratory tract was the focus of infection in 64% of cases. Airway infection in intubated patients is the main reason for antibiotic prescription in medical ICUs. Because, no gold standard exists for the diagnosis of respiratory tract infections in incubated patients, two different classes of antibiotics for patients with purulent respiratory secretions is common clinical practice in the ICU

setting. The panel shows the clinical challenges in management of respiratory tract infections in ventilated patients with a hypothetical clinical scenario. In this Review, we discuss ventilator-associated pneumonia (VAP) in adult patients, with an emphasis on diagnosis, microbiological causes, and management.[2]

National Nosocomial Infections surveillance system (NNIS) of USA data suggests nosocomial pneumonia is the second most common nosocomial infection in intensive care units. Additionally pneumonia is associated with the greatest mortality among nosocomial infections and with considerably increased costs of care. The widespread use of tracheal intubation and mechanical ventilation to support the critically ill has defined an expanding group of patients who are at particularly high risk for development of nosocomial pneumonia.[5]

Despite availability of newer antimicrobials the treatment of VAP has proved to be difficult. The clinical presentation and organisms causing the VAP are different in different set ups. Hence there is every need for early diagnosis and management of these patients to decrease morbidity and mortality.

OBJECTIVES

1) To study the incidence, clinical profile and etiological organisms causing Pneumonia in patients on Mechanical Ventilation.

REVIEW OF LITERATURE

The Roman physician Galen may have been the first to describe mechanical ventilation: "If you take a dead animal and blow air through its larynx [through a reed], you will fill its bronchi and watch its lungs attain the greatest distention".[6]

The iron lung, also known as the Drinker and Shaw tank, was developed in 1929 and was one of the first negative-pressure machines used for long-term ventilation. It was refined and used in the 20th century largely as a result of the polio epidemic that struck the world in the 1940s. The machine is effectively a large elongated tank, which encases the patient up to the neck. The neck is sealed with a rubber gasket so that the patient's face (and airway) is exposed to the room air.[6]

Vesalius too describes ventilation by inserting a reed or cane into the trachea of animals.[6]

The design of the modern positive-pressure ventilators was mainly based on technical developments by the military during World War II to supply oxygen to fighter pilots in high altitude. Such ventilators replaced the iron lungs as safe endotracheal tubes with high volume/low pressure cuffs were developed. The popularity of positive-pressure ventilators rose during the polio epidemic in the 1950s in Scandinavia and the United States and that caused the beginning of modern ventilation therapy.

The term nosocomial comes from the Greek “nosokomein”, hospital, which is derived from the Greek word “nosos” meaning disease. Therefore a nosocomial infection is an infection associated with a hospital or a health care facility.[6]

Approximately 10-28% of critical care patients develop VAP.[6,7] The incidence of VAP increases with the duration of mechanical ventilation. It doubles the risk of mortality as compared with patients without VAP.[8,9] VAP may account for up to 60% of all Healthcare- Associated Infections. VAP increases the length of ICU stay by 28%.[10]

The crude mortality rate for VAP is 27 to 76 %. Pseudomonas and Acinetobacter pneumonia is associated with increased mortality rates when compared to other organisms.[11]

Ventilator associated pneumonia is defined as pneumonia occurring after 48 hours of endotracheal intubation and initiation of mechanical ventilation.[12]

Variability in VAP incidence might be due to the absence of a diagnostic gold standard. The standard definition used to measure VAP incidence is based on several non-specific clinical signs, with microbiological criteria included to improve specificity, but could be severely restricted by the absence of sensitivity and specificity of present criteria.

1) A total of 10000 and more patients were studied in 1417 ICUs across the Europe and overall nosocomial pneumonia prevalence was 9.6%. In this study mechanical ventilation was identified as one of the several risk factors associated with nosocomial infection.[13]
2) A study conducted by Trivedi et al showed an incidence of 9.38% of nosocomial pneumonia and out of this 38% had VAP. Most common microorganism which was isolated was as follows: Pseudomonas (55%), Acinetobacter (20%), S. aureus (14.5%) and Klebsiella (75%). Total mortality was 21.3%.VAP is associated with crude mortality rate of 20 –70%.[14]

3) In an Indian study nosocomial pneumonia was found to have a 9% incidence using radiological and microbiological criteria.[15]
4) The attributable mortality of VAP is controversial; this condition prolongs mechanical ventilation and length of stay in the ICU.[15] The overall mortality due VAP was estimated to be 13 % in a Meta-Analysis.[16] Pneumonia was associated with increased in-hospital death rates (42•9% for patients with pneumonia vs 11•5% for those without, p=0•01).[17]
5) Melsen and colleagues reported that VAP development decreased the daily probability of discharge from the ICU by 26%, suggesting that the disorder lasts throughout the stay. The overall daily risk of discharge after ventilator associated pneumonia was 0•74 (0•68–0•80).[15]
6) Study conducted in India by Neelima Ranjan and colleagues reported incidence of VAP was 57.14%. Study showed that the incidence of VAP is directly proportional to the duration of mechanical ventilation. The most common pathogens causing VAP were Acinetobacter spp. and Pseudomonas aeruginosa and were associated with a high fatality rate.[18]
7) Another study conducted by Behnia M and colleagues showed that 43 patients were diagnosed with nosocomial pneumonia in ICU over a span of one year. One or more gram negative organisms as the causative agents were present in 85% of microbiologic samples. The three most prevalent gram negatives were Stenotrophomonasmaltophilia (34%), Pseudomonas aeruginosa (40%), and Acinetobacter baumannii (32%). Twenty eight percent of bronchoalveolar samples contained Staphylococcus aureus. Acinetobacter baumannii, Klebsiella

pneumonia extended spectrum beta lactam (ESBL) and P. aeruginosa had the highest prevalence of multi drug resistance (MDR). Mortality from pneumonia was 37%.[19]

8) Sandiumenge and colleagues reported S aureus, P aeruginosa, and A. baumannii to be the three main causes of infection in patients in ICUs. Enterococcus spp and Candida spp, on the other hand, should be interpreted as oral contaminants.[20]
9) VAP caused by multi drug resistant bacterial infection such as Pseudomonas and Acinetobacter species are associated with high mortality. [21]
10) A study conducted by Kollef showed that mortalities due to ventilator associated pneumonia were 37.5% as compared with 8.5% mortalities due to other then pneumonia. [22]
11) Rakshit and colleagues observed that the incidence of VAP is directly proportional to the duration of MV. They also found that Gram-negative bacteria followed by methicillin resistant Staphylococcus aureus (MRSA) are among the commonest incriminating organisms. Further they observed that APACHE-III (Acute Physiology and Chronic Health Evaluation) score on admission is a useful parameter to assess the prognosis of patients developing VAP. The mortality rate in patients who acquired VAP was found to be 37%.[23]
12) Heyland and group showed that there was no significant difference between bronchoalveolar lavage and endotracheal aspiration when used as diagnostic technique for the growth of microorganisms causing VAP.[24]

13) A Study done by Iregui and associates showed that patients who had a delay in receiving antibiotics for more than 24 hours after being diagnosed as VAP were at greater risk of mortality. The study suggested that clinicians should avoid delaying the administration of appropriate antibiotic treatment to patients with VAP in order to minimize the risk of mortality.[25]

14) In a study done by Andrade and colleagues the incidence of VAP was found to be 24.59 per 1000 ventilator days and the mortality rate was 32.1%. The major pathogens isolated were Pseudomonas, Staphylococcus aureus and Enterobacteriaceae and were found to be resistant to Imipenem, Oxacillin and third and fourth generation cephalosporins.[26]

15) In a study done by Alp and his associates VAP was the leading cause of morbidity and mortality in intensive care units with incidence of 7% to 70 and the mortality rates of 20–75%. The study also showed that Aspiration of colonized pathogenic microorganisms from the oropharynx and gastrointestinal tract is the main route for the development of VAP.[27]

16) Study done by Dey etal showed increased incidence and association of multidrug resistant organisms causing VAP in CCU.[28]

17) In a study done by Rodrigues and his associates Multidrug-Resistant Pseudomonas aeruginosa are increasing in clinical-surgical intensive care unit in a Brazilian University Hospital with high mortality rates.[29]

18) In a study done by Katherson and his colleagues found that the incidence of VAP was comparable to that found in the National Nosocomial Infection

Surveillance System and Klebsiella was the most common organism. The incidence of VAP was found to increase with the duration of MV.[30]

19) A study done by Hussain and his associates observed no difference in the results with Quantitative Bronchoscopic Lavage Cultures (B-BAL) when compared with Blind NG Tube Lavage (N-BAL) Cultures in the Diagnosis of Ventilator Associated Pneumonia (VAP).[31]

20) In a study done by Erbay and his colleagues the cost of VAP was approximately five-fold higher than non-infected patients.[32]

VENTILATOR ASSOCIATED PNEUMONIA (VAP)

Definition

Ventilator associated pneumonia (VAP) is defined as pneumonia occurring after 48 hours of endotracheal intubation and initiation of mechanical ventilation.[33]

Categorization of VAP:

a) **Early-onset VAP:** Ventilator associated pneumonia occurring within 4 days of endotracheal intubation and initiation of mechanical ventilation.

b) **Late-onset VAP:** Ventilator associated pneumonia occurring after 4 days of endotracheal intubation and initiation of mechanical ventilation

This categorization helps predict the implicated pathogens and guides us in the initial empiric therapy with antibiotics, which is known as the epidemiological approach.[34]

Pneumonia acquired within 48 hours after hospital admission as a consequence of emergency intubation, aspiration due to decreased level of consciousness and coma, or cardiopulmonary resuscitation is excluded from definition of VAP.[13]

Incidence:

The accuracy of epidemiologic data of NP and VAP has been in question because of the difficulties in defining a "gold standard" for diagnosis. The incidence of nosocomial pneumonia varies from hospital to hospital. The incidence of nosocomial pneumonia in the intensive care units ranges from 9 to 24 % with variation relating to care presented in the ICUs and differences in the diagnostic techniques used. In an Indian study nosocomial pneumonia was found to have a 9% incidence using radiological and microbiological criteria.[35]

Among a total of more than 10000 patients in 1417 ICUs across Europe, the overall nosocomial pneumonia prevalence was 9.6%. In this study logistic regression analysis identified mechanical ventilation as one of the several risk factors for ICU-acquired infections.[36]

The rates differ according to the population and the diagnostic criteria used. Using a protected specimen brush (PSB) during fiber optic bronchoscopy to diagnose pneumonia in ventilated patients, Fagon reported a nosocomial pneumonia incidence rate of 9%.[37]

An incidence of 16.6% was reported at a later period using bronchoscopic protected specimen brush (PSB) and Broncho alveolar lavage (BAL) with quantitative culture techniques.[38] The wide differences in incidence rates is due to the difference in the number of patients in each study, the case mix, the hospital setting, the diagnostic criteria used to confirm pneumonia, and the mean duration of mechanical ventilation in the study population.

The risk of acquiring pneumonia appears to increase with the duration of mechanical ventilation. In one study it was found to be 7% at 10 days and 19% at 20 days.[39] In that study the incremental risk of pneumonia was virtually constant with a mean rate of around 1% per day of ventilation. In another large series[40], maximum cumulative risk of developing VAP was up to day 5, with the rate declining thereafter. The risk per day was estimated to be 3% on Day 5, 2% on Day 10 and 1% on Day 15. The predictors of VAP also depended on the type of patient and were different for different types of illness.

Trivedi et al reported an incidence of 9.38% of nosocomial pneumonia and 38% had ventilator associated pneumonia. Commonest isolates were pseudomonas (55%), Acinetobacter (20%), Staph. aureus (14.5%) and Klebsiella (75%). Total mortality was 21.3%. VAP is associated with crude mortality rate of 20 –70%.

Mortality as a result of VAP is especially high when it is caused by multi-drug resistant organisms like pseudomonas or Acinetobacter species.[41] Kollef reported that overall mortalities in patients with VAP were 37.5% as compared with 8.5% in patients without pneumonia.[42]

In recent studies it has been found that in early onset VAP, the most common isolated pathogen was staph aureus & in late onset VAP it was pseudomonas aeruginosa.[43]

The P. aeruginosa and staphylococcus aureus are the most common organisms and are usually frequent and more antibiotic resistant. There appears to be three key risk factors that influence the type of infection in VAP, the underlying disease condition, the duration of mechanical ventilation before the onset pneumonia and prior antibiotic exposure.

Pseudomonas aeruginosa & other multidrug resistant pathogens are common in patients who have previously received antibiotics, steroids or ventilation for more than 6 days (late onset) & this is associated with a higher mortality rate. There is an enormous impact of antimicrobial agents on the organisms responsible for NP. The organisms of the normal oropharyngeal flora virtually disappear & are being replaced by gram negative bacilli in the patients who are on prior antibiotics and in those who are seriously ill.[44]

Patients with COPD are at increased risk for streptococcus pneumonia and hemophilus influenzae infection, and those with bronchiectasis have infections frequently with Pseudomonas aeruginosa and Staphylococcus aureus.

Chronic renal failure, diabetes, head trauma and neurological patients are at increased risk for staphylococcus aureus infection. Prior antibiotic exposure reduces the chances of acquiring streptococcus pneumonia or H. influenza infection, while it increases the risk for Pseudomonas aeruginosa infection.[34]

Feldman and colleagues[45] assessed the sequence of colonization in the oropharyngeal, gastrointestinal tract, lower respiratory tract & endotracheal tube (ET) in mechanically ventilated patients. They studied 10 patients, who on admission showed no evidence of any infection, and cultured the oropharynx, gastric content, the interior of the airway tube, and endotracheal secretions twice a day for 5 days. Nine patients became colonized; subsequently the oropharynx was the first site at. 36 hours; followed by the stomach at 36 to 60; and there after the lower respiratory tract at 60 to 84 hours. Organisms isolated from the endotracheal tube at 48 hours but occurred in significant amounts later at 60 to 96 hours. Gram-positive isolates did not colonize the endotracheal tube in significant amounts. Nosocomial Pneumonia was diagnosed in 3 of the 10 patients. In two cases, Acinetobacter, the pathogen considered to be responsible for VAP, was first isolated from tracheal aspirates and from the interior of the endotracheal tube (between 60 to 84 hours) and at 96 hours there was clinical evidence of nosocomial pneumonia. It was found oropharyngeal colonization was followed by gastric; lower respiratory tract & eventually ET colonization suggesting

early colonization of oropharynx may be an important precursor for subsequent LRT colonization.[44]

Microbiology of VAP:

Each of the microbes known to cause VAP shares an ability to exploit some defect in the patient's lung defenses. VAP usually results from the aspiration of oropharyngeal secretions through the endotracheal tube or from inoculation directly into the airway. It has been known for decades that the microbial flora of hospitalized and critically ill patients becomes drastically altered within days after admission particularly, when antibiotics have been administered. The usual mixed flora of the oropharynx and anaerobic flora of the colon have low virulence. In critically ill patients these organisms become overgrown by endogenous aerobic Gram-negative bacilli, which can then colonize the airway and lead to lung infection.[45]

Bacteria causing VAP include Staphylococcus aureus, Streptococcus pneumonia, Enterococci, Haemophilus influenza, Escherichia coli, Klebsiella species, Enterobacter species, Proteus species, Citrobacter species, Pseudomonas aeruginosa and Acinetobacter baumannii.

Fungi include Candida species and Aspergillus species. Viruses include Influenza and other Respiratory viruses, Herpes simplex virus and Cytomegalovirus.

Early onset VAP is often due to antibiotic sensitive bacteria. (Staphylococcus aureus, Hemophilus influenza and Streptococcus pneumonia), whereas late onset VAP is frequently caused by antibiotic resistant pathogens (oxacillin-resistant Staphylococcus aureus, Pseudomonas aeruginosa, Acinetobacter species and Enterobacter species)[46]

A] Early onset VAP

1. Gram-positive cocci

• Streptococcus pneumonia

• Methicillin sensitive staphylococcus aureus (MSSA)

2. Gram negative bacilli

• E. coli

• Klebsiella species (spp)

• Serratia marcescens

B] Late onset VAP:

1. Gram-positive cocci

• Methicillin resistant staphylococcus aureus (MRSA)

2. Gram negative bacilli

• Enterobacteriaceae species

• Pseudomonas aeruginosa

• Acinetobacter baumanii.[44]

Streptococcus pneumonia is a Gram-positive diplococcus. It colonizes the upper respiratory tract and invades the lung after micro aspiration of oropharyngeal secretions. It is the most common cause of community acquired pneumonia. Most S. Pneumonia isolates remain susceptible to traditional beta-lactam antibiotics. It causes VAP predominantly in the early days after intubation and is rapidly cleared after beginning antibiotic therapy.

Haemophilus influenzae is a small pleomorphic gram-negative coccobacillus. It is easily eradicated by antibiotic therapy and causes VAP most often early after the initiation of mechanical ventilation.

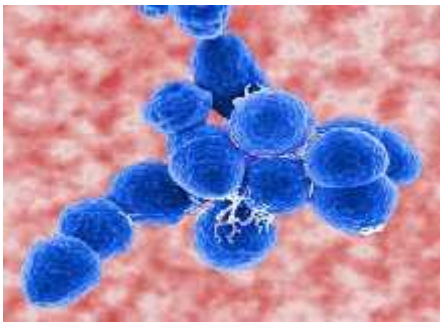
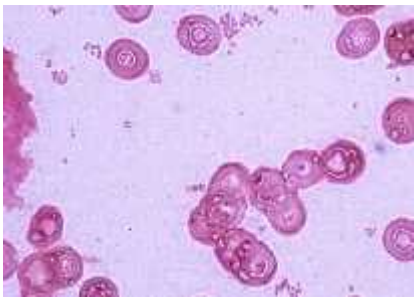
Staphylococcus aureus is a gram-positive coccus that frequently colonizes the anterior nares. Most of the strains are susceptible to pencillinase-resistant beta-lactam antibiotics (methicillin-sensitive S. aureus), but the prevalence of methicillin-resistant Staph.Aureus (MRSA) strains are increasing in community isolates.

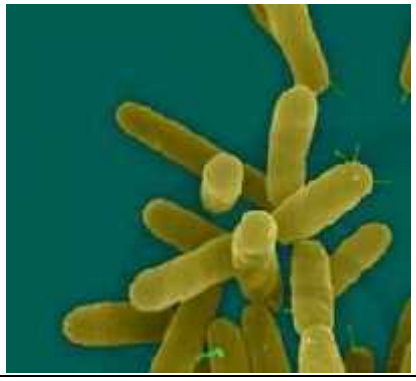
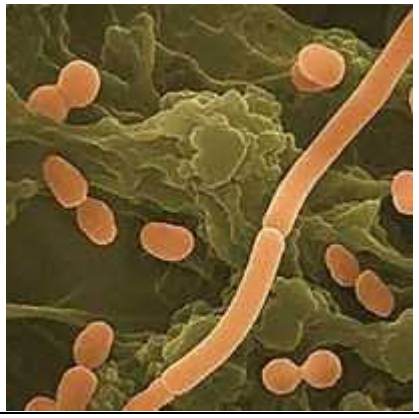
The Enterobacteriaceae are gram-negative bacilli that normally reside in the lower gastrointestinal tract. Antibiotic therapy and critical illness can suppress the normal bacterial flora and lead to an overgrowth of Enterobacteriaceae in the gut and colonization of the skin, upper gastrointestinal and respiratory tract. They exhibit resistance to penicillins and cephalosporins.

Pseudomonas aeruginosa is an aerobic gram-negative bacillus and is intrinsically resistant to many classes of antibiotics. It is the most common cause of fatal episodes of VAP. Pseudomonas VAP is unusual early in the hospital course in previously healthy patients. It typically occurs with prolonged duration of mechanical ventilation.

