"VENTILATOR ASSOCIATED PNEUMONIA: STUDY OF CLINICAL PRESENTATIONS, ORGANISMS INVOLVED AND OUTCOME."

By

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Dissertation Submitted to the

Sri Devaraj Urs University, Kolar,

Karnataka

In Partial fulfillment

Of the Requirements for the Degree of

M.D

In

GENERAL MEDICINE

Under the guidance of

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April 2011

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to be submitted to the Sri Devaraj Urs University, Kolar, Karnataka

Signature of Member Secretary

ACKNOWLEDGEMENT

It is with deep sense of gratitude and respect, I have taken an opportunity to thank my teacher and guide **Dr. P. N. Venkatarathnamma**, M.D, Professor, Department of General Medicine, Sri Devaraj Urs Medical College, Tamaka, Kolar, for her constant inspiration and valuable guidance at various stages of preparation of this dissertation.

I express my gratitude to **Late Dr. Prof. A. R. Patil ,** professor & director of post graduate studies for his encouragement invaluable inputs for the study.

My sincere thanks to **Dr. Prof. V Lakshmaiah** M.D. H.O.D. Dept of General Medicine, and all other staff members without whose excellent guidance and constant encouragement, this study would not have been possible.

I express my deep sense of gratitude and humble thanks to **Dr. K. Prabhakar, Dr. B.N. Raghvendra Prasad, Dr. Srinivasa Rao, Dr. Raveesha A,** Professors, for their advice and encouragement throughout the present study.

I thank **Dr Paawan Wadhawan** for his constant source of encouragement, and help during the period of my study. I thank **Mr. K P Suresh** for the statistical help rendered to me for the analysis of this study.

I thank all my colleagues for having rendered their co-operation during the study.

I would like to acknowledge the opportune help and permission rendered by the Medical Director, Principal and Medical superintendent, SDUMC/RLJH, in conducting this study. I thank my parents for their constant support. Lastly, I thank everyone concerned including the patients for their co-operation without which this dissertation would have never materialized.

Signature

Dr. Chandan Bansal

LIST OF ABBREVIATIONS USED

VAP	Ventilator-Associated Pneumonia
HAP	Hospital-Acquired Pneumonia
ICU	Intensive Care Unit
CDC	Centers for Disease Control
HICPAC	Hospital Infection Control Practices Advisory Committee
SDD	Decontamination Of The Digestive Tract
CFU	Colony Forming Unit
ETA	Endo Tracheal Aspirate
PSB	Protected Specimen Brush
BAL	Bronchoalveolar Lavage
ET	Endotracheal Tube
MRSA	Methicillin Resistant Staph Aureus
LUZ	Left Upper Zone
LMZ	Left Middle Zone
LLZ	Left Lower Zone
RUZ	Right Upper Zone
RMZ	Right Middle Zone
RLZ	Right Lower Zone

ABSTRACT

TITLE OF THE STUDY: "ventilator associated pneumonia: study of clinical presentations, organisms involved and outcome."

INTRODUCTION: During the past 30 years our ability to care for critically ill patients has improved greatly, in part due to the expanded use of invasive techniques such as tracheal intubation and mechanical ventilation. Unfortunately, the widespread application of these techniques has resulted in increasing new nosocomial infection hazards, such as ventilator associated pneumonia (VAP).

OBJECTIVE: To study the occurrence, risk factors and outcome of ventilator associated pneumonia in Intensive Care Unit of R. L. Jalappa hospital and Research Center, Tamaka, Kolar attached to Sri Devaraj Urs Medical College.

MATERIAL AND METHODS: The study of ventilator associated pneumonia is a prospective noncontrolled observational study. A total of 50 patients of VAP were evaluated during the study period and different parameters analyzed.

RESULTS: It was found that crude mortality rate was 38%. Most of the patients were in age group of 30 – 50 years with male dominance. Right lower zone was most commonly involved and had statistically significant mortality rate. *Pseudomonas aeruginosa* was the commonest organism cultured in the Endo Tracheal Aspirate and mortality associated with it was higher although not statistically significant. Most effective antibiotic overall was Imipenam in the study group. The data obtained in the given study were comparable to the contemporary studies done.

KEYWORDS: Ventilator Associated Pneumonia, Mechanical Ventilation, Antibiotics.

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INTRODUCTION

For more than a century, it has been known that patients acquire infections in the hospital. These infections are variously referred to as cross infection, hospital acquired infection and nosocomial infection. Ventilator-associated pneumonia (VAP), an important form of hospital-acquired pneumonia (HAP), specifically refers to pneumonia developing in a mechanically ventilated patient more than 48 h after tracheal intubation or tracheostomy.