Pseudomonas is difficult to eradicate from the airways. Persistent or recurrent episodes of pneumonia is common with this organism. Acinetobacter species are aerobic gram-negative bacilli .It has low virulence. Acinetobacter species are important as causes of outbreaks and are readily spread from one patient to another. They are resistant to many common antibiotics.[47]

Table no.1- Risk Factors for Specific VAP Pathogens:

Pathogen		**RiskFactor**
Streptococcus pneumonia		• Smoking • COPD • Absence of antibiotic therapy
Haemophilus influenzae		• Smoking • COPD • Absence of antibiotic therapy
Staphylococcus aureus		**(MSSA)** • Younger age • Traumatic coma • Neurosurgery **(MRSA)** • Steroid therapy • Longer duration of MV • Prior antibiotic therapy • Prior bronchoscopy

Pseudomonas aeruginosa		• COPD • Steroid therapy • Longer duration of MV • Prior antibiotic therapy
Acinetobacter species		• ARDS • Head trauma • Neurosurgery • Gross aspiration • Prior cephalosporin therapy

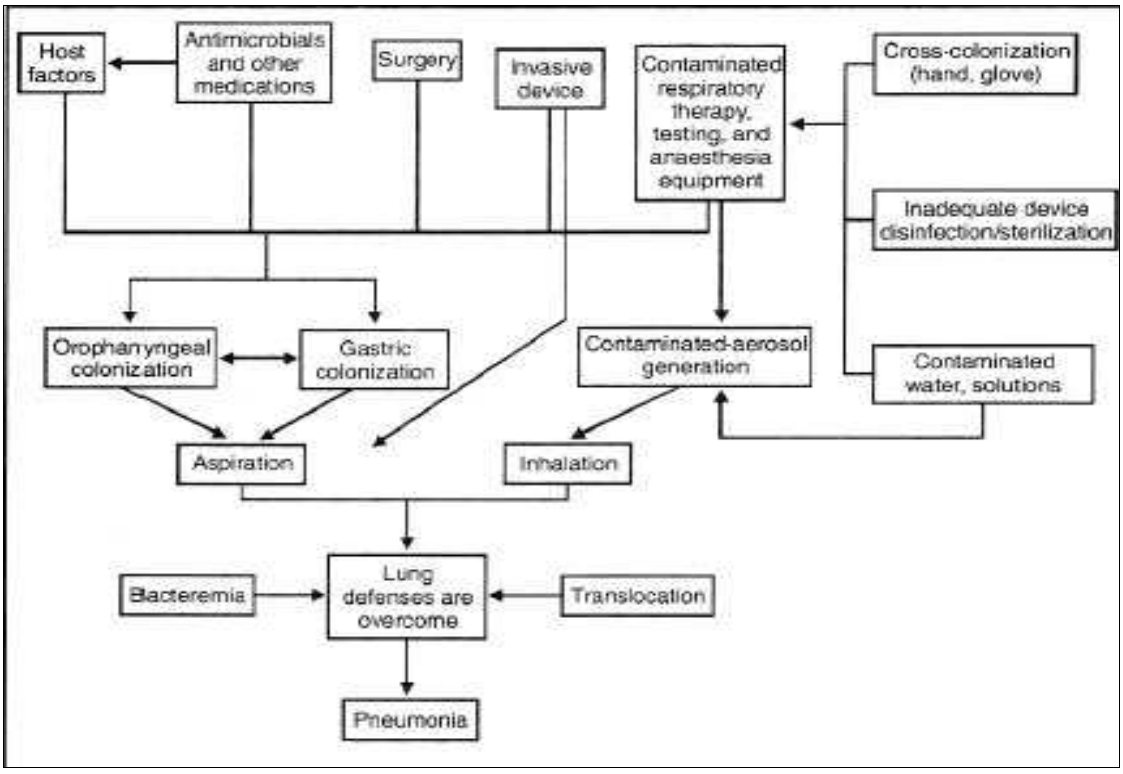
PATHOGENESIS

Pathogenesis and routes of entry: For any infection to occur there must be interplay of 3 factors i.e.; impaired host defense, access of pathogenic bacteria in sufficient numbers to the lower respiratory tract and the virulence of the organism.[48]

The organism may gain access into the lungs by one of several routes i.e.; micro aspiration of oropharyngeal secretions, aspiration of gastric contents, inhalation, hematogenous spread, direct inoculation and exogenous penetration (e.g. pleural space). Out of these micro aspiration is the most common.[48]

Fig. 1: The pathogenesis of nosocomial pneumonia and VAP [48]

(Chart Diagram)



Routes of bacterial entry[34]

a) Micro aspiration of oropharyngeal secretions colonized with pathogenic bacteria.

b) Aspiration of esophageal / gastric contents.

c) Inhalation of an infected aerosol.

d) Hematogenous spread of infection from a distant site of infection.

e) Exogenous penetration from an infected site (i.e. pleural space).

f) Direct inoculation into the airway of incubated patients from ICU personnel

Oropharyngeal Colonization:

Nosocomial gram negative bacterial pneumonias develop in hospitalized patients and are due to changes in the bacterial flora. Colonization of the upper respiratory tract by gram negative bacilli is mediated by alterations in the surface properties of the epithelial cells. In healthy individuals a film of fibronectin covers the epithelium lining the mucosa of the mouth and oropharynx, and prevents the Gram-negative bacteria from adhering to the epithelial cells. This protective coating is lost in very ill individuals, so that

Pathogenic Gram-negative organisms adhere to receptors present on epithelial cells of the mucosa and soon colonize it. The number of these bacterial receptors on both upper and lower airway epithelial cells is increased in many illnesses. The risk factors responsible for oropharyngeal colonization with gram.

Negative bacteria include neutropenia, prior antibiotic therapy, alcoholism, azotemia, coma, diabetes, serious illness, hypotension, intubation, smoking, surgery and neutralization of gastric acid.[34]

Aspiration:

The potential routes of infection, micro aspiration of a small volume of oropharyngeal secretions previously colonized with pathogenic bacteria is most common. Micro aspiration is reported even in healthy people during sleep, but it is the presence of pathogenic bacteria which are able to overwhelm the lower respiratory tract defenses that are most important in the development of pneumonia.

The incidence of aspiration increases when the gag reflex is impaired, if there is an alteration in level of consciousness, when certain devices such as nasogastric tube or endotracheal tubes (ET) are used or if esophageal disease is present.

Among mechanically ventilated patients additional routes of entry exists. The ET tubes by pass host defenses above the vocal cords and impair lower respiratory tract defenses such as cough and mucocilliary clearance. Contaminated secretions can pool above the inflated ET cuff and are not easily removed by suctioning. The secretions can leak around the ET cuff and directly enter the lower respiratory tract when there are changes in airway caliber during swallowing and breathing.[34]

Gastric Colonization:

The acid within the stomach serves as a major deterrent to bacteria swallowed in the saliva. If gastric acidity is suppressed by the use of antacids and H2-antagonists, the bacteria within the stomach survive, multiply and soon colonize the upper gastrointestinal tract. Gastric contents laden with Gram-negative bacteria could easily regurgitate and be aspirated into the lungs, causing aspiration pneumonia. This is particularly frequent in obtunded patients, sedated patients or following a large vomit. Prophylaxis and treatment of bleeding stress ulcers with sucralfate which does not

significantly increase gastric pH in most patients, has resulted in a reduced incidence of nosocomial pneumonias.[34]

Hematogenous spread:

Rarely infected emboli from a septic thrombophlebitis can, lead to septic infarcts within the lung. Catheter related sepsis or any other source of sepsis can cause bacteremia with hematogenous spread of infection into the lungs, causing pneumonia.[34]

Inhalation:

Contaminated respiratory equipment's (nebulizers, humidifiers, ventilator tubing etc) are a source of infected aerosols. Infected particles 3-5 microns in size can be deposited into the terminal bronchioles and alveoli, thereby causing a lower respiratory tract infection.[34]

Iatrogenic Causes:

Lack of aseptic precaution during suction of tracheobronchial secretions, either through an endotracheal tube or tracheostomy is an important cause of lower respiratory tract infection. Medical staff or respiratory therapy equipment's harbor's pathogenic flora and bacteria can be directly inoculated into tracheobronchial tree.[34]

In this closed milieu the major reservoir of nosocomial organisms is the infected or colonized patient. Most bacteria, many viruses, and possibly even fungi are spread primarily via the hands of the medical, paramedical and nursing staff. Mycobacteria, Legionella, and in granulocytopenic patients, Aspergillus are transmitted by the airborne droplets. Aspiration of infected pharyngeal and mouth secretions, exposure to invasive devices and procedures, surgery, impairment of immune mechanisms or overwhelming illnesses amplify colonization and vulnerability to nosocomial

infections, and promote their easy transmission. In most patients, antibiotic use promotes sooner or later antibiotic resistance to a number of organisms that prevail in a particular ICU. These resistant organisms contaminate the whole closed environment of the ICU; they can contaminate the curtains, the walls, floor and ceilings, the side tables, the wash basins and the soap dishes, the detergents used as antiseptics, and the clothing and hands of the ICU staff. Bacteria from colonized or infected patients can also be perpetuated in urine bottles, bedpans, commodes, respiratory therapy equipment, ventilators, chamber domes of transducers used in hemodynamic monitoring, and in bronchoscopes or other endoscopes.

In short, the closed milieu of the ICUs provides an environment that is as conducive to the growth and preservation of resistant organisms.[34]

HOW SPECIFIC RISK FACTORS LEAD TO PNEUMONIA?

The risk factors include patient related risk factors, infection control related factors and intervention related factors.[34]

1. Patients related risk factors:

Certain illnesses predispose to colonization and pneumonia because of disease associated impairment in host defense function. These include acute or chronic illness, coma, malnutrition, prolonged hospitalization or preoperative period, hypotension, metabolic acidosis, cigarette smoking and the presence of co-morbid illness. These illnesses include CNS dysfunction, COPD, diabetes mellitus, alcoholism, azotemia & respiratory failure. Advanced age is associated with an increased risk of pneumonia primarily because of the increased frequency of serious comorbidity among the elderly but age associated immune changes may also play a role.[34]

2. Infection control related factors:

Poor infection control practices can lead to the transmission of hospital acquired pathogens by the hands of medical personnel. This can occur either by not washing hands or not changing gloves between patients or through use of contaminated respiratory therapy devices and equipment.[34]

3. Intervention related factors:

A number of procedures and therapies can impair host defense. Certain therapeutic agents, particularly sedatives can suppress CNS function and can lead to increased incidence of aspiration. Corticosteroids and cytotoxic agents impair a number of vital host defensive functions. Endotracheal tubes can impair mucocilliary clearance from lower respiratory tract as well as injure the epithelial surface and predispose to increased bacterial binding to the surface of the lower respiratory tract. Prolonged and inappropriate antibiotics may increase colonization by antibiotic resistant bacteria, including potentially virulent gram negative bacilli.

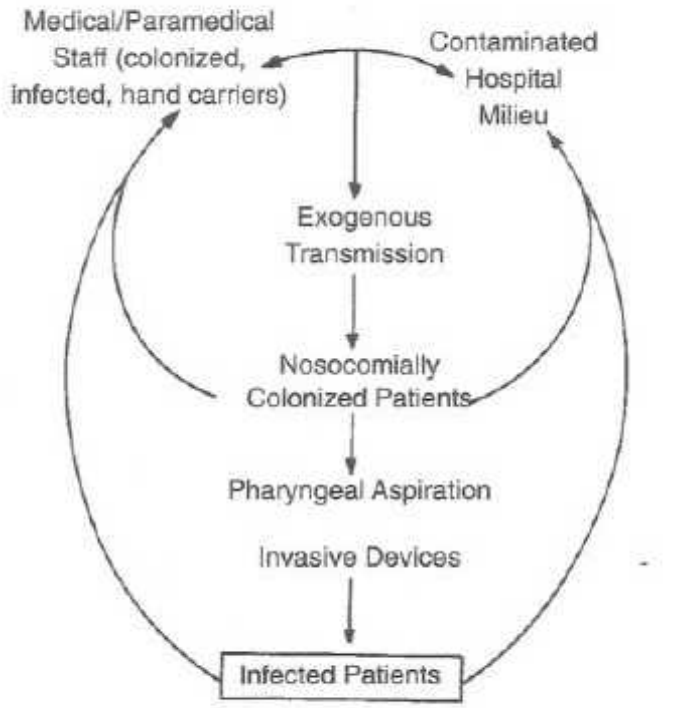
Antacids & H2 blockers are commonly used for prophylaxis against stress ulcers but may increase frequency of gastric colonization by enteric gram negative organisms and possibly incidence of pneumonia.

Enteral feeding via a nasogastric tube can result in increased gastric volume, reflux and gram negative overgrowth in stomach. Nasogastric tube themselves can impair the function of the lower esophageal sphincter thereby promoting aspiration and bacterial contamination of the tracheobronchial tree.

The effect of all these manipulations is augmented if patients are maintained in the supine position because this position increases the rate of reflux of gastric contents into the lung.[34]

Fig-2

CYCLE OF TRANSMISSION OF NOSOCOMIAL *PNEUMONIA*



PATHOLOGY:

Definition

Nosocomial pneumonia is usually defined pathologically as foci of consolidation with intense leukocyte accumulation in the bronchioles and adjacent alveoli.

The collection of pathogenic material in the air filled alveoli is called consolidation. The pathogenic material may be inflammatory cells, blood and exudates.[49]

Classically pneumonias are classified pathologically and radiologically according to the portion of the lung involved as followed.

- Lobar pneumonia: is a confluent consolidation of a part of a lobe or whole lobe or many lobes of the one or both lungs.

Classically caused by Streptococcus pneumoniae which has 4 pathologic stages.

1. Congestion
2. Red hepatization
3. Gray hepatization,
4. Resolution.

- Interstitial pneumonia: It pathologically characterized by a patchy consolidation with presence inflammatory exudates and cells with predominant lymphocytes infiltrating the interstitium associated with deposition of collagen and diffuse alveolar damage. It is caused by viruses and Mycoplasma etc.

- Bronchopneumonia: is a sub segmental, patchy, non-confluent consolidation involves multiples lobes. The inflammatory exudates tend to spread into the alveolar parenchyma immediately surrounding terminal bronchioles. Necrosis of the alveolar walls and abscesses appear in subsequent periods.[49]

Severity and distribution of lesions are not taken into account in this classical definition of pneumonia. In an animal study, Johansson et al**.** classified VAP as mild, moderate, or severe bronchopneumonia. Mild bronchopneumonia was defined as the presence of scattered neutrophilic infiltrates localized to terminal bronchioles and surrounding alveoli. Moderate bronchopneumonia was defined 'as extension of this process with gross confluence of infiltrates between adjacent lobules; purulent sputum was often present in bronchioles. Severe bronchopneumonia was diagnosed when this process was extensively confluent both grossly and microscopically and was occasionally associated with tissue necrosis. Rouby et al[50] defined four stages of VAP severity:

1. Bronchiolitis: intense proliferation of polymorphonuclear leukocytes localized within the lumen of bronchioles and associated with purulent mucus plugs and bronchiolar wall alteration.
2. Focal bronchopneumonia: presence of scattered neutrophilic infiltrates localized to terminal bronchioles and surrounding alveoli.
3. Confluent bronchopneumonia: extension of these elementary lesions to several adjacent lobules.

4. Lung abscess: confluent bronchopneumonia associated with tissue necrosis and disruption of the normal lung architecture.

Recent postmortem human studies have used modified histologic criteria to define VAP. In a postmortem study of mechanically ventilated patients, the authors group defined VAP as a consolidation at the level of secondary lobules with intense accumulation of polymorphonuclear leukocytes, fibrinous exudate, and cellular debris within alveolar spaces. Lung abscess was defined as pneumonia associated with tissue necrosis and destruction of the lung architecture.[50]

Fabregas et also described four evolutionary stages of VAP:[51]

1. Early phase (0 to 2 days): capillary congestion with increased number of polymorphonuclear leukocytes at this level.
2. Intermediate phase (3 to 4 days): presence of fibrin, few erythrocytes, and several polymorphonuclear leukocytes in the alveoli.
3. Advanced phase (5 to 7 days): polymorphonuclear leukocytes filling up most of the alveoli and macrophages incorporating cellular debris in the' cytoplasm.
4. Resolution phase (> 7 days): the inflammatory exudate is eliminated because of phagocytic activity of mononuclear cells.

DIAGNOSIS:

Clinical Diagnostic Criteria of VAP:

Clinical suspicion of pneumonia with a new or progressive chest radiographic infiltrates after 48 hrs of patients on mechanical ventilation & one of the following.[13,49]

1. Fever > 38.3 C

2. Leukocytosis > 12000/cmm or Leucopenia < 4000/cmm.

3. Purulent respiratory secretions with gram stain demonstration of bacteria and polymorphs.

4. Quantitative ET aspirate cultures with growth > 106 colony forming units (cfu)/ml.

For adults 70 years or older, altered mental status with no other recognizable cause and at least 2 of the following

- New onset of purulent sputum or change in character of sputum, increased respiratory secretions or increased suctioning requirements.
- New-onset or worsening cough, dyspnea or tachypnea
- Rales or bronchial breath sounds
- Worsening gas exchange (e.g.: O2 desaturations [PaO2/FiO2 ≤ 240], increased O2 requirements or increased ventilation demand).

However those who had other cause for the radiological infiltrates like pulmonary embolism, pulmonary hemorrhage, atelectasis, CCF and ARDS were excluded.

Table no.2- CPIS:

I	Temperature °C		≥36.5 and ≤ 38.4			0 points
			≥38.5 and ≤ 38.9			1 point
			≥39.0 and ≤ 36.0			2 points
II	Blood leukocytosis, mm^{-3}		≥4000 and ≤ 11000			0 points
			<4000 and > 11000			1 point
			+ band forms ≥ 500			+ 1point
III	Tracheal secretions		<14+ of tracheal secretions			0 point
			≥ 14 + secretions			1 point
			+ purulent sputum			+ 1 point
IV	Oxygenation PaO_2/FiO_2,		> 240 or ARDS			0 points
	mmHg		≤ 240 and ARDS			2 points
V	Pulmonary radiography		No infiltrate			0 points
			Diffuse	or	patchy	1 point
			infiltrate			
			Localized infiltrate			2 points
VI	Culture of tracheal aspirate		(semi-quantitative :0-1-2 or			
	3+)					
	Pathogenic	Bacteria	≤ 1 or no growth			0 point
	Cultured					
			> 1+			1 point
			>1+ and	same	pathogenic	2 points
			bacteria seen in Gram stain			
Total points = CPIS, varies from 0 to 12 points, >6 points is pneumonia.						

Other diagnostic criteria's for a VAP

1. CDC criteria of VAP

(> 3 of the following criteria):

i. Rectal temperature >38°C or < 35.5oC

ii. Blood leukocytosis >10*109/L and or left shift or leucopenia <3109/L

iii. Ten leucocytes per high power field in Gram stain of endotracheal aspirate

iv. Positive culture from endotracheal aspirate and New, progressive or persistent radiographical infiltrate

2. Radiological signs (2 or more serial chest x-rays) with at least one of the following:

• New or progressive and persistent infiltrate

• Consolidation

• Cavitation

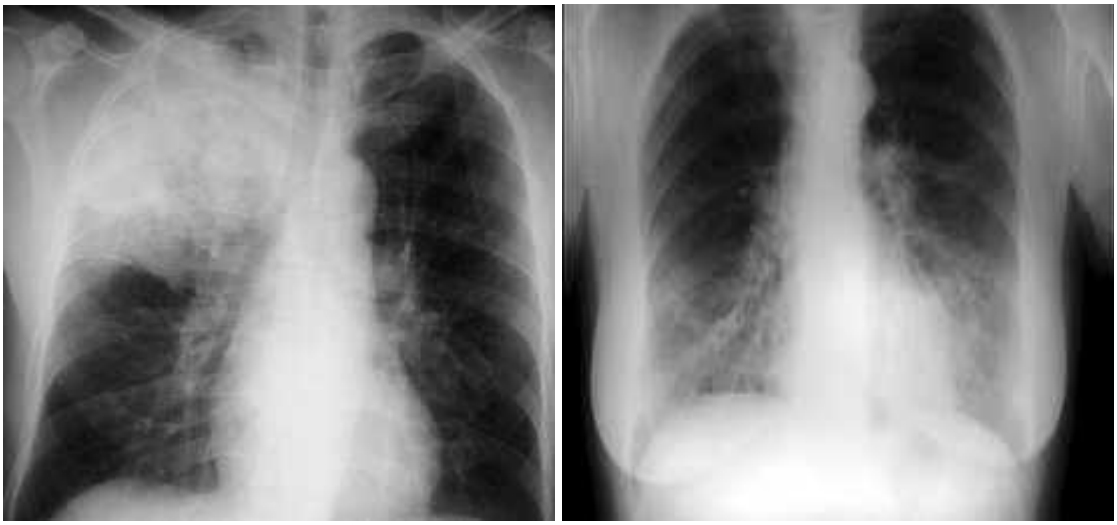


Fig 3: Chest X-ray showing consolidation and cavitation

3. Microbiological criteria

At least one of the following:

- Positive growth in blood culture not related to another source of infection.

- Positive growth in culture of pleural fluid.
- Positive quantitative culture from Broncho alveolar lavage (≥104 colony forming units/ml) or protected specimen brushing (≥103colony forming units/ml).
- 5% or more of cells with intracellular bacteria on direct microscopic examination of Gram-stained Broncho alveolar lavage fluid.
- Histopathological evidence of pneumonia.

4. Clinical pulmonary infection score criteria of VAP: CPIS at baseline was assessed on the basis of the first five variables, i.e. temperature, blood leukocyte count, tracheal secretions, oxygenation, and the character of pulmonary infiltrate. CPIS at 72 hrs was calculated based on all seven variables and took into consideration the progression of the infiltrate and culture result of the tracheal aspirate. A score of >6 at baseline or at 72 hrs was considered suggestive or pneumonia.[52]

Table no.3- CPIS

	CPIS points		
Criterion	0	1	2
Temperature (°C)	≥36.5 and <38.4 In the case of external cooling, give 1 point	≥38.5 and <38.9	≤ 36 or ≥ 39
Blood leukocytes ($x10^3$/l)	>4.0 and <11.0	• 1 <4.0 • 2 ≥11.1 and absence of band forms	• 4 >11.1 and presence of band forms
		• 3 ≥11.1 and ≤17.0, no differentiation done	• 5 ≥17.1, no differentiation done
Tracheal secretions	Absence	Presence and non-purulence (colour: white or light yellow)	Presence and purulence (colour: yellow, green or brown)
Oxygenation (PaO_2 (mmHg)/FiO_2)	>240 or ARDS		<240 and no acute respiratory distress syndrome (ARDS)
Chest X-ray	No infiltrate	Diffuse or patchy infiltrate	Localised infiltrate
Semi-quantitative tracheal aspirate culture (cfu/ml)	• 1 <10^5 • 2 No previous culture	≥10^5 and ≤10^6	>10^6

Clinicians use Clinical Pulmonary Infection Score (CPIS) to diagnose VAP .Most clinicians after observing the above values at the same time, in the same patient, would most certainly consider VAP and begin treatment with a broad range antibiotic while awaiting culture results. Combining knowledge gained from microbiologic examination of Broncho alveolar lavage with the CPIS and good clinical judgment give the best road map for patient treatment.[53]

CPIS Advantages:

• Can easily be calculated at the bedside.

• No special equipment needed.

• May be performed by nursing or respiratory therapy staff.

CPIS Limitations:

- Clinical parameters easier to obtain in ICU than general ward.
- Clinical parameters often not available initially or during course of treatment
  - Oxygenation values
  - Presence of tracheal secretions
  - Serial Chest X-rays
- Unreliable in certain populations
  - Trauma (sensitivity 61%, specificity 43%)
  - Thermal injury (sensitivity 30%, specificity 80%)
  - Immunocompromised patients.

Risk Factors for developing VAP include:

- Mechanical ventilation with endotracheal intubation including tracheostomy.
- Prolonged mechanical ventilation.
- Advanced age.
- Pre-existing sinusitis and lung disease.
- Micro or macro aspiration of oropharyngeal or gastric contents.
- Malnutrition and immunosuppression.
- Obesity.
- Chronic lung disease.

Controversies in the Diagnosis of NP and VAP:

Despite numerous high quality studies addressing different diagnostic strategies in the setting of suspected VAP, no single approach meets with anything close to majority approval. The optimal diagnostic and management strategy for VAP remains controversial.

Unlike community-acquired pneumonia identification of an infiltrate in the lungs as pneumonia in the ICU setting is far more complex as there are several pitfalls in the diagnosis:

1. The clinical diagnosis is based on the presence of fever, leukocytosis, purulent secretions and persistent radiological infiltrates. These systemic features of infection may be due to extra pulmonary infections or due to noninfectious causes that stimulate inflammatory response such as trauma, surgery and pancreatitis. In a study conducted in 84 patients Fagon et al[54] compared prospectively the diagnostic predictions based on clinical radiological and

laboratory criteria by a team of physicians with those resulting from a full work up with invasive methods. They found that only 27 out of 84 clinically suspected patients were actually found to have pneumonia. Among those found to have pneumonia only 62% had had positive predictions on clinical grounds. The main values of temperature, leucocytes, Pa02/Fi02 and radiologic scores in the 3 days preceding the onset of pneumonia did not differ among those who were found to have pneumonia and those who did not. It is estimated that the rate of false positive clinical judgement is 10-25% and that of the false negative is 20-40%.[55]

2. The existence of purulent secretions signifies the presence of tracheobronchitis but not of pneumonia. Tracheobronchitis alone does not appear to carry additional mortality risk and antibiotic therapy does not alter the clinical outcome in the absence of pneumonia.[21]
3. The appearance of a new infiltrate on chest x-ray cannot be relied upon as evidence of pneumonia in the ICU setting. Infiltrates may represent atelectasis, pulmonary embolism, heart failure or alveolar hemorrhage. Wunderink et also studied 69 patients of VAP who subsequently died and 24 of whom had autopsy-proven pneumonia. They found that no radiological sign either alone or in combination with clinical features had a diagnostic accuracy more that 68%.[56]
4. Even if the diagnosis is correct, bacteriological diagnosis can be misleading because of heavy colonization of the upper respiratory tract. Thus, recovery of bacteria does not mean infection of lung tissue. Hill et al found that culture from

lung biopsies correlated with only 40% of cultures from endotracheal specimen (ETA) obtained simultaneously.[58] For patients with histologically proven pneumonia, endotracheal aspirate sensitivity was 82% but specificity was only 27%. Fagon and Chastre found that only 1/3rd of the antibiotics proposed on the basis of ETA sampling were found to be appropriate. However, ETA qualitative culture has a high negative predictive value and in the absence of prior antibiotic exposure, a negative culture result virtually excludes VAP[45] (ATS). ETA culture is also an easy-to apply surveillance tool to detect potential pathogens and to direct empirical therapy in the event of the occurrence of VAP.

5. NP can be diagnosed more reliably if there is cavitation of a pulmonary infiltrate, or the same organism is found from respiratory secretions and blood or by lung biopsy or percutaneous needle aspiration .However, these conditions are seen only in a small minority and lung biopsy or needle aspiration are usually contraindicated in patients on mechanical ventilation.[54]

In a study they offered the following three important findings:

1. The accuracy of clinical criteria (infiltrates on the chest radiograph and two of the following: leukocytosis, fever, purulent secretions) for the diagnosis of pneumonia was reasonable (sensitivity 69%, specificity 75%) and the CPIS was not more accurate.
2. Non-invasive (ETA) and invasive (PSB, BAL, protected BAL) sampling techniques were not superior to these clinical criteria.

3. When microbiological results were added to clinical criteria, adequate diagnoses originating from the microbiological investigation which might have corrected false positive and false negative clinical judgements were countered by a similar proportion of inadequate diagnoses.[55]

Clinical Criteria for Presence of VAP:

The major clinical features suggestive of hospital acquired pneumonia are fever, purulent sputum and a new or changing pulmonary infiltrates on chest radiograph (CXR). Although the sensitivity of a clinical diagnosis of VAP is high, the specificity is low. Specificity is a problem in patients with pre-existing pulmonary infiltrates such as patients with ARDS. Although an abnormal CXR is essential, the diagnosis of VAP cannot be based on CXR alone. No single radiographic sign or combination of signs increases the likelihood of a diagnosis of hospital acquired pneumonia. There is poor agreement between readers and the interpretation of infiltration is affected by alteration of ventilator settings. The combination of any one clinical feature with an abnormal chest x- ray is associated with a high likelihood of hospital acquired pneumonia. Basing the diagnosis of VAP on a new or changing pulmonary infiltrate on CXR and one clinical feature of hospital acquired pneumonia has a good sensitivity but poor specificity. Increasing the number of criteria required increases the ability to distinguish hospital acquired pneumonia from other entities that mimic pneumonia clinically. If all 4 features are required for a positive diagnosis, however sensitivity drops to unacceptable levels.[55]

VARIOUS PROCEDURES FOR DIAGNOSING VAP: [57,58,59,60,61,62.]

Bronchoscopic sampling of the lower airways by using a protected specimen brush or bronchoalveolar lavage is currently the most accurate method of establishing a microbiologic diagnosis of VAP short of direct tissue examination. Quantitative or semi quantitative cultures are usually performed by using bronchoscopic specimens, and VAP is diagnosed when an appropriate threshold is exceeded. In most clinical studies, thresholds of 1000 or 10,000 colony-forming units (cfu)/ml for samples obtained with a protected specimen brush or with bronchoalveolar lavage, respectively, yielded the best operating characteristics. From a practical standpoint, quantitative cultures of 100–1000 or–10,000 cfu/ml for specimens from protected specimen brushing or bronchoalveolar lavage, respectively, should be considered positive for VAP. Quantitative tests of endotracheal aspirate specimens have acceptable overall sensitivity for identifying pathogens associated with VAP, and serial sampling in intubated patients may improve the likelihood of appropriate initial therapy. However, tests of endotracheal aspirates lack diagnostic specificity because of tracheobronchial bacterial colonization that occurs as a consequence of biofilm formation on the surface of endotracheal tubes. If available, quantitative-culture thresholds (≥ 100,000 cfu/ml) should be used with tracheal-aspirate specimens to increase specificity for the etiologic agent of VAP.

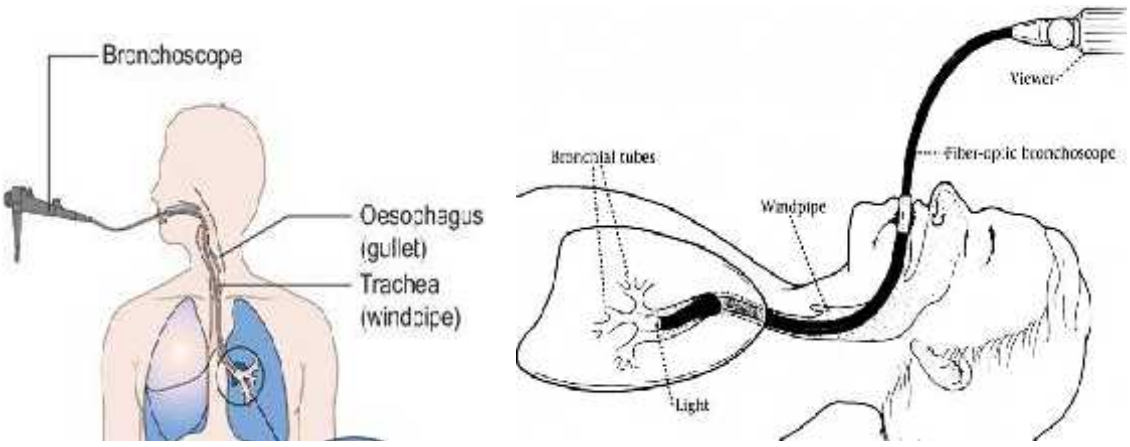


Fig 4: Continuous aspiration of subglottic secretions in preventing VAP.

INVESTIGATIONS

IMAGING:

The radiographic interpretation of pulmonary disease in ICU setting is challenging as on, abnormal immune response often alters the appearance of the chest radiographic findings of the pneumonias. Although portable chest X-ray are the most frequently performed radiographic examinations they are often of suboptimal quality despite recent advances in diagnostic imaging. Inadequate exposure, breathing pattern, and variations in techniques such as poor patient positioning, different degrees of inspiration and short focus film distance, all may compromise film quality. Many ICU patients who develop pneumonia show diffuse parenchymal opacifications with either interstitial, alveolar or mixed patterns. Resolution after therapy in these patients often is delayed. And it is difficult to determine the organism causing pneumonia from the radiographic appearance. The radiographic changes in aspiration pneumonia generally develop from 12 –24 hrs after aspiration. In supine patients, the abnormal opacities usually develop in the posterior aspect of the upper lobes and in the superior and posterior basal segments of the lower lobes.

Lobar type of pattern (non – segmental peripheral airspace, consolidation) is frequently caused by bacteria (commonly streptococcus pneumonia and Klebsiella pneumonia and others). Most hospital acquired pneumonia, begins as bronchopneumonia and is caused by gram positive and Gram negative bacteria.[63]

Other infections (e.g. Fungal, viral, rickettsial and tubercular) and noninfectious disorders (pulmonary thromboembolism, vasculitis, drug reactions) may also be responsible for similar shadows. Interstitial pneumonia is often viral. Radiologically

these findings appear as peribronchial cuffing, increased reticular markings or ill defined nodules.

Atelectasis is common in post-thoracic surgical and upper abdominal surgery but is also seen in other patients in ICU. Most commonly it is due to inspissated mucus plug which is due to excessive secretion, poor respiratory effort and poor cough reflex due to anesthesia and analgesics. The lobar atelectasis more commonly involves lower lobes with right lower lobe 5 times more commonly involved than the left. After lobar atelectasis evidence of volume loss appears within 18 to 24 hours and complete lobar atelectasis may not appear radiologically for days & weeks. CT is definitely more sensitive than plain X-rays but is not routinely available. It is helpful in diagnosing lung abscess, pleural effusion and pneumothorax more efficiently than X-rays.

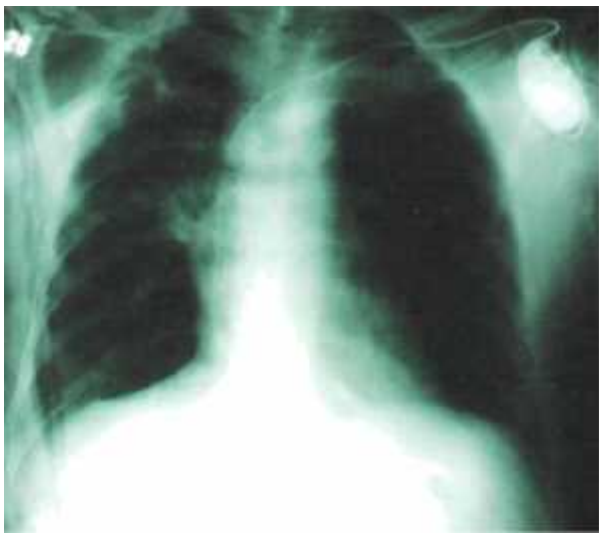


Fig no 5: Chest x-ray of IHD patient on admission

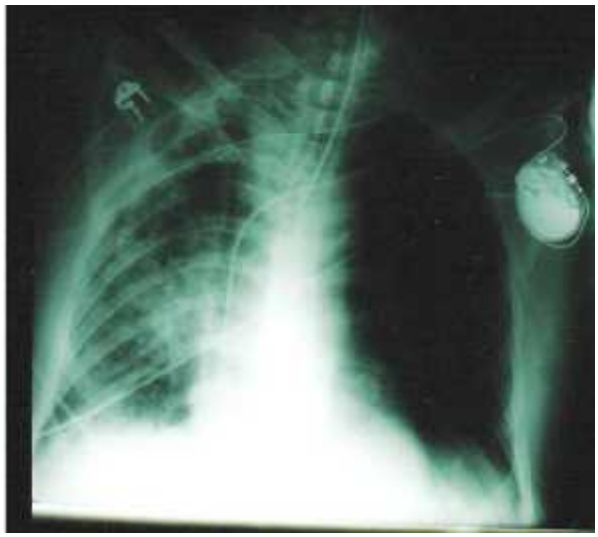


Fig no 6: Chest x-ray of the same patient with VAP on 5th day of Ventilator

Gallium scanning and Indium111 radio nucleotide labeled leucocyte imaging is often used as screening procedure for detecting area of infection. Although these scans are quite sensitive but they lack specificity and are best used for detecting extra thoracic foci of infection in these patients.[49]

Microbiologic diagnosis.[63]

The methods to obtain culture material from the lower respiratory tracts are:-

A. **Non invasive (minimally invasive)**

- Endotracheal aspirate – (standard)
- Simplest method

B. Non bronchoscopic techniques

1. Plugged telescoping catheter (PTC),

2. Protected bronchoalveolar mini-lavage (mini-PBAL), and

3. "Blind" Protected specimen brushing.

C. Invasive

Bronchoscopic techniques –

1. Protected specimen brushing (PSB)

2. BAL

Open Lung Biopsy

Quantitative culture techniques:

In view of the unreliability of qualitative microbiological evaluation of ETA and lower respiratory tract secretions, quantitative culture techniques were developed.

Since there is a bacterial burden in the respiratory tract even in the absence of active infection, cutoff values for bacterial concentration to separate infection from colonization were defined. Threshold values are difficult to determine as there is a large overlap between bacterial counts in the presence and absence of histologically proven pneumonia. Marquette et al have shown that quantitative culture of ETA secretions may have an acceptable diagnostic accuracy, when histological diagnosis was used as a "gold standard".[64] Some studies have shown that quantitative ETA cultures correlate well with the result of invasive diagnostic techniques . The consensus threshold values of quantitative culture are 106 cfu/ml for ETA secretions, 10^5 cfu/ml for BAL specimens and 10^3 cfu/ml for PSB material.

Bronchoscopic techniques [BAL] for the diagnosis of VAP:

The protected specimen brush [PSB] and Bronchoalveolar lavage (BAL) are the two techniques that have evolved for the diagnosis of VAP Both these techniques have developed on the premise that samples from the affected lower airways together with quantitative culture will improve the chances of obtaining uncontaminated secretions and the reliability of microbiological results. Several investigators believe that bronchoscopic sampling is the gold standard of care in the diagnosis and management of VAP[65]. However, many problems remain with respect to their proper use and interpretation that cast doubts regarding their routine use.

Due to the inaccuracy of the “clinical diagnosis and overuse of antibiotics has led to use “specialized” diagnostic procedure for quantitative culture of the specimens obtained from the lower airways. Using this bronchoscopic BAL was developed to

obtain distal lung samples by wedging the bronchoscope in the distal third of the lung and lavaging with saline to obtain microbiologic samples for quantitative analysis.

Bronchoscopic BAL has been in use since 1988. The amount of liquid instilled into the lung for specimen retrieval varies from 130 to 150 ml; with the first sample being discarded. The sensitivity of quantitative BAL is 42 to 93% with a mean of 73%. Specificity is 45 to 100% with a mean of 82%. This procedure is relatively safe with a major risk of desaturation for several hours after the procedure.

Advantages:

- Specific affected area of the lung can be visualized and sampled.
- More accurate than sputum or tracheal aspirates.
- May enable physician to identify non-infectious lesions.
- Detects intracellular organisms in BAL cultures quickly and specifically with highly positive predictive value.

Disadvantages:

- More aggressively invasive than some of the other methods.
- Reduced positive end expiratory pressure (PEEP) during procedure.
- Limited to larger sizes of endotracheal tubes because of the diameter of the bronchoscope.
- Additional personnel needed to assist during procedure.
- It Must be performed by physician (usually a pulmonologist).
- Sterilization of the scope is costly, technically difficult, and time consuming (spread of infection due to inadequate sterilization may occur).
- Expensive.

Table–4: Guidelines for bronchoscopic procedures for the diagnosis of VAP.

- Endotracheal tube size should be > 1 .5mm larger than external diameter of the bronchoscope ventilator settings: FiO2 at 100%
- Inspiratory flow rate <60L/min.
- Titrate ventilator settings to maximize exhaled tidal volume.
- Sedatives with or without a short acting paralytic agent
- Monitor pulse oximetry, ECG and exhaled tidal volume during procedure.

Protected Specimen Brush (PSB):

The protected specimen brush technique for the diagnosis of pneumonia has been used for 20 years. This technique was initially described by Wimberley et also, who using an in vitro model of upper airway colonization showed that protection against contamination was provided by a sampling device protected by a double sheathed plugged catheter. The methodology was later standardized by Meduri et. Since the bronchoscope becomes contaminated by the bacterial flora in the endotracheal tube and proximal airways during its introduction, proper technique is vital to the reliability of the results.

This bronchoscopic technique uses a sample collection brush (protected by a sheath) inside the scope channel until the suspect portion of the lower airway has been reached. The brush is then extended into the desired specimen and withdrawn.

Sensitivity of the PSB is from 36 to 95% and specificity 50 to 100%. Because the sample is small, sampling is often delayed to increase the probability of obtaining infected tissues. No studies have shown BAL or PSB being superior to the other as BAL is more sensitive and PSB is generally more specific.

In 1984, Chastre et al[66] compared the results of PSB samples with histopathology and quantitative cultures of lung biopsy specimen obtained at the same time. Using a diagnostic threshold of 103 cfu/ml for quantitative cultures the PSB sampling technique identified every case of histologically proven pneumonia. The sensitivity of PSB was 100% the specificity was 80%, the positive predictive value was 43% and the negative predictive value was 100%. The values of the PSB technique thereafter has been extensively evaluated in both human and, animal studies including those where its accuracy was determined using the "gold standard" of cultures from lung biopsies. The overall accuracy based on pooled results of 18 studies is high, with a sensitivity of 89% and specificity of 94%.[65]

In the study by Rouby et also, autopsy findings of lung histology and quantitative lung cultures were correlated with BAL data collected in living patients within 24 hours of autopsy. Even in those lobes with histopathologically proven pneumonia only 55% had a bacterial concentration more than 103 cfu/gm of tissue. In 39% of the patients whose lung tissue contained <103 cfu/gm there was histologic evidence of pneumonia or lung abscess. They also identified the "bronchiolitis" lesion that may be the earliest and treatable stage of pneumonia. This stage of pneumonia may be undiagnosed on account of low organism burden and the existing threshold values for bacteriologic diagnosis. The same holds good that the accepted threshold value of

103cfu/ml cannot identify resolving pneumonia. It is also important that no new antibiotic is introduced .at the time of sampling as it leads to an unacceptable level of false negative results. False negative values can also result if sampling is not done from the affected area.[67]

However, it remains that if properly performed and carefully interpreted, PSB samples are able to identify the presence of pneumonia and the aetiologic agents when combined with quantitative culture technique.

Advantages:

- Specific area of the lung can be visualized and sampled.
- May enable physician to identify non-infectious lesions.
- Highly specific.
- More accurate than sputum or tracheal aspirates.

Disadvantages:

- More aggressively invasive than other pulmonary specimen collection methods.
- Limited to larger endotracheal tubes due to the diameter of the bronchoscope.
- Additional personnel needed.
- Pneumothorax may result if brush is mishandled.
- Reduced PEEP during procedure.
- Must be performed by pulmonologist.
- Sterilization of the scope is costly and technically difficult with failure reported.
- Expensive.

Table -5: Guidelines for the PSB technique

- Perform suction through the endotracheal tube prior to bronchoscopy.
- No suction is performed while introducing the bronchoscope.
- No lidocaine is injected through the suction channel of the bronchoscope
- The bronchoscope tip is advanced into the involved area as seen on a chest x-ray/fluoroscopy.
- A triple-lumen protected brush is advanced 2 cms out of the FOB
- The inner cannula protruded to eject the gelatin plug into the bronchus while keeping the tip of the protected brush in the field of vision.
- The inner cannula is containing the brush is then advanced into a bronchial segment leading into the involved area.
- The brush is then advanced out of the inner catheter and turned several times to obtain a specimen.
- After sampling, the brush is retracted into the inner cannula, and the inner cannula into the outer cannula and entire bronchoscope is removed.
- The outer sheath is cleaned with 70% alcohol, cut with sterile scissors, and discarded.
- The brush is then re-advanced, cut with sterile wire clippers into a container with 1 ml of sterile saline.
- The specimen should be sent for quantitative culture within 15 minutes.

Bronchoalveolar Lavage:

In this technique the bronchoscope is wedged in the airway of the lung to be sampled, and the lavage fluid is introduced and aspirated in a standardized manner**.** BAL samples approximately 10 million alveoli and thus represents a larger area than PSB. However, as with the PSB technique there can be contamination by tracheobronchial secretions.

Analysis of postmortem lung biopsy has shown that BAL fluid cultures to be as useful as PSB cultures. When the results of 11 studies evaluating BAL fluids from a total of 435 ICU patients with suspected VAP were pooled, the overall accuracy of this technique was similar to that of PSB[68]. Therefore it is not necessary to perform both BAL and PSB in the same patient[69]. BAL is easier to apply, less expensive and does not require the specialized brush. It also allows a larger area of the lung to be sampled.

Table no 6: Guidelines for BAL technique

- Perform suction through the endotracheal tube prior to bronchoscopy.
- No suction is performed while introducing the bronchoscope.
- No lidocaine is injected through the suction channel of the bronchoscope.
- The bronchoscope is wedged in the segmental bronchus of the lobe that is affected.
- Three aliquots of 40 ml sterile saline are infused through the working channel of the bronchoscope.
- Suction is applied and the first aliquot is discarded or saved as bronchial lavage.
- The second and third aliquots of aspirate are saved as bronchoalveolar lavage.
- The specimen should be sent for quantitative culture within 30 minutes.

Post Procedure Care for Bronchoscopic BAL & PSB:

1. Hypoxemia should be avoided during and immediately following the BAL procedure.
2. Low flow oxygen therapy for 30 minutes post procedure. Patients receiving mechanical ventilator support may benefit from increased FIO2.
3. Oxygen saturation and pulse rate monitoring with a pulse oximeter may be desirable.
4. Slight hemoptysis may occur in some patients during the first 24 hours after a BAL procedure. Additional clinical assessment is indicated if hemoptysis is significant or prolonged.

Complications of bronchoscopic techniques for VAP:

The most common complication of bronchoscopic PSB and BAL in ventilated patients is hypoxia during the procedure. This is particularly so in the presence of ARDS or patient's restlessness with consequent dyssynchorony with the ventilator. The hypoxemia may persist for up to 2 hours after the procedure. Other complications include pulmonary hemorrhage and pneumothorax with PSB, fever related to the release of cytokines and transient worsening of pulmonary infiltrates. In general the risk of complications increases as the duration of the procedure increases.