Ventilator associated pneumonia (VAP) is associated with prolonged mechanical ventilation, increased duration of intensive care unit (ICU) stay and highest mortality rate of all hospital acquired infections.[4] VAP occurs approximately in 9-27% of all intubated patients.[4,10] VAP may be caused by a wide spectrum of bacterial pathogens, which may be polymicrobial and are rarely due to viral or fungal pathogens in immunocompetent hosts.[4] Common pathogens include aerobic gram-negative bacilli, such as *Pseudomonas aeruginosa* , *Escherichia coli* , *Klebsiella pneumoniae* and *Acinetobacter* species.[4] Selection of appropriate antibiotics in the initial stages is an important determinant of clinical outcome. Various studies have shown that as much as 50% of antibiotic use is inappropriate.[3] Use of appropriate antibiotics directed towards the most prevalent organism not only improves the cure rate and survival but also reduces the emergence of resistant strains.[3,4] Given the rapid emergence of antimicrobial resistance and the limited number of new antimicrobial agents, clinicians treating patients with suspected ventilator-associated pneumonia not only must prescribe appropriate initial antimicrobial regimens to optimize outcomes but also must minimize the development of resistance by rigorously using a de-escalation strategy.[8] Over the past several decades our understanding of VAP has grown significantly with regard to pathogenesis, risk factors, diagnostic testing, therapies, and prevention by modifying risk factors.[10] There is still a great paucity of data on incidence, risk factors and aetiology of VAP. There is also lack of studies on antimicrobial susceptibility of the microorganisms causing VAP. There is also need to know the organisms causing VAP in a particular institution, as they may differ in different institutions. The knowledge of these factors will help in the prevention and management of VAP. The incidence of patients who are being admitted to ICU and requiring mechanical ventilation is increasing. To date, however, there are very few studies in India evaluating VAP.

Knowledge of the incidence of VAP, risk factors implicated, and causative microbial flora in the local setting would be immensely helpful in management of these patients to improve outcome.

AIMS AND OBJECTIVES

1. To study the occurrence and risk factors of VAP.
2. To study the clinical profile of the patients with VAP.
3. To study the outcome of the patients developing VAP.
4. To study the factors associated with increased mortality in patients developing VAP.

REVIEW OF LITERATURE

Patients in the intensive care unit (ICU) are at risk for dying not only from their critical illness but also from secondary processes such as nosocomial infection.

DEFINITION

VAP is defined as the occurrence of new and persistent radiographic infiltrate not otherwise explained, appearing on chest radiograph > 48hrs after onset of mechanical ventilation (or) within 48 hrs of extubation , and any two of the three criteria are met.[3,4,7,8,9,10.]

1. Fever with temperature more than 38^{o}C or hypothermia with temperature of less than 35^{o}C.
2. Increased peripheral total leukocyte count (more than 16000/mm^{3}) or leucopenia (less than 3000/mm^{3}).
3. Positive endotracheal tube culture.

CLASSIFICATION

It is commonly classified as either early onset (occurring within 96 hours of start of mechanical ventilation) or late onset (>96 hours after start of mechanical ventilation). [3,5,10.]

Early-onset ventilator-associated pneumonia is most often due to antibiotic-sensitive bacteria (e.g., oxacillin-sensitive *Staphylococcus aureus*, *Haemophilus influenzae*, and *Streptococcus pneumoniae*), whereas late-onset ventilator-associated pneumonia is frequently caused by antibiotic-resistant pathogens (e.g., oxacillin-resistant *Staph. aureus*, *Pseudomonas aeruginosa*, *Acinetobacter species*, and *Enterobacter species*.[8,9,10.]

EPIDEMIOLOGY AND INCIDENCE

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For more than a century, it has been known that patients acquire infections in the hospital. These infections are variously referred to as cross infection, hospital acquired infection and nosocomial infection. Accurate information concerning the epidemiology of VAP is lacking, as there is no universally accepted criteria for