Table-7: High-risk for complications of bronchoscopic procedures

- Pa02 > 70 mmHg on Fi02 > 70%.
- PEEP> 15cm H_20.
- Bronchospasm
- Recent (<48h) Myocardial infarction.
- Unstable arrhythmia.
- Hypotension or receiving vasopressor therapy
- Platelet count < 20,000/cmm
- Moderate risk for complications
- PEEP> 1Ocm H_20
- PT or APTT > 1.5 times control
- Raised ICP.

Non Bronchoscopic distal airways sampling:[70]

The endotracheal tube bypasses the proximal airways and allows catheters to be passed blindly to sample secretions from distal airways. The potential advantages of non bronchoscopic sampling techniques are less invasiveness, less cost, absence of contamination by the bronchoscopic channel, and less procedure- related risks to the patient. It does not require the special skills as with bronchoscopy and it can be passed through small endotracheal tubes. However, sampling errors can be inherent in a blind technique where the airways are not visualized.

The non bronchoscopic techniques include:

1. Plugged telescoping catheter (PTC).

2. Protected bronchoalveolar mini-lavage (mini-PBAL), and

3. "Blind" PSB.

1. Plugged telescoping catheter (PTC):

It can be inserted blindly into the lung bronchus, and wedged into position. The inner catheter is then pushed 2 to 3 cm beyond the tip of the outer sheath and 3 brief aspirations applied. One ml of saline solution is then flushed through the inner catheter and collected in a sterile vial and distal segment of the catheter is aseptically transected and collected in the same vial for microbiological processing.

2. Protected bronchoalveolar mini-lavage (mini-PBAL):

Non-bronchoscopic BAL (mini BAL) specimens may also be obtained using a flexible catheter inserted via the endotracheal tube into the main bronchus of the affected lung. Lavage is performed as for bronchoscopic BAL and a specimen obtained for culture. This is blind technique leading to a false positive result in a heavily colonized patient or a patient with bronchitis.

3. "Blind" PSB:

The PSB is a double-lumen brush system that avoids upper airway contamination of the sample. The brush is introduced via the endotracheal tube into the main bronchus of the affected lung with infiltrates seen on chest X-ray. The inner cannula is then advanced further revealing the brush which is turned several times to obtain a specimen. Marik and Brown compared the results of "blind" PSB catheter with

bronchoscopically directed procedure in 55 patients, who had not received prior antibiotic therapy. The bronchoscopic PSB was taken as the "gold standard" and based on this premise there was a sensitivity of 86% and a specificity of 85%.

In a study in which procedures were conducted in 27 patients on mechanical ventilation who died, protected mini-BAL and simple distal protected suction were compared with postmortem biopsies**.** Both techniques provided a specificity of 100% and 86% respectively with a sensitivity of 78%.

The overall concordance between the bronchoscopic and non bronchoscopic techniques is around 80% which would mean the diagnosis could be missed by non bronchoscopic techniques especially when the pneumonia affects the upper lobes or the left lung[68]. Therefore the bronchoscopic methods are perhaps the preferred technique whenever the option is available and the patient's condition is stable.

Invasive V/s Noninvasive diagnostic strategies:

Despite voluminous literature available the controversies related to diagnostic and management strategies remain. This is because we now recognize that there is no reference point that can be regarded as "gold standard" against which the results can be validated[71]. The value of these various invasive techniques over clinical assessment and endotracheal aspirate is still debated[72]. Thus invasive strategy can no longer be insisted upon as the standard of care. Invasive techniques are not routinely required and it’s routine use is not justified.[73]

The difficulties with most studies on the diagnostic tools for VAP are that the criteria for suspected pneumonia are based on the nonspecific criteria of fever, leukocytosis, purulent secretions and infiltrates on chest x-ray. Quantitative scoring would

reflect the degree of likelihood of that suspicion. A clinical pulmonary infection score (CPIS) was used by incorporating six different clinical variables, to determine the likelihood of VAP.

When this score was used prospectively, there was acceptable correlation with diagnosis, by BAL with quantitative cultures. This highlights the value of a careful clinical evaluation before resorting to more complicated sampling techniques.

The argument in favor of bronchoscopic techniques is that they enhance the accuracy of aetiologic diagnosis. It is well established that inappropriate initial antibiotic therapy is associated with higher mortality.

Therefore it is crucial that clinical recognition and initiation of empiric antibiotics is not delayed. Accurate aetiologic diagnosis enables suitable modifications of antibiotics later. Despite extensive research, there is no clear evidence that the type of diagnostic tool, invasive or noninvasive changes outcome. Several studies have shown that mortality or morbidity does not change whether invasive or noninvasive techniques were used. Quantitative endotracheal aspirates (QEA) when compared with PSB and BAL resulted in similar mortality figures in a randomized, open study by Sanchez-Nieto[74]. In this pilot study the impact of bronchoscopy only led to more frequent antibiotic changes. Also, QEA cultures did not miss any microorganisms detected by PSB and/or BAL. Similar findings that QEA is as reliable as bronchoscopic techniques were reported by several others. The advantage of QEA is its simplicity and easy repeatability. All these studies were on small populations and importantly antibiotics were continued in all irrespective of the quantitative culture results.

Thus the potential advantages of diagnostic accuracy and salutary effects of withholding unnecessary antibiotics were not realized. However it is clear that techniques using quantitative cultures, whether invasive or noninvasive are superior to empiric treatment in terms of clinical outcome

Tracheal Aspirates:

Niederman[74] and others have recommended the use of tracheal aspirates before subsequent growth of the specimen or as soon as VAP is suspected by CPIS.

Gram stain can be used to make early decisions concerning which broad range antibiotic to use for treatment. Sensitivity and specificity vary widely when analyzed quantitatively. However, tracheal aspirates can easily be contaminated with colonizing pathogens rather than the culprit causing the VAP.

Bacteria from the biofilm on the inside of the endotracheal tube may contaminate the sample. Studies by both Neiderman[74] and we recommend confirmation with an invasive BAL or PSB. They opine that all clinical information should be used to guide clinical decisions (i.e., CPIS, tracheal aspirates, gram stain, BAL or PSB) without the extended necessity of using broad spectrum antibiotics.

Advantages:

- Easily performed at the bedside in the ICU.
- May be performed by Respiratory Therapists or Nurses.
- Inexpensive.

Disadvantages:

- Specimen easily contaminated.
- Low specificity (38 to 100%).
- Low sensitivity (14 to 100%).
- Can cause incorrect selection of antibiotic treatment.

Table- 8: Sensitivity and specificity of procedures for diagnosing NP & VAP

Method	Sensitivity specificity*	Comment
Bronchoscopic Protracted Specimen brush	33% - 100% sensitivity 50%-100% specificity Applies to presence of pneumonia	Assessment limited by absence of gold standard
Bronchoscopic BAL	50%-90% sensitivity 45%-100% specificity Applies to presence of pneumonia	No gold standard
Non bronchoscopic BAL	Similar to bronchoscopic methods, with close to 90% agreement when both done in the same patient	No gold standard
Quantitative Endotracheal Aspiration	38%-82% sensitivity 72%-85% specificity Up to 100% sensitive with specificity as low as <20% for the	No gold standard

	diagnosis of pneumonia; sensitivity still high (>90%) for presence of etiologic pathogen	
CPIS of at least 6	Sensitivity of up to 90% for presence of pneumonia	May help to guide discontinuation of antibiotics after 3 days if score starts and remains low.

* All cultures are less accurate if patient is on antibiotics during testing. BAL, bronchoalveolar lavage: CPIS: clinical pulmonary infection score.

GENERAL PREVENTIVE STRATEGY AND NONPHARMACOLOGIC STRATEGIES:[75]

Effective Hand Washing and the Use of Protective Gowns and Gloves:

The use of protective gowns and gloves has also been found to reduce the rate of acquired nosocomial infections. However, their use appears to be most effective when directed at specific antibiotic-resistant pathogens, such as vancomycin-resistant enterococci.

Thorough hand washing as the most effective means of preventing infection, compliance by ICU staff is inadequate. Use of hand washing disinfectants may achieve better compliance and prevention. Disposable gloves and gowns may also prevent cross infection.

Semi recumbent Positioning of Patients:

Patients should be placed in a semi recumbent position i.e. their upper body elevated for as long as possible rather than supine. Accidental self extubation with consequent reintubation should be avoided through appropriate analgesia/sedation and physical restraints. Reintubation performed with the patient in semi recumbent supine position may also be beneficial.

Avoidance of Large Gastric Volumes:

The stomach, upper airway, teeth, artificial airway, ventilator-circuit condensate, and nasal sinuses have all been implicated as potential sources of aspirated secretions. Gastric over distention should be avoided by reducing the use of narcotics and anticholinergic agents, monitoring gastric residual volumes after intragastric feedings, using agents that increase gastrointestinal motility (e.g., metoclopramide) and

when necessary, supplying enteral nutrition through small-bore feeding tubes directed into the small bowel instead of the stomach.

Oral (Non-Nasal) Intubation:

Prolonged nasal intubation (for more than 48 hours) should be avoided because of the association between nosocomial sinusitis and ventilator-associated pneumonia.

Nosocomial sinusitis may predispose the patient to pneumonia through the aspiration of infected secretions from the nasal sinuses. Therefore, the preferred route of intubation is the oropharynx.

Routine Maintenance of Ventilator Circuits:

Ventilator circuits should also be monitored regularly so that accumulated condensate in the tubing can be removed. A high concentration of pathogenic bacteria is found in condensate fluid, which may cause pneumonia if aspirated. Several clinical studies found no benefit from routinely changing ventilator-circuit tubing.

Continuous Subglottic Suctioning:

The secretions that pool above inflated endotracheal-tube cuffs may be a source of aspirated material and thus ventilator-associated pneumonia. Endotracheal tubes with a separate dorsal lumen above the cuff to suction pooled secretions from the subglottic space are available.

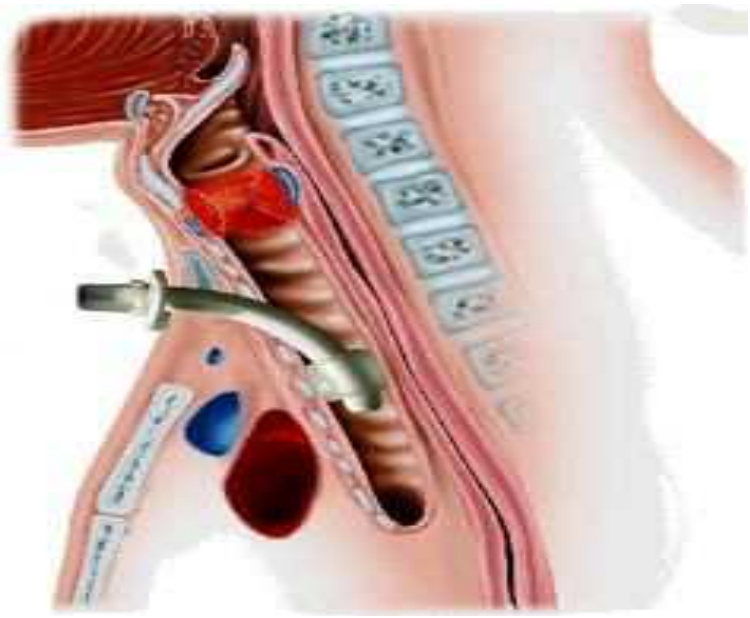


Fig no 7: Continuous subglottic suctioning

Type of Suction Catheter and Its Replacement:

Two types of suction-catheter systems are available: the open, single-use system and the closed, multiuse system. The risk of nosocomial pneumonia appears to be similar with both systems.

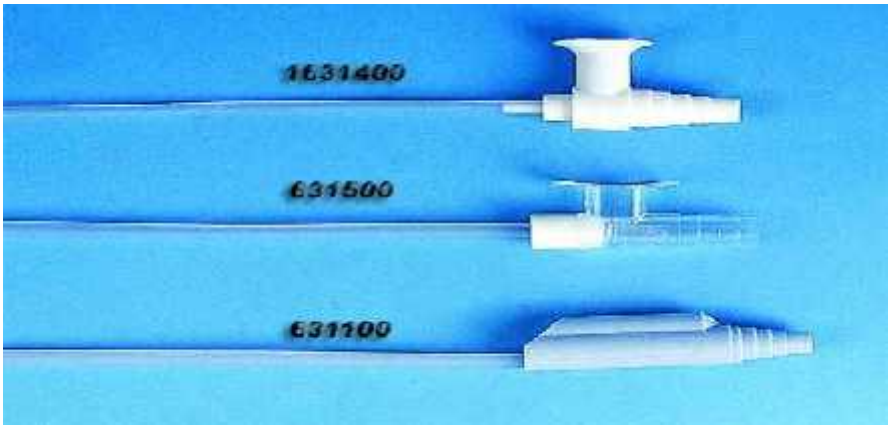


Fig no 8: Types of Suction Catheters

Humidification with Heat and Moisture Exchangers:

Heat and moisture exchangers reduce the incidence of ventilator-associated pneumonia by minimizing the development of condensate within ventilator circuits. They are cost-effective for providing humidification to patients receiving ventilation if there are no contraindications.

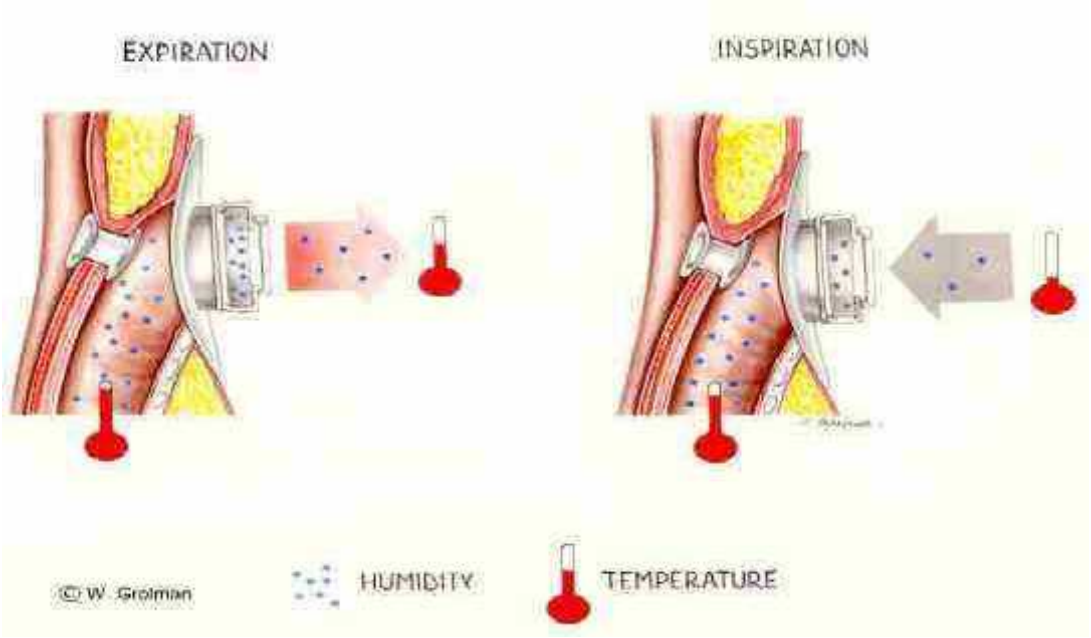


Fig no 9: Humidification with Heat and Moisture Exchangers

Postural Changes:

Kinetic therapies that change the patient's position by means of specialized beds or medical devices are hypothesized to help prevent ventilator- associated pneumonia by improving the drainage of pulmonary secretions.

TREATMENT

The current treatment of NP relies on appropriate antimicrobial therapy and inadequate antibiotic therapy is associated with increased mortality rates.

However adequate treatment can be a challenge due to the range of organisms encountered the high incidence of resistant organisms & frequency of polymicrobial nature of nosocomial infections.

Administration of Antibiotics:

Previous exposure to antibiotics is an important risk factor for ventilator associated pneumonia because of the presence of antibiotic-resistant bacteria. Eliminating or reducing the unnecessary use of antibiotics should be the primary goal in preventing antibiotic-resistant nosocomial infections.

Combination Antibiotic Therapy:

The routine use of combination antibiotic therapy has been advocated as a means of reducing the subsequent emergence of bacterial resistance.

Prophylactic Antibiotic Therapy:

The use of aerosolized antibiotics for the prevention of ventilator-associated pneumonia has been abandoned because of its lack of efficacy and the subsequent emergence of antibiotic-resistant infection. The use of broad-spectrum parenteral antibiotics for the prevention of ventilator-associated pneumonia is also not recommended, because of the increasing frequency of antibiotic resistance.

Chlorhexidine Oral Rinse:

Chlorhexidine has been shown to be effective in the control of ventilator-circuit colonization and pneumonia caused by antibiotic-resistant bacteria. Oropharyngeal

decontamination with chlorhexidine solution has also been shown to reduce the occurrence of ventilator-associated pneumonia. Trials regarding administration of immunoglobulins and vaccines for prevention of VAP have been tried but not found to be effective.

Antibiotic issues:

Several specific issues relating to antibiotic selection were considered, including the expected efficacy of an appropriate therapeutic choice. Specific pharmacologic features of antimicrobial agents should also be considered, including cost. The penetration of antibiotics to the site of infection is important, but it remains unclear whether concentrations in bronchial secretions or in epithelial lining fluid are most relevant for predicting efficacy. Some agents penetrate into respiratory secretions better than others. Aminoglycosides have relatively poor penetration, while fluroquinolones can achieve better concentration in bronchial secretions. Agents such as the aminoglycosides and quinolones are bactericidal in a concentration dependent fashion. In addition these agents have a prolonged post antibiotic effect (PAE), allowing them to suppress bacterial growth even after their concentrations are below target level. Other agents such as vancomycin and the beta-lactams are also bactericidal but act in a time-dependent rather than in a concentration-dependent fashion. No or a very short post antibiotic effect against gram negative bacilli, is seen with beta-lactam antibiotics (penicillin's, cephalosporin's, aztreonam). One exception is the beta-lactam carbapenums antibiotic's such as impenum.

Generally speaking empiric therapy should be commenced once NP is suspected and altered as microbiologic data become available. The ATS has produced a consensus statement suggesting various treatment strategies, based on the division of patients into groups according to the severity of their disease & the presence of associated risk factors.

- ✓ Mild to moderate infection and without significant risk factors or / with severe, but early onset infection, mono therapy is generally considered adequate in these patients.
- ✓ Mild to moderate infection with risk factors. These patients are more likely to be infected by more virulent pathogens including pseudomonas aeruginosa and additional antibiotics coverage is needed.
- ✓ Severe infection with risk factors many of these patients will require combination antibiotic therapy.

There are few data assessing the optimal duration of therapy and this must be evaluated on an individual patient basis according to clinical response. Antibiotics are frequently given for at least 7 days but in certain patients for eg., those with multilobe involvement ,cavitation or necrotising gram negative infection, treatment may need to be prolonged for 14 – 21 day**.**[76]

Table-9: General framework for empirical initial antimicrobial treatment of VAP (Based on the ATS guidelines)

Ventilated patients	**Class of antimicrobial agents**	**Agents and dosages**
Early onset, no risk factors	Cephalosporin – II or Cephalosporin – III or Aminopenicillin/β lactamase inhibitor or Third or fourth G Quinolone or Clindamycin/ Aztreonam	Cefuroxime 3 x1.5g Cefotaxime 3 x 2 g or Ceftriaxone 2 x 1 g Amoxicillin/Clavulanic acid 3 x 2.2 g Levofloxacin 2 x 500mg Moxifloxocin 1 x 400mg Clindamycin 3 x600mg Azteonam 3 x 2g
Late onset, no risk factors	Quinolone or Aminoglycoside + Antipseudomonal β-lactam/ β-lactamase inhibitor or Ceftiazidime or Carbapenems +/- Vancomycin*	Ciprofloxacin 3 x400mg Gentamicin 5-7mg/kg Tobramycin 5-7mg/kg Amikacin 1x15mg/kg Piperacillin/ Tazobactam 3x4.5g Ceftazidime 3x2g Imipenem/Cilastatin 3x1g Meropenem 3 x1g Vancomycin 2x1g

Early or late onset, risk factors	Risk factors for P.aeurginosa, see late Onset Risk factors for MRSA, vancomycin* Risk factor for legionellosis; macrolide	Vancomyin 2x1g Erythromcyin 4x1g OR Azithromycin 1x500g OR Clarithromycin 2x500g OR Levofloxacin 2x500mg OR Moxifloxacin1x400mg

* Consider also linezolid and synercid.

PREVENTION

The two important processes involved in the pathogenesis of hospital acquired pneumonia are

- ✓ Bacterial colonization of the aero digestive tract and Aspiration of the contaminated secretions into the lower airway.

Therefore, preventive strategies for hospital acquired pneumonia are directed at reducing the bacterial burden colonizing the aero digestive tract, and decreasing the occurrence of aspiration.[77]

Reducing the bacterial burden colonizing the aero digestive tract:

1. Reducing the use of antibiotics:

VAP occurring late during mechanical ventilation are more likely to be due to the high risk multidrug resistant bacteria such as pseudomonas aeruginosa and methicillin-resistant staphylococcus aureus.[77] VAP due to antibiotic resistant pathogens are associated with greater hospital mortality and longer lengths of hospital stay than those due to antibiotic sensitive bacteria**.**[78]

Therefore, reducing the unnecessary use of antibiotics should be the primary objective in order to prevent the more serious forms of VAP. The recent trends in treatment strategies reflect this approach (see preceding section "treatment strategies). Changing or rotating antibiotic class periodically in an ICU may also reduce incidence of antibiotic resistance.[77]

2. Stress ulcer prophylaxis:

Critically ill patient on ventilator support frequently receives antacids and H2 blockers to prevent the occurrence of stress ulcers and gastrointestinal bleeding. Bacterial colonization of the stomach is encouraged by agents that increase the gastric pH and thereby promote the occurrence of VAP. Sucralfate may be less likely to increase the risk of pneumonia, but may, however be less efficacious in preventing hemorrhage.[79] The routine use of H2 blockers should be avoided, except where the risk of gastrointestinal bleeding is high.

3. Selective digestive decontamination (SDD):

Most studies have shown that SDD reduces the risk of pneumonia. Sanchez Garcia et al[80] showed that SDD reduced the incidence of VAP (11 % Vs 29%, $p<0.001$). However, there are the potential risks of antibiotics resistance and toxicity, and the absence of demonstrable effect on mortality has prevented widespread acceptance.[77]

4. Noninvasive ventilation:

Noninvasive ventilation by avoiding conduit placement in the airway has been associated with reduced rates of VAP[81] and should be considered wherever applicable. Excessive sedation increases risk of respiratory complications.

5. Infection control programs employing several interventions:

Interventions aimed at controlling both colonization of the aero digestive tract with pathogenic bacteria and aspiration have been successful in preventing VAP and are also cost effective.[82] Chemicals that block genes in bacteria that form biofilms, antibodies that block fibronectin-building protein adhesion bacteria, and the use of

specialized coating that block bacterial adherence are the future directions in the area of prevention.

Treatment Infection control measures in ICUs

Identify reservoirs:

1. Colonized & infected patients.
2. Environmental contamination.

Halt transmission among patients:

1. Improve hand washing and asepsis.
2. Barrier precautions (Gloves, gown) for colonized & infected patients.
3. Separate susceptible patients.
4. Close unit to new admissions if necessary.

Halt progression from colonization to infection:

1. Discontinue compromising factors when possible e.g., extubate, remove nasogastric tube and use noninvasive ventilation in appropriates patients.
2. Patients to be nursed in semi recumbent position rather than supine position - Kinetic beds.
3. Continuous subglottic suctioning of secretions that pool above ET cuff in mechanically ventilated patients.
4. Avoid excessive sedation in mechanically ventilated patients.[82]
5. To use sucralfate instead of antacids and H2 blockers.

Modify host risk factors:

1. Treat underlying disease & complications.
2. Nutritional support.
3. Immunomodulation.
4. Control antibiotic use.

The APACHE 3 (Acute Physiology, Age, Chronic Health Evaluation) Prognostic System:[83]

Risk Prediction of Hospital Mortality for Critically Ill Hospitalized Adults:

The objective of this study was to refine the APACHE methodology in order to more accurately predict hospital mortality risk for critically ill hospitalized adults. Data was collected data from 17,440 unselected adult medical and surgical intensive care unit (ICU) admissions at 40 US hospitals. They analyzed the relationship between the patient's likelihood of surviving to hospital discharge and the following predictive variables: major medical and surgical disease categories, acute physiologic abnormalities, age, preexisting functional limitations, major comorbidities and treatment location immediately prior to CCU admission.

The APACHE 3 prognostic system consists of two options:

1. An APACHE 3 score, which can provide initial risk stratification for severely ill hospitalized patients within independently defined patient groups.
2. An APACHE 3 predictive equation, which uses APACHE III score and reference data on major disease categories and treatment location immediately prior to CCU admission to provide risk estimates for hospital mortality for individual CCU patients. APACHE 3 score ranges from 0 to 299. The

development of APACHE III was based on the association between acute changes in a patient's physiologic balance and short-term risk of death.

APACHE lll Scoring:

Have the following parameters

1. Age

2. Chronic health

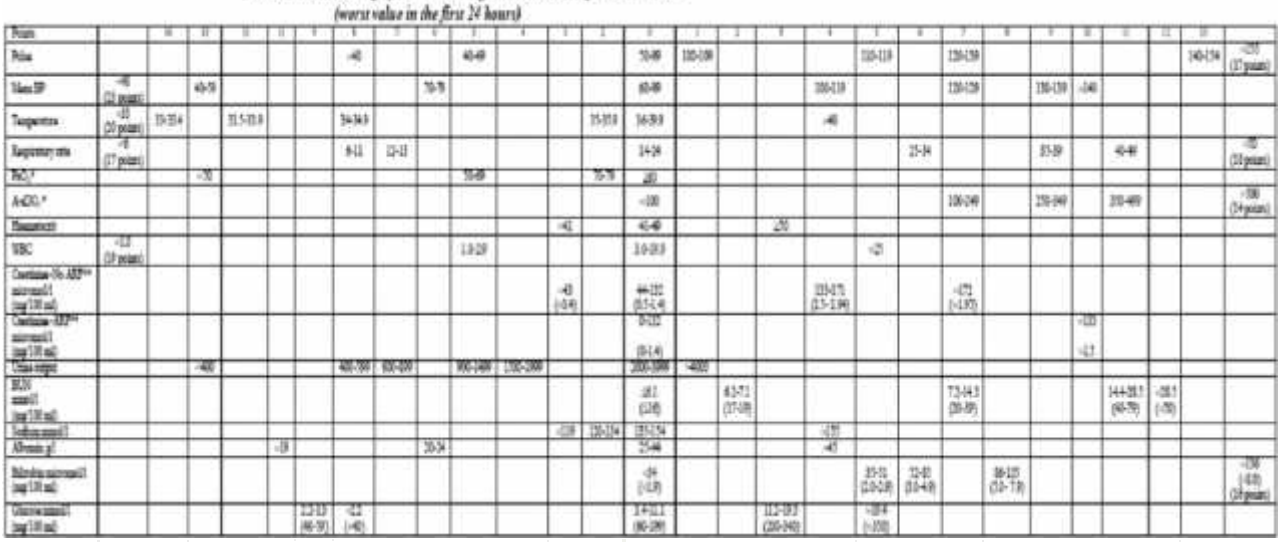
3. Acute physiologic abnormalities (most initial 24 h):

- ✓ Pulse rate.
- ✓ Mean blood pressure.
- ✓ Temperature.
- ✓ Respiratory Rate.
- ✓ PaO2/P(A-a)02.
- ✓ Hematocrit.
- ✓ White blood cell count.
- ✓ Creatinine.
- ✓ Urine output.
- ✓ Blood urea nitrogen.
- ✓ Sodium.
- ✓ Albumin.
- ✓ Bilirubin.
- ✓ Glucose.
- ✓ Acid-base.

4. Neurologic status

TABLE NO 10: APACHE SCORINGS DIAGRAMS AND CHARTS

APACHE III Scoring System – Vital Signs and Laboratory Abnormalities
(worst value in the first 24 hours)



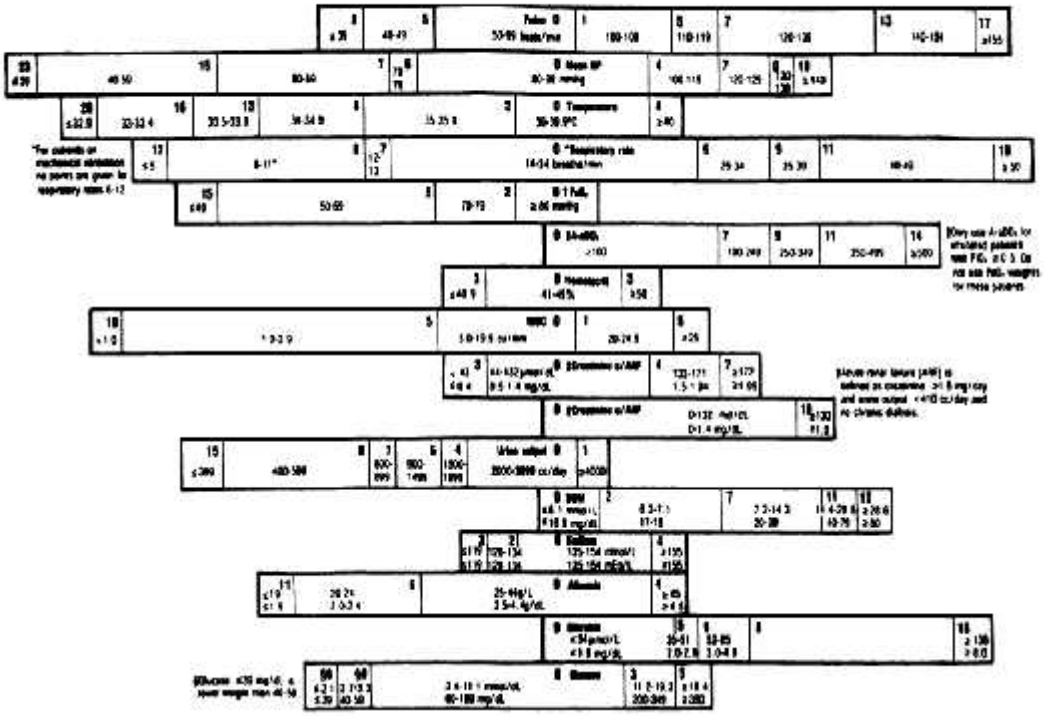
* For non-intubated patients or intubated patients with $FiO_2 \leq 0.5$. For intubated patients with $FiO_2 > 0.5$ use A-aDO_2.

** Acute renal failure (ARF) defined as creatinine ≥1.5 mg/100 ml, urine output <410 ml/day and no chronic dialysis.

APACHE III points for Age and Chronic Health Evaluation

	Points
Age, years	
<45	0
45-59	5
60-64	11
65-69	13
70-74	16
75-84	17
>84	24
Co-morbid condition AIDS	23
Hepatic failure	16
Lymphoma	13
Metastatic cancer	11
Leukemia/multiple myeloma	10
Immunosuppression	10
Cirrhosis	4

APACHE III PHYSIOLOGIC SCORING FOR VITAL SIGNS AND LABORATORY TESTS



METHODOLOGY

MATERIALS AND METHODS:

SOURCE OF DATA:

- The study will be conducted on patients getting admitted in Intensive Care Unit of BLDEU'S Shri B M PATIL medical college hospital and research centre, Bijapur.
- Period of study will be from January2015 to June 2016.

METHOD OF COLLECTION OF DATA:

This study is a cross-sectional study.

It is classified into 2 categories:

1) Early onset VAP: Ventilator associated pneumonia occurring within 4 days of endotracheal intubation and initiation of mechanical ventilation.
2) Late onset VAP: Ventilator associated pneumonia occurring after 4 days of endotracheal intubation and initiation of mechanical ventilation.

All the patients getting admitted to ICU and fulfill the criteria of VAP as mentioned below are thoroughly examined clinically and radiologically for the presence of pneumonia followed by which endotracheal aspirate is cultured to detect the presence of bacteria thus completing bacteriological part of examination.

Data is collected

- By detail history
- By detail examination
- By required investigations including routine and specific.

Specific Tests:

a) Total and differential leucocyte count.

b) Chest X-ray

c) Blood Culture

d) Endotracheal aspirate for culture and sensitivity.

e) Arterial blood gas analysis

Routine Tests:

a) Complete blood count

b) ESR

c) Urine examination

d) Random blood sugar

e) HbA1c

f) HIV

g) Blood Urea and Serum creatinine

h) Serum Electrolytes

INCLUSION CRITERIA:

Patient included in this study are those who are on mechanical ventilator for more than 48 hours and should fulfill one of the criteria mention below.

a) Temperature> 38.2 C or < 36 C

b) Leukocytosis>12000/cmm or Leucopenia <4000/cmm.

c) Evidence of pneumonia based on Clinical, respiratory secretions and radiographic features.

EXCLUSION CRITERIA:

a) Patients who develop respiratory infection in less than 48 hours on mechanical ventilator, i.e. pneumonia acquired within 48 hours after hospital admission as a consequence of emergency intubation, aspiration due to decreased level of consciousness and coma, or cardiopulmonary resuscitation are excluded from definition of VAP.

b) Patients getting admitted to ICU with respiratory infection.

c) Patients getting discharge from ICU within 48 hours of admission.

d) Patients who died within 48 hours of ICU admission.

SAMPLE SIZE:

Time period of study is from January2015 to June 2016. With incidence of 5-67% of ventilator associated pneumonia, at 95% confidence level and 20% allowable error, the sample size is 47(≅50).

$n = Z\alpha^2 \times p \times (100-p)/L^2$

$Z\alpha$ = Z value at α level = 95%

P = incidence rate of VAP = 67%

L = Allowable error = 20%

Hence minimum 47(≅50) cases of ventilator associated pneumonia will be included in the study to co-relate pneumonia is due to mechanical ventilator.

STATISTICAL ANALYSIS:

- ✓ Data will be analysed with
    a) mean +_SD
    b) Diagrams
- ✓ Results will be compared by Chi square test.

All characteristics were summarized descriptively. For continuous variables, the summary statistics of N, mean, standard deviation (SD) were used. For categorical data, the number and percentage were used in the data summaries. Chi-square (χ^2)/Fisher exact test was employed to determine the significance of differences between groups for categorical data. If the p-value was < 0.05, then the results will be considered to be significant. Data were analyzed using SPSS software v.23.0.

INVESTIGATIONS REQUIRED:

- ✓ Complete blood count.
- ✓ Total and differential leucocyte count.
- ✓ ESR.
- ✓ Urine examination.
- ✓ Serum Electrolytes.
- ✓ Blood Urea and Serum creatinine.
- ✓ Random Blood sugar.
- ✓ HbA1c.

- ✓ HIV.
- ✓ Arterial blood gas analysis.
- ✓ Blood Culture.
- ✓ Endotracheal aspirate for culture and sensitivity.
- ✓ Chest X-ray.

RESULTS

In total 612 patients were admitted to MICU/ICCU of Shri B.M. Patil Medical College Hospital and Research Center and were put on mechanical ventilator in the span of January 2015 to June 2016 out of which 50 patients developed ventilator associated pneumonia.

Incidence: 8.16%

Table no 11: Distribution of cases by Age and Onset of VAP

Age (Yrs)	Early Onset		Late Onset		Total		p value
	N	%	N	%	N	%	
16-25	7	25.0%	1	4.5%	8	16.0%	
26-35	6	21.4%	3	13.6%	9	18.0%	
36-50	4	14.3%	3	13.6%	7	14.0%	
51-70	8	28.6%	4	18.2%	12	24.0%	0.027 (Sig)
>70	3	10.7%	11	50.0%	14	28.0%	
Total	28	100.0%	22	100.0%	50	100.0%	
Mean ±SD	44.2±21.2		64.5±23.4		53.1±24.2		

The age of the patients ranged from 16 years to 96 years, the mean age being 56 years.

Graph no 1: Distribution of cases by Age and Onset of VAP

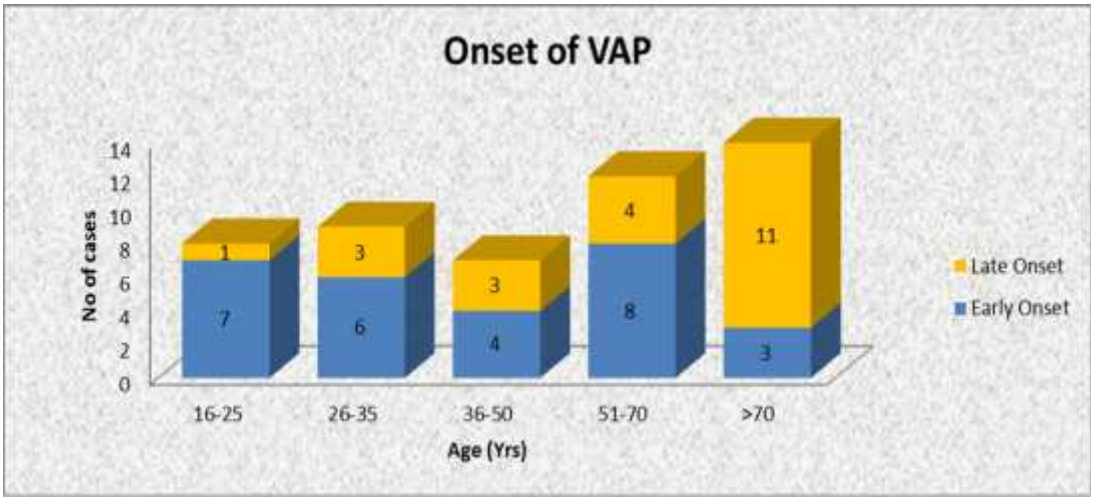


Table no 12: Distribution of cases by Sex and Onset of VAP

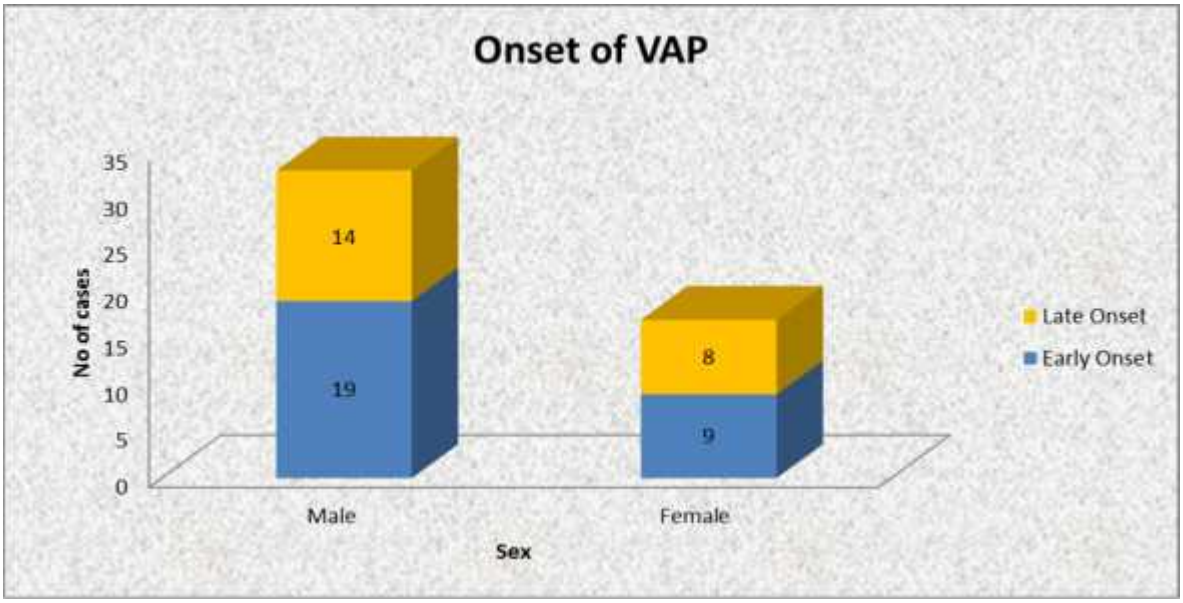
Sex	Early Onset		Late Onset		Total		p value
	N	%	N	%	N	%	
Male	19	67.9%	14	63.6%	33	66.0%	0.754
Female	9	32.1%	8	36.4%	17	34.0%	
Total	28	100.0%	22	100.0%	50	100.0%	

Out of 50 patients with VAP, 33 were males (66%) and 17 were females (34%).

Out of 28 patients with early onset VAP, 19 were males (67.9%) and 9 were females (32.1%).

Out of 22 patients with late onset VAP, 14 were males (63.6%) and 8 were females (36.4%).

Graph no 2: Distribution of cases by Sex and Onset of VAP



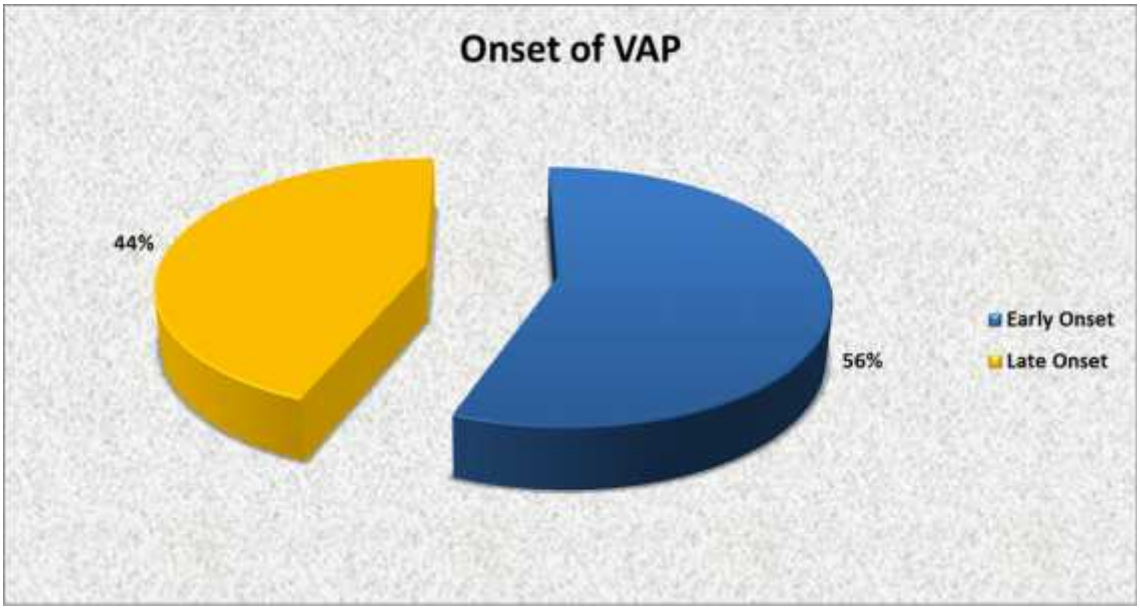
Primary diagnosis of critically ill patients who developed VAP was:

1) Stroke:	11
2) IHD & other cardiac causes:	10
3) Organophosphorus poisoning:	4
4) Cirrhosis of liver:	4
5) Septic shock:	4
6) Chronic Kidney Disease:	3
7) Neurological Causes:	3
8) Unknown compound poisoning:	2
9) Diabetic Ketoacidosis:	2
10) Pyrexia of Unknown origin:	2
11) G.B syndrome:	2
12) Seizure Disorder and Drug overdose:	1
13) Myasthenia Gravis:	1
14) Hypocalcemic Periodic Paralysis:	1

Table no 13: Distribution of cases according to Onset of VAP

Onset of VAP	N	%
Early Onset	28	56.0
Late Onset	22	44.0
Total	50	100.0

Graph no 3: Distribution of cases according to Onset of VAP

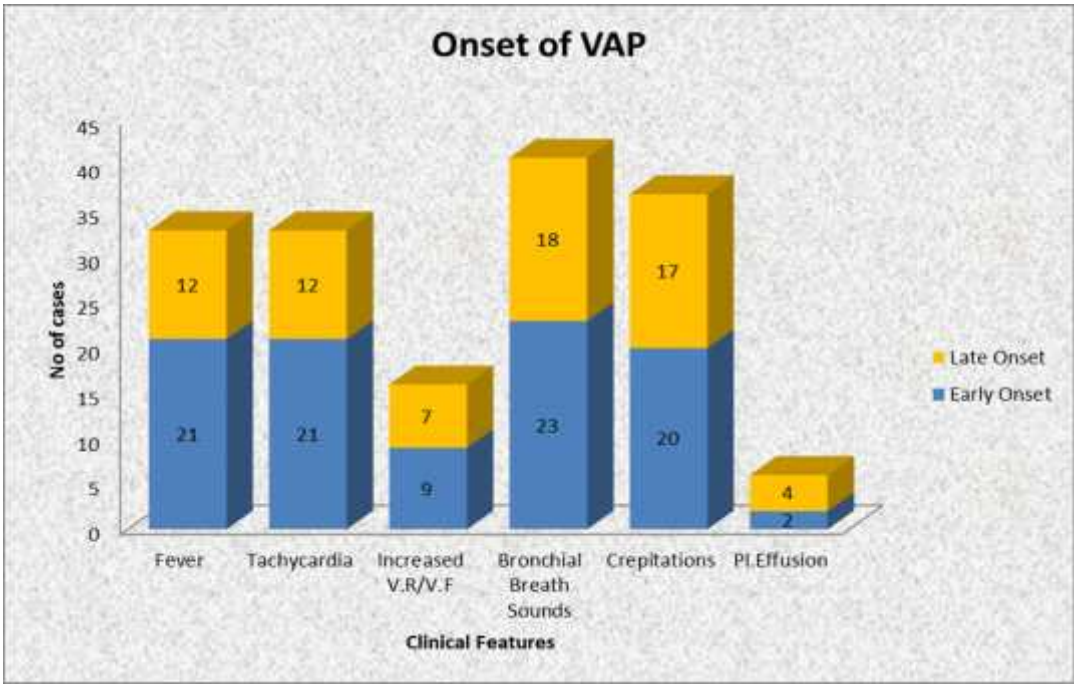


Out of 50 patients, 28 patients (56%) developed early onset VAP, while 22 patients (44%) developed late onset VAP.

Table no 14: Distribution of Clinical Features by Onset of VAP

Clinical Features	Early Onset		Late Onset		Total		p value
	N	%	N	%	N	%	
Fever	21	75.0%	12	54.5%	33	66.0%	0.026 (Sig)
Tachycardia	21	75.0%	12	54.5%	33	66.0%	0.026 (Sig)
Increased V.R/V.F	9	32.1%	7	31.8%	16	32.0%	0.981
Bronchial Breath Sounds	23	82.1%	18	81.8%	41	82.0%	0.976
Crepitations	20	71.4%	17	77.3%	37	74.0%	0.64
Pl.Effusion	2	7.1%	4	18.2%	6	12.0%	0.233

Graph no 4: Distribution of Clinical Features by Onset of VAP



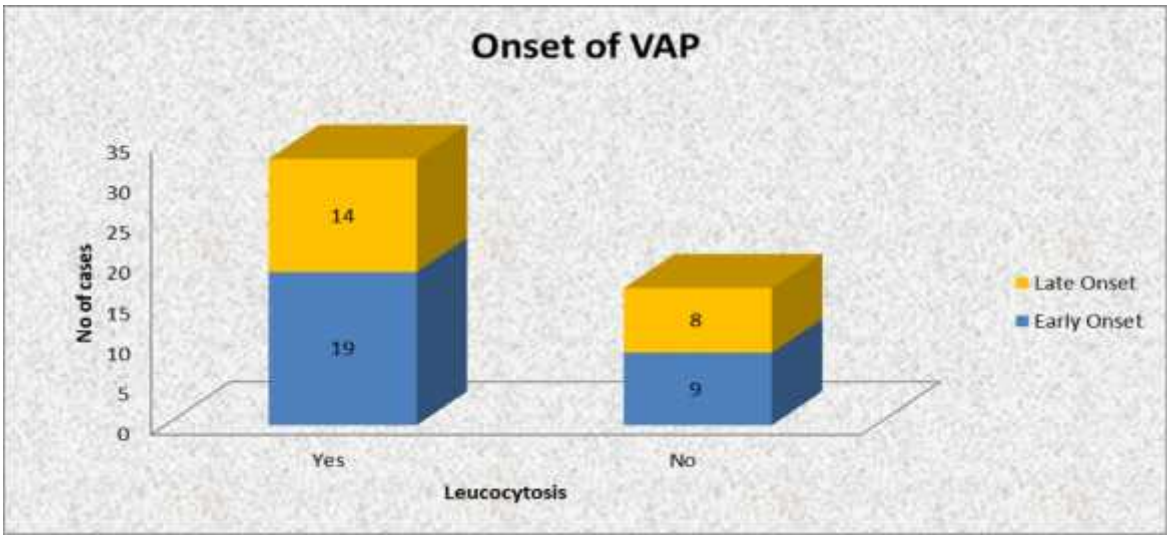
The most common clinical feature in early onset VAP is Bronchial breath sounds (82.1%) followed by Fever and Tachycardia (75%) each followed by Crepitation's (71.4%).

Similarly Bronchial breath sound (81.8%) is most common sign seen in late onset VAP followed by crepitation (77.3%) which is followed by Fever and Tachycardia (66%) each.

Table no 15: Distribution of Leucocytosis by Onset of VAP

Leucocytosis	Early Onset		Late Onset		Total		p value
	N	%	N	%	N	%	
Yes	19	67.9%	14	63.6%	33	66.0%	0.754
No	9	32.1%	8	36.4%	17	34.0%	
Total	28	100.0%	22	100.0%	50	100.0%	

Graph no 5: Distribution of Leucocytosis by Onset of VAP

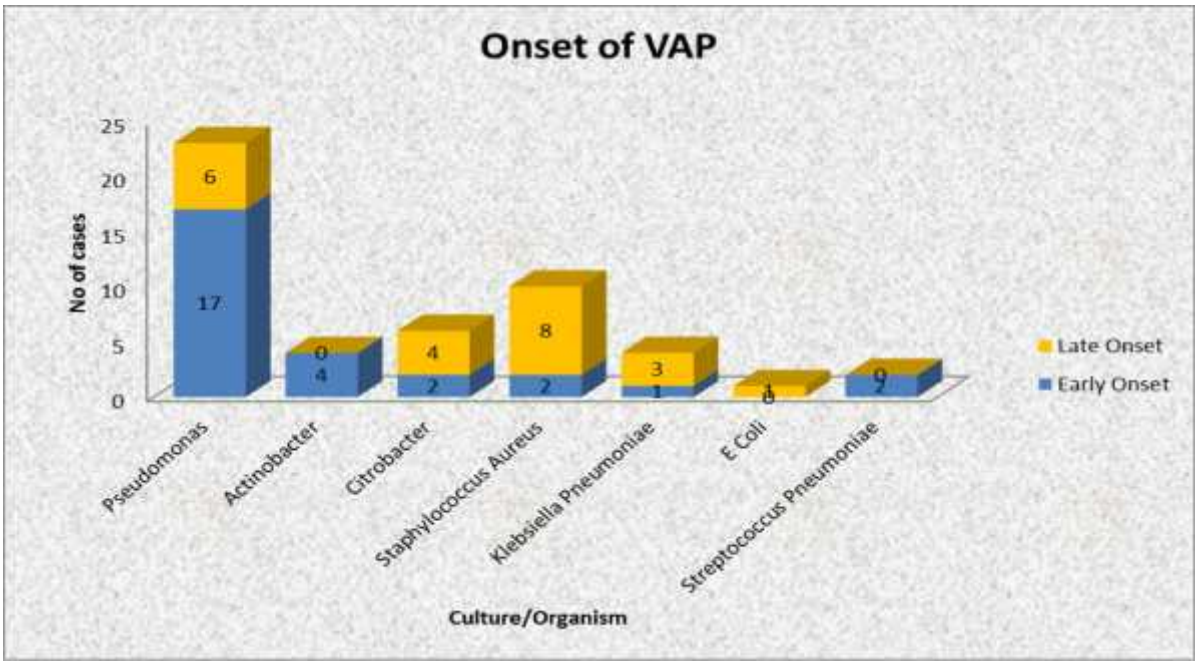


In early onset VAP, 67.9% patients had leukocytosis while 63.6% patients of the late onset VAP had leukocytosis.

Table no 16: Distribution of Culture/Organism by Onset of VAP

Culture/Organism	Early Onset		Late Onset		Total		p value
	N	%	N	%	N	%	
Pseudomonas	17	60.7%	6	27.3%	23	46.0%	0.002 (Sig)
Actinobacter	4	14.3%	0	0.0%	4	8.0%	
Citrobacter	2	7.1%	4	18.2%	6	12.0%	
Staphylococcus Aureus	2	7.1%	8	36.4%	10	20.0%	
Klebsiella Pneumoniae	1	3.6%	3	13.6%	4	8.0%	
E Coli	0	0.0%	1	4.5%	1	2.0%	
Streptococcus Pneumoniae	2	7.1%	0	0.0%	2	4.0%	
Total	28	100.0%	22	100.0%	50	100.0%	

Graph no 6: Distribution of Culture/Organism by Onset of VAP



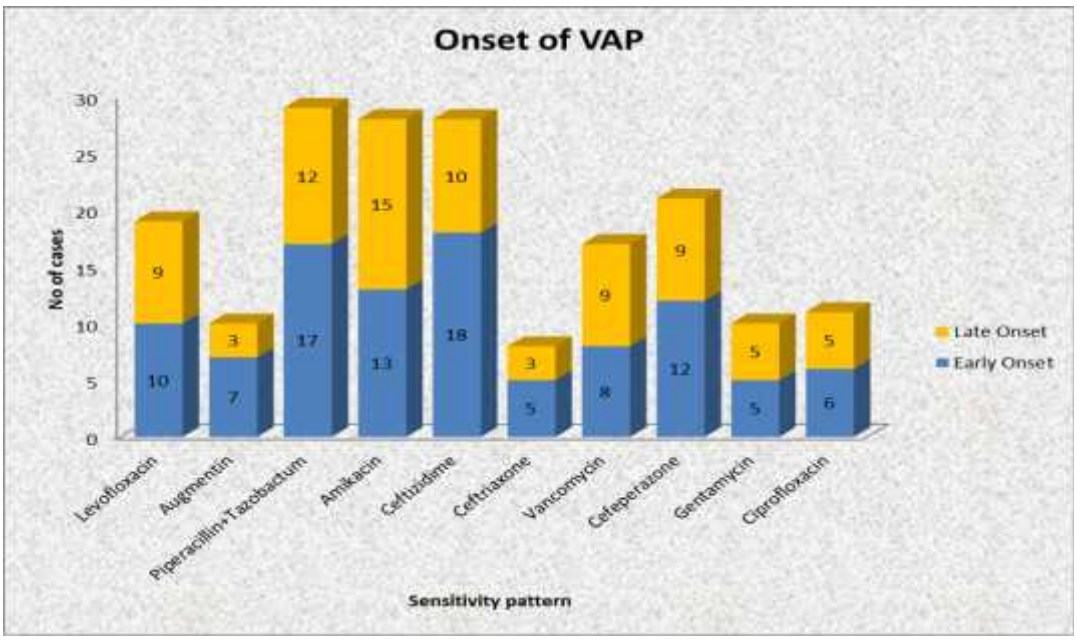
Most common organisms isolated in early onset VAP were pseudomonas (60.7%) and Actinobacter (14.3%). Other organisms isolated were Citrobacter (7.1%), Staphylococcus Aureus (7.1%), Streptococcus Pneumoniae (7.1%) and Klebsiella (3.6%).

Most common organism isolated in late onset VAP was Staphylococcus (36.4%) and pseudomonas (27.3%), followed by Citrobacter (18.2%), Klebsiella (13.6%) and E.coli (4.5%).

Table no 17: Sensitivity pattern by Onset of VAP

Parameters	Early Onset		Late Onset		Total		p value
	N	%	N	%	N	%	
Levofloxacin	10	35.7%	9	40.9%	19	38.0%	0.707
Augmentin	7	25.0%	3	13.6%	10	20.0%	0.319
Piperacillin+Tazobactum	17	60.7%	12	54.5%	29	58.0%	0.661
Amikacin	13	46.4%	15	68.2%	28	56.0%	0.124
Ceftizidime	18	64.3%	10	45.5%	28	56.0%	0.183
Ceftriaxone	5	17.9%	3	13.6%	8	16.0%	0.686
Vancomycin	8	28.6%	9	40.9%	17	34.0%	0.361
Cefeperazone	12	42.9%	9	40.9%	21	42.0%	0.89
Gentamycin	5	17.9%	5	22.7%	10	20.0%	0.669
Ciprofloxacin	6	21.4%	5	22.7%	11	22.0%	0.912

Graph no 7: Sensitivity pattern by Onset of VAP



Most common antibiotic for which most bacteria were sensitive in early onset VAP was Ceftizidime (64.3%). Followed by Piperacillin & Tazobactum (60.7%), Amikacin (46.4%), Cefeperazone (42.9%), Levofloxacin (35.7%), Vancomycin (28.6%), Augmentin (25%), Ciprofloxacin (21.4%), Gentamycin & Ceftriaxone (17.9% each).

In case of Late onset VAP, Amikacin (68.2%) was most sensitive antibiotic followed by Piperacillin+Tazobactum (54.5%), Ceftizidime (45.5%), Levofloxacin (40.9%), Vancomycin (40.9%), Cefoperazone (40.9%), Gentamycin & Ciprofloxacin (22.7% each) and Augmentin (13.6%).

An overall, Piperacillin & Tazobactum (58%) was the most sensitive antibiotic in patients with VAP.

Table no 18: Antibiotic Relieved by Onset of VAP

Antibiotic Relieved	Early Onset		Late Onset		Total	
	N	%	N	%	N	%
Piperacillin+Tazobactum+Amikacin	6	21.4%	7	25.0%	13	46.4%
Piperacillin+Tazobactum+Amikacin+Metronidazole	0	0.0%	1	3.6%	1	3.6%
Piperacillin+Tazobactum+Gentamycin	2	7.1%	0	0.0%	2	7.1%
Piperacillin+Tazobactum+Gentamycin+Levofloxacin	1	3.6%	1	3.6%	2	7.1%
Piperacillin+Tazobactum+Metronidazole	1	3.6%	0	0.0%	1	3.6%
Piperacillin+Tazobactum+Levofloxacin	2	7.1%	2	7.1%	4	14.3%
Cefoperazone+sulbactum	0	0.0%	1	3.6%	1	3.6%
Amikacin+Cefoperazone+sulbactum	1	3.6%	1	3.6%	2	7.1%
Amikacin+Ceftriaxone	0	0.0%	1	3.6%	1	3.6%
Amikacin+Vancomycin	1	3.6%	0	0.0%	1	3.6%
Amikacin+Meropenam	1	3.6%	0	0.0%	1	3.6%
Gentamycin+Metronidazole	2	7.1%	1	3.6%	3	10.7%
Gentamycin+Ceftriaxone	1	3.6%	1	3.6%	2	7.1%
Gentamycin+Ceftriaxone+Levofloxacin	1	3.6%	0	0.0%	1	3.6%
Gentamycin+Ceftizidime	1	3.6%	0	0.0%	1	3.6%
Gentamycin+Ceftizidime+Levofloxacin	1	3.6%	3	10.7%	4	14.3%
Ceftizidime+Levofloxacin	2	7.1%	1	3.6%	3	10.7%
Levofloxacin+Cefoperazone+sulbactum	0	0.0%	1	3.6%	1	3.6%
Levofloxacin+Vancomycin	1	3.6%	0	0.0%	1	3.6%
Vancomycin	4	14.3%	1	3.6%	5	17.9%
Total	28	100.0%	22	78.6%	50	178.6%

Most common antibiotic used for treatment in early onset VAP was Piperacillin & Tazobactum (21.4%) followed by Vancomycin (14.3%).

Similarly for late onset VAP, commonest antibiotic used was Piperacillin & Tazobactum (25%) followed by combination of Gentamycin, Ceftizidime and Levofloxacin (10.7%).

An overall, Piperacillin & Tazobactum (46.4%) was the most common antibiotic used for treatment of VAP followed by Vancomycin (17.9%).

Graph no 8: Antibiotic Relieved by Onset of VAP

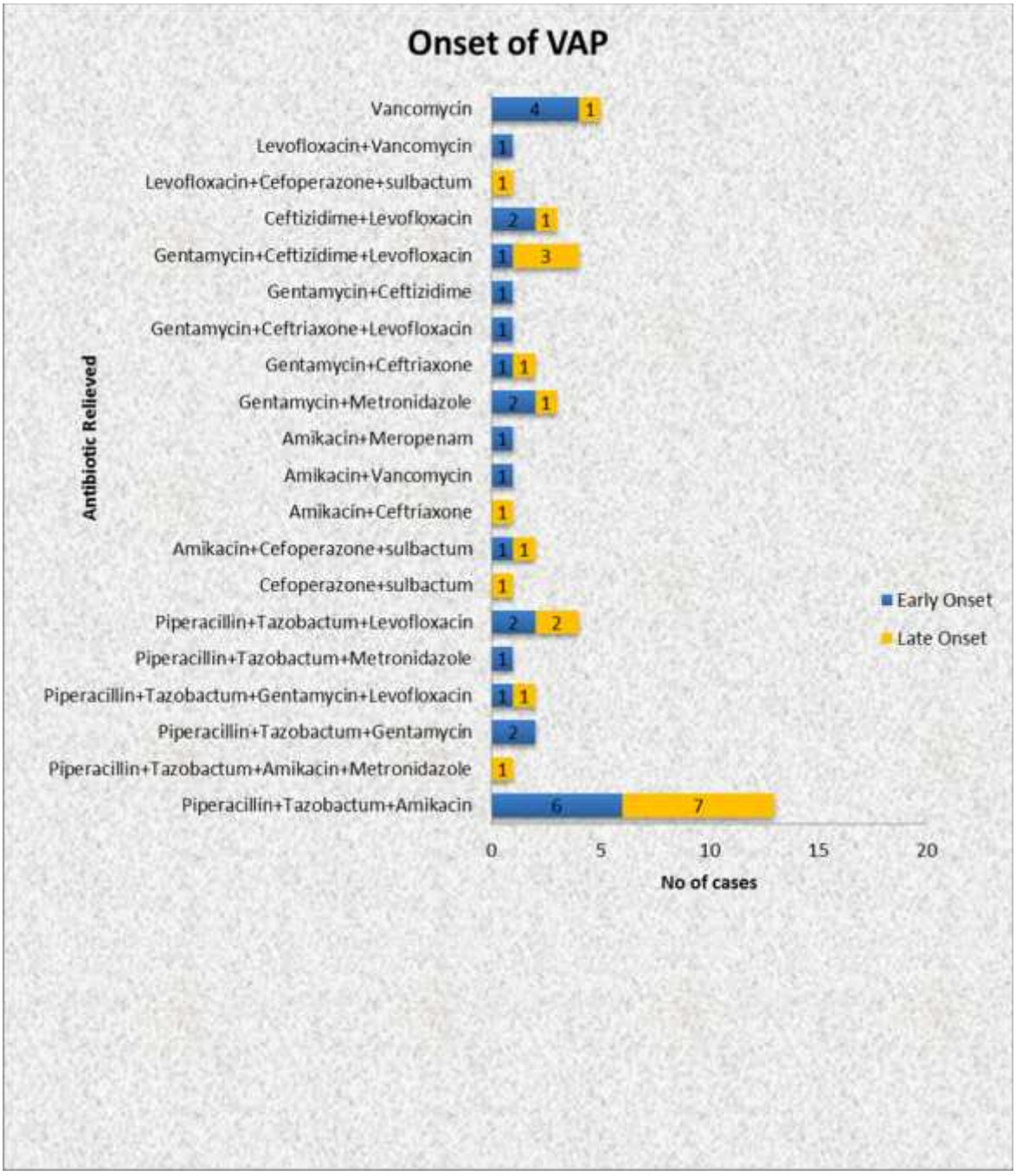
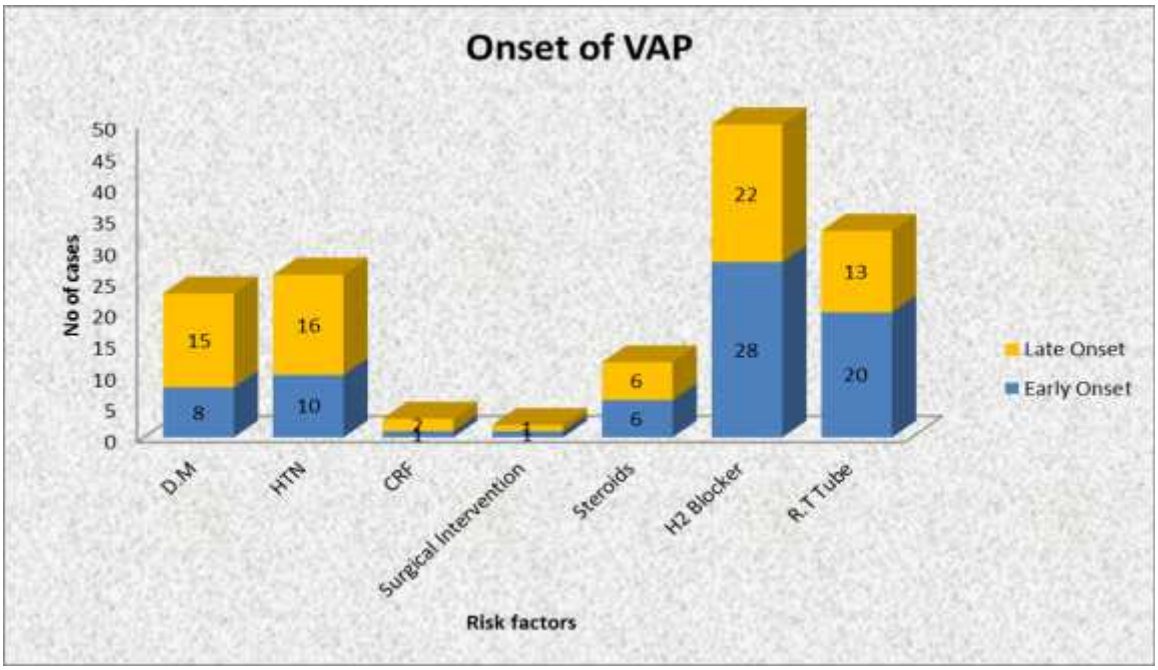


Table no 19: Distribution of Risk factors by Onset of VAP

Risk factors	Early Onset		Late Onset		Total		p value
	N	%	N	%	N	%	
D.M.	8	28.5%	15	68.1%	23	46.0%	0.038 (Sig)
HTN	10	35.7%	16	72.7%	26	52.0%	0.009(Sig)
CRF	1	3.6%	2	9.1%	3	6.0%	0.415
Surgical Intervention	1	3.6%	1	4.5%	2	4.0%	0.861
Steroids	6	21.4%	6	27.3%	12	24.0%	0.631
H2 Blocker	28	100.0%	22	100.0%	50	100.0%	NA
R.T Tube	20	71.4%	13	59.1%	33	66.0%	0.361

Graph no 9: Distribution of Risk factors by Onset of VAP



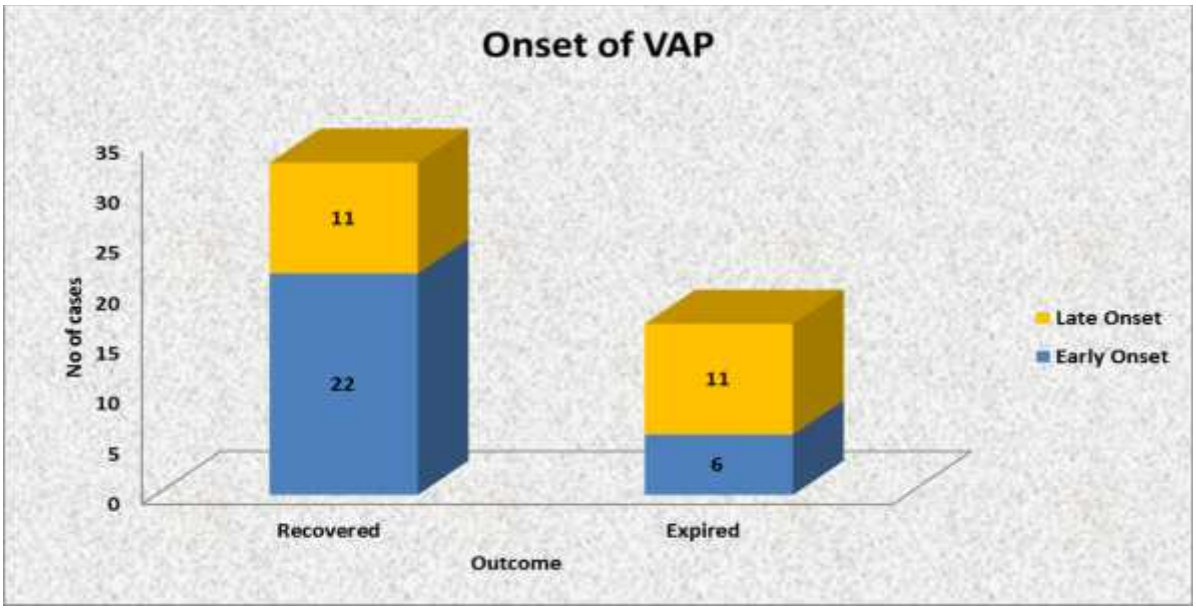
The commonest risk factor predisposing to early onset VAP was use of proton pump inhibitor (100%) followed by Ryle's tube insertion (71.4%), Hypertension (35.7%), Diabetes Mellitus (28.5%), Steroids (21.4%), chronic renal failure and surgical intervention (3.6%).

In late onset VAP, most common risk factor predisposing was Proton pump inhibitor (100%) followed by Ryle's tube insertion (66%), Hypertension (52%), Diabetes Mellitus (46%) and Steroids (24%), Chronic renal failure (6%) and surgical intervention (4%).

Table no 20: Outcome by Onset of VAP

Outcome	Early Onset		Late Onset		Total		p value
	N	%	N	%	N	%	
Recovered	22	78.6%	11	50.0%	33	66.0%	
Expired	6	21.4%	11	50.0%	17	34.0%	0.034(Sig)
Total	28	100.0%	22	100.0%	50	100.0%	

Graph no 10: Outcome by Onset of VAP



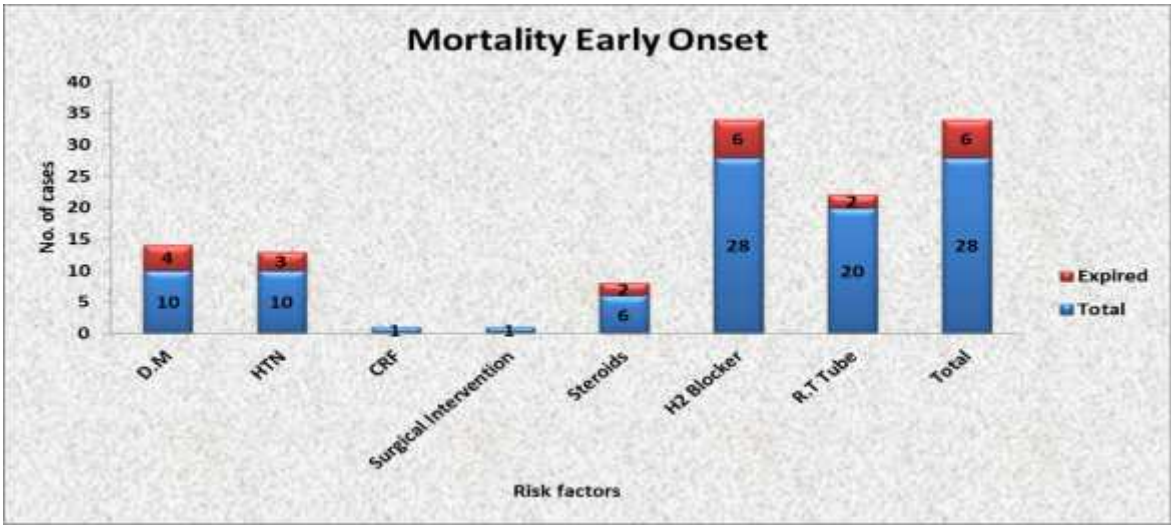
In early onset VAP totally 22 (78.6%) patients recovered and 6 (21.4%) patients expired.

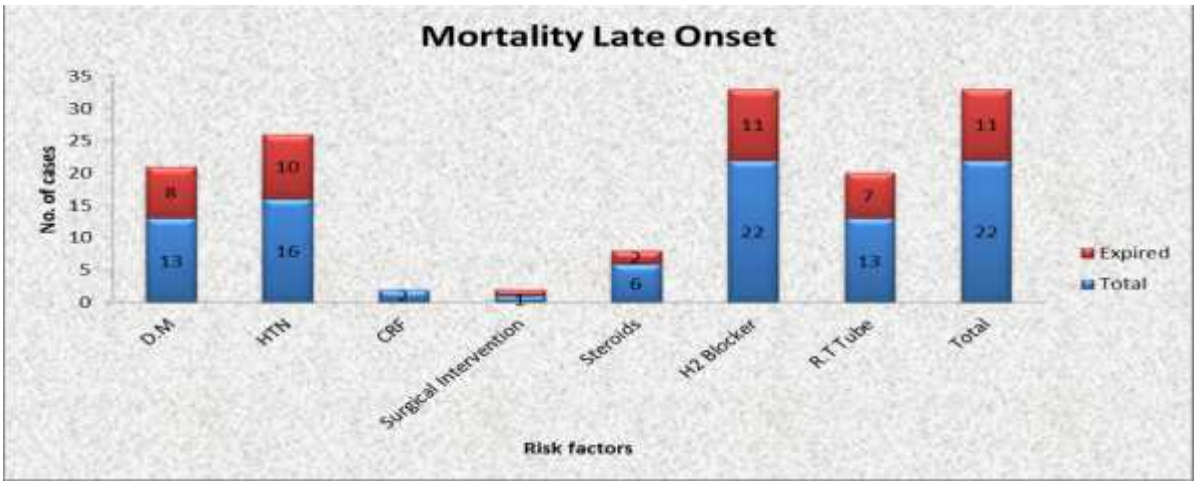
While in late onset VAP, 11 (50%) patients recovered and 11 (50%) patients expired.

TABLE NO 21: MORTALITY WITH RELATION TO RISK FACTORS

Risk factors	Early Onset			Late Onset			Total		
	Total	Expired		Total	Expired		Total	Expired	
		N	%		N	%		N	%
D.M	10	4	40.0	13	8	61.5	23	12	52.2
HTN	10	3	30.0	16	10	62.5	26	13	50.0
CRF	1	0	0.0	2	0	0.0	3	0	0.0
Surgical Intervention	1	0	0.0	1	1	100.0	2	1	50.0
Steroids	6	2	33.3	6	2	33.3	12	4	33.3
H2 Blocker	28	6	21.4	22	11	50.0	50	17	34.0
R.T Tube	20	2	10.0	13	7	53.8	33	9	27.3
Total	28	6	21.4	22	11	50.0	50	17	34.0

GRAPH NO 11: MORTALITY WITH RELATION TO RISK FACTORS IN EARLY ONSET VAP





GRAPH NO 12: MORTALITY WITH RELATION TO RISK FACTORS IN LATE ONSET VAP.

The mortality was high in patients of early onset VAP with Diabetes (40%) followed by steroids (33.3%) and Hypertension (30%).

The mortality was high in patients of late onset VAP with Surgical intervention (100%) followed by Hypertension (62.5%) and Diabetes (61.5).

DISCUSSION

Critically ill patients admitted to ICU benefit from close surveillance, cardiovascular monitoring and invasive devices such as mechanical ventilator, urinary bladder catheterization and vascular acess.[25]

VAP is the most common nosocomial infection among patients receiving mechanical ventilation in ICU. A total of 50 patients admitted to the ICU of our hospital who were on Mechanical Ventilation for more than 48 hours were studied. Present study was conducted to determine the predisposing factors, clinical pattern and organisms causing VAP.

Diagnosis of VAP using clinical criteria alone is often not accurate because fever and leukocytosis occur in many febrile conditions and colonization of respiratory tract with gram negative bacilli is common in intubated patients even in absence of pneumonia.[25]

Also chest x-ray infiltrates in patients on mechanical ventilator may be due to causes other than pneumonia. Diagnostic bronchoscopy with protected brushing of specimen or BAL culture increase the specificity of diagnosis.[63]

However invasive diagnostic testing is not needed routinely to manage suspected VAP[71] and diagnostic bronchoscopy was not used routinely in the present study as it was not considered safe in critically ill patients.

The incidence in our study was 8.16% which is almost in accordance with other studies conducted by Trivedi et al[14], and Fagon et al[37].

Our study included 33(66%) male and 17(34%) female patients. There was no sex predilection to VAP in our study and was the same in other studies done by Wagh etal[9] and Rodrigues etal[27].

In the present study the distribution of VAP was same in all the age groups, which is similar in other Indian studies (Rakshit[11], Joseph[85] and Dey[28]) and Western studies (Alp[86] and Rodrigues[27]).

The clinical spectrum of diseases in this study was similar to other Indian studies. The prevalence of VAP was greater in patients with diseases necessitating prolonged MV. Cases such as poisonings were uncommon in Western studies done by Heyland[56] and Katherson[55].

The significant risk factors for development of VAP were prolonged ventilation, severe illness and presence of co morbid condition like diabetes, stroke, renal diseases etc. The patients who developed VAP had prolonged stay in the hospital and high mortality rate (34%) in our study. Patients with neurological disorders and CNS infections in our study group were predisposed to the development of VAP. These patients had impaired consciousness and inadequate cough reflexes which predisposed them for developing VAP.

Co morbid illness and VAP: It was found that the risk of developing VAP was more in patients who had medical illnesses like diabetes, hypertension, Stroke, CRF and Surgical intervention than patients without them. This was similar to the studies done by Rakshith[11] and Heyland etal[56].

Table no 22. Co-morbid illness and VAP

Comorbid illness & VAP	This Study	Rakshith et al[11]	Heyland et al[56]
Diabetes	23	3	80
Hypertension	26	2	40
Stroke	11	1	51
Chronic kidney disease	3	3	4

In this study, VAP was not independently associated with mortality. Mortality was predominantly associated with severity of underlying disease, presence of co morbid factors and older age groups.

In the present study, 56% of cases were early-onset VAP and 44% of the cases were late-onset VAP, which is similar to other studies reporting. This shows that VAP increases with the duration of mechanical ventilation. The risk of acquiring pneumonia appears to increase with the duration of MV in a study done by Fagon etal[87] was found to be 7 % at 10 days and 19 % at 20 days.

Table no. 23: VAP and its relation to Onset.

VAP	This study	Dey et al[28]	Abdel et al[89]
Early onset	56%	47.7%	42%
Late onset	44%	52.3%	44%

The most common organisms isolated in early onset VAP was Pseudomonas. And the most common organisms isolated in late onset VAP was Staphylococcus Aureus. These results go in accordance with previous studies conducted by Jordi et al[43] and Brennan et al[44].

Most of the organisms isolated were potentially antibiotic resistant in this study. Multidrug resistant organisms are increasing in ICU. This emphasizes the need for judicious selection of patients for antibiotic therapy. The prophylactic use of antibiotics is not recommended and exposure to antibiotics is a significant risk factor for colonization and infection with nosocomial MDR pathogens has been observed by many authors.

Trivedi etal[63] reported 38% of his patients had VAP. The organisms were Pseudomonas (55%), Acinetobacter (20%), Staphylococcus (14.5%) and Klebsiella (15%). In this study the most common offending organisms isolated were Acinetobacter (25%) and Klebsiella (25%).

Currently the exact role of VAP in worsening the prognosis of ICU patients is difficult to assess because the patients are critically ill and thus their clinical status is severe enough to require ICU care and potentially cause death. Therefore it is difficult to establish whether the patients would have survived if pneumonia did not occur.

This study helped in the early diagnosis of VAP and also to determine MDR organisms causing VAP in our ICU. The antibiotic susceptibility pattern of these isolates also helped the clinicians to choose appropriate antimicrobial therapy for prophylaxis and for treatment purposes.

Most common antibiotic used for treatment in early and late onset VAP was Piperacillin & Tazobactum (46.4%). In this study, antibiotics as initial VAP treatment were adequate in the most patients (50%). Antibiotics were changed in 50% of the patients after the culture sensitivity report. This was similar to other studies done by Rodrigues etal[27] and Kollef etal[88].

Antibiotic de-escalation consists of initial institution of empirical broad spectrum antibiotics followed by antibiotic streamlining driven by microbiological documentation is shown to have benefit in other studies like Andrade etal[46]. Due to the increasing incidence of MDR organisms in CCUs, an early and correct diagnosis of VAP is a challenge for optimal antibiotic treatment. The emergence of MDR pathogens can be prevented by adopting an antibiotic policy and dose de-escalation regimens.

Total mortality of VAP in our study was 34%, while the study conducted by Rajesh Chawla[84] showed mortality in VAP of 37-43% in India.

Table no. 24: VAP and its relation to Outcome.

Authors	Study years	No. of patients studied	Diagnostic Criteria	Mortality rates (%)
Kerver et al.	1986	39	Clinical	30
Torres et al.	1987-88	322	Clinical/PSB	33
Kollef et al.	1982-83	277	Clinical	37.5
Fagon et al.	1989-94	1118	PSB/BAL	53
Rakshit etal	2003-04	51	Clinical	37
This study	2015-16	50	Clinical	34

The overall mortality was 34%. VAP has a crude mortality rate of 20 to 70 %. Kollef reported that in his study the overall mortality was 37.5%.The mortality rates in patients with VAP is higher than patient without VAP, but whether this reflects the cause and affect relationship is uncertain.

Reintubation should be avoided, if possible, as it increases the risk of VAP. Noninvasive ventilation should be used whenever possible in selected patients with respiratory failure.

In summary, prior administration of antibiotics for short duration may be beneficial in some patient groups, but when given for prolonged periods may well place others at risk for subsequent infection with antibiotic-resistant microorganisms.

Pugin and co-workers[58] developed the clinical pulmonary infection score (CPIS), which combines clinical, radiographic, physiological (PaO2/FiO2), and microbiologic data into a single numerical result. When the CPIS exceeded 6, was a good correlation of the presence of VAP. The CPIS has a sensitivity of 77% and a specificity of 42%.

Singh and co-workers[90] have shown that some patients with a low clinical suspicion of VAP (CPIS of 6 or less) can have antibiotics safely discontinued after 3 days, if the subsequent course suggests that the probability of pneumonia is still low.

The incidence of colonization in hospitalized patients in general and even more in patients requiring endotracheal intubation is high. Antibiotic treatment of simple colonization is strongly discouraged. The clinical strategy emphasizes prompt empiric therapy for all patients suspected of having HAP. Although these criteria should raise suspicion of VAP, confirmation of the presence of pneumonia is much more difficult, and clinical parameters cannot be used to define the microbiologic etiology of pneumonia.

The driving force behind this strategy is the consistent findings that delay in the initiation of appropriate antibiotic therapy for patients with VAP is associated with increased mortality. The selection of initial antibiotic therapy is based on risk factors for specific pathogens, modified by knowledge of local patterns of antibiotic resistance and organism prevalence. Therapy is modified on the basis of the clinical response on Days 2 and 3, and the findings of semi quantitative cultures of lower respiratory tract

secretions. Use of an ICU-specific, broad-spectrum empiric therapy regimen can reduce the incidence of inappropriate initial therapy to less than 10%.

Quantitative cultures can be performed on endotracheal aspirates or samples collected either bronchoscopically or non-bronchoscopically, and each technique has its own diagnostic threshold and methodologic limitations. Quantitative cultures of tracheal aspirate (TA) are not a specific diagnostic method because of the lower respiratory tract colonization and a high percentage of false-positive results. However, investigators reported that quantitative cultures of TA have equal diagnostic accuracy to the other invasive techniques.

Iregui and coworkers[91] also documented an adverse outcome with initially delayed appropriate antimicrobial therapy in 107 patients with VAP and examined factors leading to such delays.

One of the consequences of increasing antimicrobial resistance is inappropriate initial empiric antimicrobial treatment of infections. Combination therapy should include agents from different antibiotic classes to avoid antagonism of therapeutic mechanisms. For gram-negatives, regimens usually involve combinations of two drugs from the beta lactam, quinolone, or aminoglycoside classes. A trend to greater rates of relapse for short duration therapy was seen if the etiologic agent was P. Aeruginosa or an Acinetobacter species.

The variation and differences in the clinical and bacteriological pattern are related to the

a) Health seeking behavior in our patients is different when compared to that of the western population. By the time the patient is referred to the tertiary care center his underlying disease would have progressed and may be irreversible. This may necessitate longer duration of MV which is directly proportional to the development of VAP.

b) ICU case mix

c) Difference in the definition and diagnostic studies used.

d) The paucity of the nursing staff that leaves lacunae in ideal patient care. The patient nurse ratio in our CCU set up is 4:1, the desired ratio being 1:1.

Such differences make direct comparison between studies difficult.

Not with standing these reservations this study confirms the magnitude of the problem of VAP. So the best approach to manage this problem seems to be adaptation of preventive strategies.

CONCLUSION

- Incidence of VAP was 8.16% in our study.
- Out of 50 patient studied 28 had developed early onset and 22 had developed late onset VAP.
- The clinical examination revealed that patients to have increased body temperature, tachycardia, tubular breath sound and crepitation's. The patients with associated pleural effusion had decreased air entry with dull note on percussion.
- The most common sign evident in early onset VAP was bronchial breath sounds (82.1%), Fever and tachycardia (75%) followed by crepitation (71.4%), increased VR/VF (32.1%) and pleural effusion (7.1%).
- The most common sign evident in late onset VAP was bronchial breath sounds (81.8%) followed by crepitation (77%), fever and tachycardia (54.5%), increased VR/VF (31.8%), pleural effusion (18.2%).
- 67.9% of early onset and 63.6% of late onset VAP had leukocytosis.
- Most common organisms isolated in early onset VAP were pseudomonas (60.7%) and Actinobacter (14.3%). Followed by Citrobacter, Staphylococcus Aureus, Streptococcus Pneumoniae (7.1% each) and Klebsiella (3.1%).

- Most common organism isolated in late onset VAP was Staphylococcus Aureus (36.4%), followed by Pseudomonas (27.3), Citrobacter (18.2%) Klebsiella (13.6%) and E.Coli (4.5%).

- Most common antibiotic for which most bacteria were sensitive in early onset VAP was Ceftizidime (64.3%). Followed by Piperacillin & Tazobactum (60.7%), Amikacin (46.4%), Cefeperazone (42.9%), Levofloxacin (35.7%), Vancomycin (28.6%), Augmentin (25%), Ciprofloxacin (21.4%), Gentamycin & Ceftriaxone (17.9% each).

- In case of Late onset VAP, Amikacin (68.2%) was most sensitive antibiotic followed by Piperacillin Tazobactum (54.5%), Ceftizidime (45.5%), Levofloxacin (40.9%), Vancomycin (40.9%), Cefoperazone (40.9%), Gentamycin & Ciprofloxacin (22.7% each) and Augmentin (13.6%).

- An overall, Piperacillin & Tazobactum (46.4%) was the most common antibiotic used for treatment of VAP followed by Vancomycin (17.9%).

- The commonest risk factor predisposing to early onset VAP was use of proton pump inhibitor (100%) followed by Ryle's tube insertion (71.4%), Hypertension (35.7%), Diabetes Mellitus (28.5%), Steroids (21.4%), chronic renal failure and surgical intervention (3.6%).

- In late onset VAP, most common risk factor predisposing was Proton pump inhibitor (100%) followed by Ryle's tube insertion (66%), Hypertension (52%), Diabetes Mellitus (46%) and Steroids (24%), Chronic renal failure (6%) and surgical intervention (4%).

- In early onset VAP totally 22 (78.6%) patients recovered and 6 (21.4%) patients expired. While in late onset VAP, 11 (50%) patients recovered and 11 (50%) patients expired.

SUMMARY

1. Out of 612 patients admitted to MICU of Shri B.M. Patil Medical College Hospital and Research Center, 50 patients who developed VAP over a period of approximately one and half years from January 2015 to June 2016 were studied.

2. Detailed history, physical examination was done and patients were investigated with chest x-ray and endotracheal aspirate culture.

3. 8.16% was total incidence.

4. 28 VAP patients had early onset and 22 VAP patients had late onset.

5. Bronchial breath sounds was the commonest sign in patients with early (82.1%) & late (81.8%) onset VAP. An overall also bronchial breath sound (82%) was the most common sign in VAP patients.

6. Pseudomonas (60.7%) and Citrobacter (14.3%) were the commonest bacteria isolated in early onset VAP. Staphylococcus (36.4%) & Pseudomonas (27.3%) were the commonest bacteria isolated in patients with late onset VAP. Overall pseudomonas (46%) was the commonest organism isolated in VAP.

7. The antibiotic to which most bacteria where sensitive in early onset VAP was Ceftizidime (64.3%) and that in late onset VAP was Amikacin (68.2%).

8. The commonest risk factor in both early and late onset VAP was use of H2 blockers (100%).

9. 78.6% patients with early onset VAP showed recovery but 21.4% expired. And 50% patients with late onset VAP expired while 50% recovered.

10. Preventive strategies should be followed in critical care units to decrease prevalence of VAP.

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ANNUXURES

ETHICAL CLEARANCE CERTIFICATE

B.L.D.E. UNIVERSITY'S
SHRI.B.M.PATIL MEDICAL COLLEGE, BIJAPUR-586 103
INSTITUTIONAL ETHICAL COMMITTEE

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this college met on 22-11-2014 *at* 3-30pm *to scrutinize the Synopsis of Postgraduate Students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected & revised version synopsis of the Thesis has been accorded Ethical Clearance.*

Title 'Study of pneumonia in patients on - mechanical ventilation"

x x x x

Name of P.G. student Dr Sandip Jagdish Singh. Dept of Medicine

Name of Guide/Co-investigator Dr S.S. Devarmani. Prof of Medicine

for

DR.TEJASWINI VALLABHA
CHAIRMAN
INSTITUTIONAL ETHICAL COMMITTEE
BLDEU'S, SHRI.B.M.PATIL
MEDICAL COLLEGE, BIJAPUR.

Following documents were placed before E.C. for Scrutinization
1) Copy of Synopsis/Research project.
2) Copy of informed consent form
3) Any other relevant documents.

BLDE University's

Shri B M Patil Medical College, Hospital & R.C

Vijayapur, Karnataka

INFORMED CONSENT FOR PARTICIPATION IN DISSERTATION/RESEARCH

I, the undersigned,_____ , S/O D/O W/O _____, aged ____years, ordinarily resident of _____ do hereby state/declare that Dr Sandip J Singh of Shri. B. M. Patil Medical College Hospital and Research Centre has examined me thoroughly on _____ at _____ (place) and it has been explained to me in my own language that I am suffering from _____ disease (condition) and this disease/condition mimic following diseases. Further Dr, Sandip J Singh informed me that he/she is conducting dissertation/research titled "Study of Ventilator Associated Pneumonia in Shri B.M. Patil Medical College Hospital & Research Center" under the guidance of Dr. S. S. Devermani requesting my participation in the study. Apart from routine treatment procedure, the pre-operative, operative, post-operative and follow-up observations will be utilized for the study as reference data.

Doctor has also informed me that during conduct of this procedure like adverse results may be encountered. Among the above complications most of them are treatable but are not anticipated hence there is chance of aggravation of my condition and in rare circumstances it may prove fatal in spite of anticipated diagnosis and best treatment made available. Further Doctor has informed me that my participation in this study help in evaluation of the results of the study which is useful reference to treatment of other

similar cases in near future, and also I may be benefited in getting relieved of suffering or cure of the disease I am suffering.

The Doctor has also informed me that information given by me, observations made/ photographs/ video graphs taken upon me by the investigator will be kept secret and not assessed by the person other than me or my legal hirer except for academic purposes.

The Doctor did inform me that though my participation is purely voluntary, based on information given by me, I can ask any clarification during the course of treatment / study related to diagnosis, procedure of treatment, result of treatment or prognosis. At the same time I have been informed that I can withdraw from my participation in this study at any time if I want or the investigator can terminate me from the study at any time from the study but not the procedure of treatment and follow-up unless I request to be discharged.

After understanding the nature of dissertation or research, diagnosis made, mode of treatment, I the undersigned Shri/Smt _____ under my full conscious state of mind agree to participate in the said research/dissertation.

Signature of patient:

Signature of doctor:

Witness: 1.

2.

Date:

Place

PROFORMA

Patient Name: Age: Sex :

Address: Occupation: I.P No.:

Date of admission: Date of discharge:

PART-1

(Reason for admission to the critical care unit)

Patient admitted in critical care unit with

CHIEF COMPLAINTS

1)

2)

3)

PRESENT HISTORY:

PAST HISTORY:

FAMILY HISTORY:

On Examination:

Level of consciousness:-

Vitals:- Pulse : Rate

Volume

Rhythm

Respiratory rate:

BP:_____ mmHg, pulse pressure

Temp:- _____ ^{o}C

Built: Nourishment: Wt. Ht.

Body mass index

Signs- Cyanosis clubbing: - Y/N grade

Lymphadenopathy - Y/N group

Signs of CCF:-

Signs of respiratory failure:-

AFFECTED SYSTEMIC EXAMINATION:

OTHER SYSTEMS:

INVESTIGATION:

Routine investigation: Hb, Tc, DC, ESR,

Urine routine, Sr Na^{+} Sr K^{+}

RBS, HbA_1C HIV test,

ABG, Blood urea, Creatinine,

E.C.G.

Chest x-ray,

Relevant special investigation:

Diagnosis:

Treatment:

PART-2

(Patient developed pneumonia after ____days of patient on mechanical ventilator)

Diagnosis of VAP is made clinically, radiologically or microbiologically.

Patient developed following clinical features,

Fever: Yes / No

Duration:

Grade: Mild/Moderate/Severe

Chills: Yes/No

Rigors: Yes/No

PAST HISTORY: H/o DM/ HT

H/o COPD/asthma

H/o TB /ILD

FAMILY HISTORY:

PERSONAL HISTORY:

Smoker: YES / NO, Duration:-_____ No of cigrates/

beedies per day._____

Alcoholic: YES / NO, Duration:-_____. , Ml per

day._____

History of exposure to professional sex workers/ multiple partners: Yes/No

GENERAL EXAMINATION:

1. Level of consciousness:- Normal / Agitated / semiconsciousness/Unconsciousness

2. Vitals: Pulse: Rate

Volume

Rhythm

Respiratory rate:-

BP:-_____mmhg, pulse pressure:-_____

Temp:- _____oC

Built:- _____. Nourishment:-_____. Wt._____kg,

Ht._____cms Body mass index:-

Signs- cyanosis: YES / NO, central / peripheral

Clubbing: YES / NO , grade-

Lymphadenopathy- YES / NO group-

Pallor- YES / NO

Icterus- YES / NO

Signs of CCF: Pedal edema- YES / NO

JVP- Raised / not, _____cm

Hepatojugular reflex -YES / NO

Signs of respiratory failure:

SYSTEMIC EXAMINATION:

1. Respiratory System:

A. Upper Resp tract - Nose:

-Oral cavity:

-Throat:

B. Lower Resp tract -

a) Inspection of chest- Shape: Normal / Abnormal, type-_____

Spine: Normal

Kyphosis

Scoliosis: Right or Left.

Intercostal spaces:-Widening /Crowding /Recession of ICS

Supra clavicular fossae-Normal / hallowed

Resp rate:-

Type of Resp: Abdo-thoracic /Thoraco-abdominal

Paradoxical resp.:- YES / NO

Trails sign- present /absent, Right /left /central

Accessory muscles in action: YES / NO

Visible pulsation;- present /absent , site-_____

b) Palpation:

Trachea- Right / left /central

Apex beat- Site-

Type-

Measurements- Anterior-posterior (AP) _____cm

Transverse-(T)_____cm

Ratio: T/AP_____.

Circumference- Inspiration-_____cms

Expiration_____cms

Expansion_____cms

Right Hemi-thorax: Inspiration-_____cms

Expiration_____cms

Expansion_____cms

Left Hemi-thorax: Inspiration-_____cms

Expiration_____cms

Expansion_____cms

Movements of chest- ↓ / on both sides –

TVF: Increased/Decreased Rt. Lt.

Areas of chest

c) Percussion: Superficial-

Deep -

Bony-sternum, clavicle, ribs

Chest wall- resonant/hyperesonant / stonydull / woody dull

Rt. Lt.

Areas

Cardiac dullness- present / absent

Tidal percussion -_____ICS shift, up/ down

Kornign's isthmus –Resonant / dull

Traube's space- present / absent

d) Auscultation:- Rt. (Areas) Lt.(areas)

Air entry

Type-Vesicular/bronchial

Adventitious sounds

- present / absent

-crepts /rhonchi/rub

Vocal Resonance- Increased/ Decreased

2. C.V.S. :

Inspection

Palpation:

Percussion

Auscultation:

3. C.N.S: Higher functions

Motor system

Sensory system

Peripheral system

3. Per Abdomen: Inspection

Palpation: Liver palpable- Yes/ No,

Tender: Yes/ No.

Percussion: Ascites - present/ absent, grade____

Auscultation: bowel sound - Yes/ No

PART-3

INVESTIGATION:

SPECIFIC	ON ADMISSION	NOW
DATE		
Total WBC count:		
Differential count:		
ABG:		
Chest x-ray:		
Blood culture:		
SPECIAL:		

Pleural fluid c/s

Endotracheal aspirate for C/S

Routine investigation-

Hb:___ , Tc_____, DC ESR

Urine routine Sr. Na Sr. K

RBS_____, HbA_1C_____.

ABG_____, Blood urea _____, Sr. Creatinine_____

E.C.G.

Chest x-ray

PART-4

TREATMENT:

COURSE IN HOSPITAL:

RESULTS- RECOVERED / UN RECOVERED / EXPIRED

COMPLICATIONS:

FINAL DIAGNOSIS:

DISCUSSION:

KEY TO MASTER CHART

Age	1= 16-20, 2= 21-25, 3=26-30, 4=31-35, 5=36-40, 6= 41-45, 7=46-50, 8= 51-55, 9= 56-60, 10= 61-65, 11= 66-70, 12= 71-75, 13= 76-80, 14= 81-85, 15= 86-90, 16= 91-95, 17= 96-100
Sex	1= Male, 2= Female
D.M	1= Yes, 2= No
HTN	1= Yes, 2= No
CRF	1= Yes, 2= No
Surgical Intervention	1= Yes, 2= No
Steroids	1= Yes, 2= No
H2 blocker	1= Yes, 2= No
RT tube	1= Yes, 2= No
Fever	1= Yes, 2= No
Tachycardia	1= Yes, 2= No
Increased VR/VF	1= Yes, 2= No
Bronchial Breath sounds	1= Yes, 2= No
Crepitations	1= Yes, 2= No
Pleural Effusion	1= Yes, 2= No
Early Onset	1= Yes, 2= No
Late Onset	1= Yes, 2= No
Leucocytosis	1= Yes, 2= No
Organism	1= Pseudomonas, 2= Actinobacter, 3= Citrobacter, 4= Staphylococcus Aureus, 5= Klebsiella Pneumoniae, 6= E Coli, 7= Streptococcus Pneumoniae
Ciprofloxacin	1= Sensitive, 2= Resistant
Gentamycin	1= Sensitive, 2= Resistant
Cefoperazone	1= Sensitive, 2= Resistant
Vancomycin	1= Sensitive, 2= Resistant
Ceftriaxone	1= Sensitive, 2= Resistant
Ceftizidime	1= Sensitive, 2= Resistant
Amikacin	1= Sensitive, 2= Resistant
Piperacillin+Tazobactum	1= Sensitive, 2= Resistant
Amoxycillin+Clavunate	1= Sensitive, 2= Resistant
Levofloxacin	1= Sensitive, 2= Resistant
Antibiotic Relieved	1= Piperacillin+Tazobactum, 2= Amikacin, 3= Gentamycin, 4= Metronidazole, 5= Ceftriaxone, 6= Ceftizidime, 7= Levofloxacin, 8= Vancomycin, 9= Meropenam, 10= Ciprofloxacin, 11= Cefoperazone+sulbactum
Outcome	1= Recovered, 2= Expired

MASTER CHART

Sl.no	I.P no	Age	Sex	Diagnosis	D.M	HTN	CRF	Surgical Intervention	Steroids	H2 Blocker	R.T Tube	Fever	Tachycardia	Increased V.R/V.F	Bronchial Breath Sounds	Crepitations	Pl.Effusion	Early Onset	Late Onset	Leucocytosis	Culture/Organism	Ciprofloxacin	Gentamycin	Cefeperazone	Vancomycin	Ceftriaxone	Ceftizidime	Amikacin	Piperacillin+Tazobactum	Augmentin	Levofloxacin	Antibiotic Relieved	Outcome
1	32749	1	1	Unknown Compound Poisoning	2	2	2	2	2	1	1	1	1	2	2	1	2	1	2	1	1	2	2	2	2	2	1	1	1	2	2	1,2	1
2	28203	2	1	Organophosphorus Poisoning	2	2	2	2	2	1	1	1	1	2	1	1	2	1	2	2	2	2	2	1	1	1	1	2	1	1	2	1,2	1
3	35171	10	1	Intracerebral Hemorhage	1	1	2	2	1	1	1	1	1	2	1	2	2	1	2	1	1	2	2	2	2	2	1	2	1	2	2	1,3	1
4	128	2	2	Drug overdose with seizure disorder	2	2	2	2	2	1	1	1	1	2	2	1	2	1	2	1	1	2	2	2	2	2	1	2	1	2	1	1,7	1
5	4248	10	1	Stroke	1	1	2	2	2	1	1	1	1	2	2	1	2	2	1	1	3	2	2	2	2	2	2	1	1	2	2	1,2	2
6	5038	9	2	Diabetic Ketoacidosis	1	2	2	2	2	1	1	2	2	1	1	2	2	1	2	2	1	1	2	2	2	2	1	2	1	2	1	3,6,7	1
7	5524	7	1	Acute kidney Injury	2	1	2	2	2	1	2	1	1	2	2	1	2	1	2	1	1	2	2	2	2	2	1	1	1	2	2	1,2	1
8	6100	12	1	MI with CCF	1	1	2	2	2	1	2	2	2	1	1	1	2	2	1	2	4	2	2	2	1	2	2	2	2	2	2	8	2
9	6778	13	1	Stroke	1	1	2	2	2	1	1	1	1	2	2	1	2	2	1	1	1	2	2	2	2	2	2	2	2	2	2	1,3,7	2
10	6798	7	1	Cirrhosis of Liver	2	2	2	2	1	1	1	1	1	2	1	2	2	1	2	1	3	1	1	1	1	1	1	1	1	1	1	3,5	1
11	8764	8	1	CRF with GE with Hypovolumic shock	1	1	1	2	2	1	2	1	1	2	1	1	1	2	1	1	4	1	2	2	1	2	1	1	2	2	1	3,6,7	1
12	8914	13	2	IHD with CCF	1	1	2	2	2	1	2	1	1	1	1	1	2	2	1	1	5	1	1	1	2	1	1	1	1	2	1	3,5,7	2
13	9860	12	2	Stroke with SAH	1	1	2	1	1	1	1	1	1	1	1	1	2	2	1	1	1	2	2	2	2	2	1	2	2	2	2	3,6,7	2
14	10536	2	2	Unknown Compound Poisoning	2	2	2	2	2	1	1	1	1	2	1	1	2	1	2	1	1	2	2	1	2	2	2	1	2	2	2	2,11	1
15	11217	13	2	Metabolic encephalopathy with sepsis	1	1	2	2	2	1	1	1	1	2	1	2	1	2	1	1	4	2	2	2	1	2	2	1	2	2	2	2,8	2
16	11520	12	2	Essential HTN with acute GE with hypovolumic shock	2	1	2	2	2	1	1	2	2	1	1	1	2	1	2	2	3,6	1	1	1	1	1	1	1	1	1	1	3,5	1
17	12167	6	1	Cirrhosis of Liver	2	2	2	2	1	1	1	1	1	2	1	1	2	1	2	1	1	2	2	2	2	2	2	2	2	2	2	1,3,7	2
18	13661	1	1	Organophosphorus Poisoning	2	2	2	2	2	1	1	1	1	2	1	1	2	1	2	1	7	1	1	1	1	1	1	1	1	1	1	3,4,5	1
19	14194	5	1	Stroke with Intracerebral hemorrhage	2	1	2	2	1	1	1	1	1	2	1	1	2	2	1	1	5	1	1	1	2	1	1	1	1	1	1	3,4,5	2
20	14190	13	1	Stroke with MCA teritory infarct	1	1	2	2	2	1	1	2	2	2	2	1	2	2	1	2	4	2	2	2	1	2	1	1	1	2	2	2,9	1
21	14725	10	1	Stroke with Intracerebral hemorrhage	1	1	2	2	1	1	1	1	1	2	1	2	1	2	1	1	6	1	1	2	1	1	1	1	2	2	1	2,5	1
22	14960	9	1	IHD with LVF	1	1	2	2	2	1	2	1	1	1	1	1	2	1	2	1	1	2	2	2	2	2	2	2	1	2	2	1,2	2
23	748	12	1	IHD with LVF	2	1	2	2	2	1	2	2	2	2	1	1	2	2	1	1	1,5	2	2	1	2	2	1	2	1	2	1	6,7	1
24	863	3	2	Acute kidney Injury	2	1	1	2	2	1	2	1	1	2	1	1	1	2	1	1	1	2	2	1	2	2	1	1	1	2	2	1,2	1
25	878	11	2	Inferior wall M.I	1	2	2	2	2	1	2	1	1	1	1	1	2	1	2	2	4	2	2	2	1	2	2	2	2	2	2	8	1
26	1731	9	1	SAH	2	1	2	2	1	1	1	1	1	2	1	2	2	1	2	1	2,3	1	2	2	2	2	2	1	1	2	1	1,2	1
27	2422	8	1	Alcoholic Hepatitis with hypovolumic shock with hypoglycemic coma	2	2	2	2	2	1	1	1	1	2	1	1	2	1	2	1	1	2	2	1	2	2	1	1	1	2	2	1,2,4	1
28	3101	8	1	IHD with LVF	1	2	2	2	2	1	2	1	1	1	1	1	2	1	2	1	1,6	2	2	2	2	2	2	2	1	2	2	1,4	2

29	3513	12	1	IHD with complete Heart Block	1	1	2	2	2	1	2	2	2	1	1	1	2	2	1	2	4	2	2	1	2	2	1	1	2	2	2	3,6,7	2
30	4405	4	1	Subdural hemorrhage	2	1	2	1	1	1	1	2	2	2	1	2	2	1	2	2	7	1	1	1	1	1	1	1	1	1	1	3,4,5	1
31	4689	10	1	Stroke with MCA teritory infarct	1	2	2	2	2	1	1	1	1	2	1	2	2	2	1	1	5	2	2	1	1	2	2	1	1	1	2	1,3	2
32	9882	5	2	DVT with CCF	2	1	2	2	2	1	2	2	2	1	1	1	2	2	1	2	3	2	1	1	2	2	2	1	1	1	1	1,7	1
33	10325	17	2	Acute Febrile Illness	1	1	2	2	2	1	2	1	1	1	1	2	2	1	2	1	1,3	2	2	2	2	2	2	1	2	2	2	1,2	2
34	10932	12	2	IHD with DKA	1	2	2	2	2	1	1	2	2	2	1	2	2	2	1	2	1	2	2	1	2	2	1	1	1	2	1	1,2	1
35	11605	4	1	Acute Febrile Illness	2	2	2	2	2	1	2	1	1	1	1	1	2	1	2	1	2	2	2	2	2	2	1	1	1	1	2	1,2	1
36	12672	6	2	Seizure disorder	1	1	2	2	2	1	1	2	2	2	2	1	2	1	2	2	5	2	2	2	2	2	1	2	1	1	1	1,7	1
37	13627	1	1	Seizure disorder with ARF	2	1	1	2	2	1	1	1	1	2	1	1	1	1	2	1	1,6	2	2	1	2	2	1	2	2	2	2	11	1
38	14736	13	1	IHD with LVF	1	1	2	2	2	1	2	1	1	1	1	1	2	2	1	1	4	2	2	2	1	2	2	2	2	2	2	7,8	2
39	16095	4	1	G.B Syndrome	2	2	2	2	2	1	1	2	2	1	1	2	2	1	2	2	2,3	2	2	2	2	2	2	1	1	2	2	1,2	1
40	16918	4	1	Cirrhosis of Liver	2	2	2	2	1	1	1	1	1	2	1	1	2	2	1	1	4	2	2	2	1	2	2	2	2	2	2	8	1
41	18225	9	2	Myocardial Infarction	1	2	2	2	2	1	2	2	2	1	1	1	2	1	2	2	1	2	2	1	2	2	1	2	2	2	1	7,11	1
42	18859	12	2	Encephalitis	2	1	2	2	2	1	1	1	1	2	2	1	2	1	2	1	1,5	2	2	1	1	2	1	2	2	2	1	6,7	2
43	18579	7	2	Myasthenia Gravis	1	2	2	2	1	1	1	2	2	1	1	2	2	2	1	2	4	2	2	2	1	2	2	2	2	2	2	8	1
44	19955	3	1	Hypocalcemic Periodic Paralysis	2	2	2	2	2	1	2	2	2	2	2	1	2	2	1	2	3,6	1	2	2	2	2	2	1	1	2	1	1,2	1
45	20287	1	1	Organophosphorus Poisoning	2	2	2	2	2	1	1	1	1	2	1	1	2	1	2	1	1	2	2	1	2	2	1	2	2	2	2	6,7	1
46	21871	3	1	Organophosphorus Poisoning	2	2	2	2	2	1	1	1	1	2	1	2	2	1	2	1	4	2	2	2	1	2	2	2	2	2	2	8	1
47	22465	3	1	Cirrhosis of Liver	2	2	2	2	1	1	2	2	2	2	1	1	1	1	2	2	1	2	2	2	2	2	2	2	2	2	2	1,7	2
48	22847	13	1	Stroke	1	1	2	2	2	1	1	2	2	2	1	1	2	2	1	1	1	2	2	2	2	2	2	1	1	2	2	1,2	2
49	23431	2	2	G.B Syndrome	2	2	2	2	1	1	1	2	2	2	1	1	2	2	1	2	3,5	2	1	1	2	2	2	1	1	2	1	2,11	1
50	24269	4	1	Meningitis	2	2	2	2	2	1	1	1	1	2	1	1	2	1	2	1	1,3	2	1	1	2	2	1	1	2	2	2	3,6	1