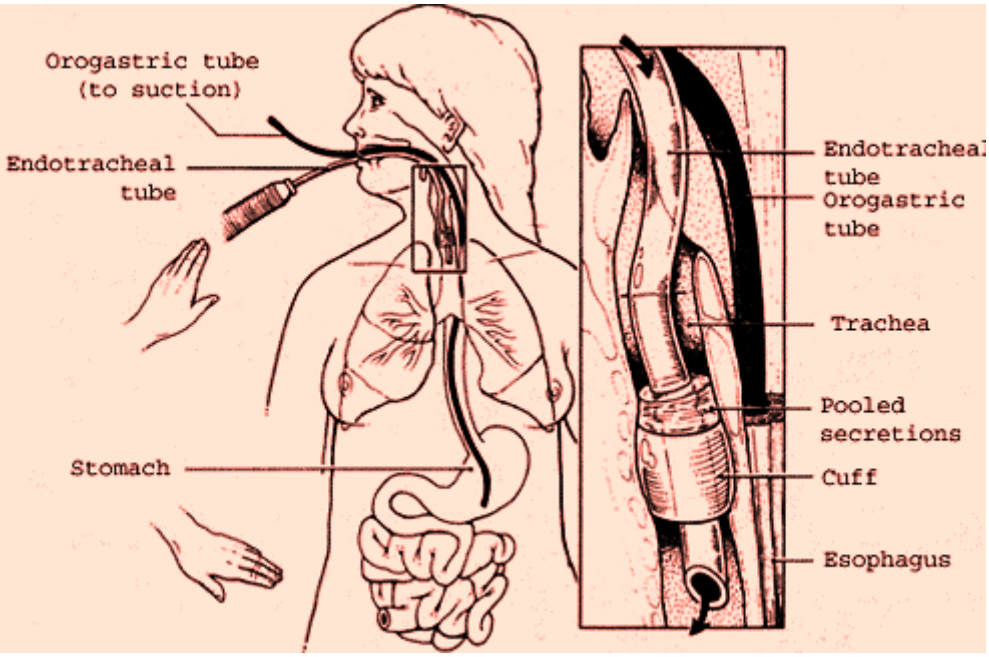
its diagnosis. Its incidence is also influenced by the case studied, and prior exposure to antibiotics. Nosocomial pneumonia is a leading cause of death from hospital-acquired infections, with an associated crude mortality rate of approximately 30 percent.[10] Pneumonia is the second most common nosocomial infection.[4,10,26.] VAP occurs approximately in 9-27% of all intubated patients. [4] Intubation of the trachea and mechanical ventilation is associated with a 7 to 21-fold increase in the incidence of pneumonia and up to 28% of patients receiving mechanical ventilation will develop this complication [6] The development of VAP prolongs the stay in the ICU and is associated with an increase in costs.[28] A study by Heyland and colleagues to determine the excess ICU stay attributable to VAP prospectively matched patients with VAP to patients who did not develop clinically suspected pneumonia. They found that the development of VAP was associated with an average of 4.3 days longer in the ICU than control subjects. Two other studies support these findings.[29,30.] The mortality attributable to VAP has been reported to range between 0 and 50%. [10] Beyond mortality, the economics of VAP include increased ICU lengths of stays (from 4 - 13 days), and incremental costs [10]

PATHOGENESIS

Pneumonia represents the host's inflammatory response to the microbial invasion of the normally sterile lung parenchyma. The magnitude of this response depends on the size and type of the inoculum, the virulence of the organisms involved, and the competence of the host's immune system.[6]

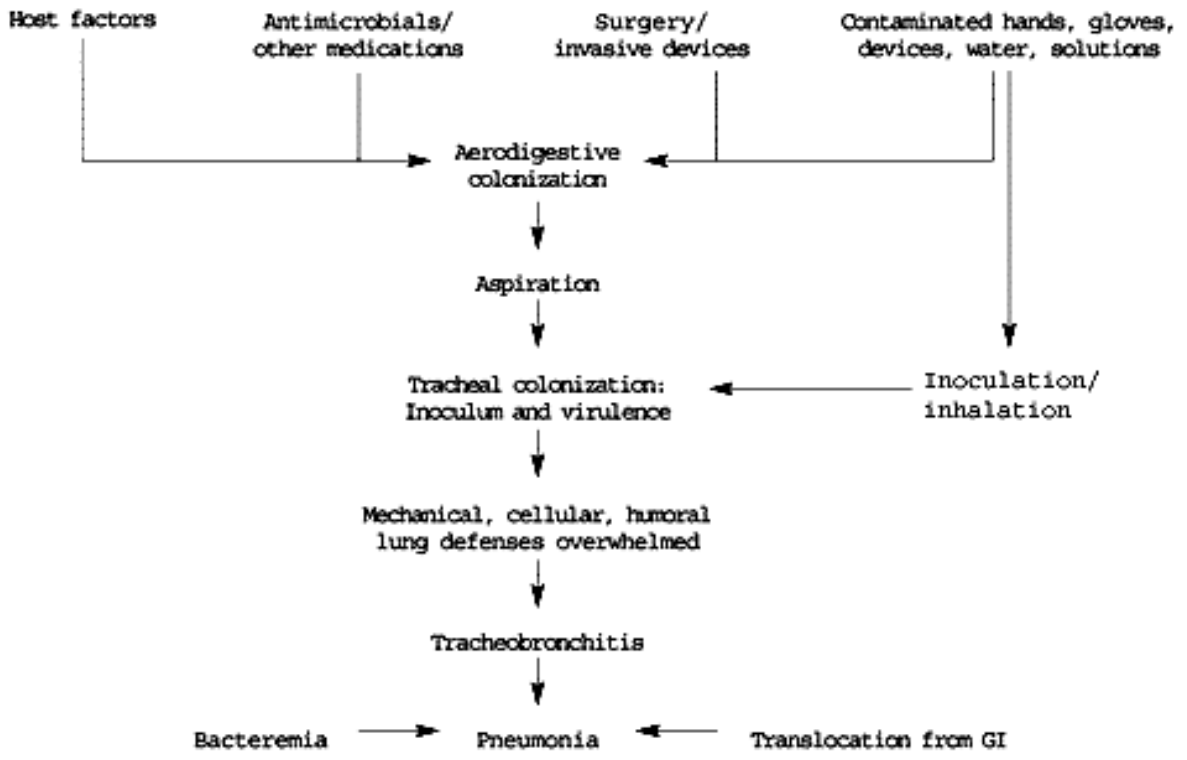
Most cases of VAP are caused by the aspiration of infected secretions from the oropharynx, although a small number of cases may result from direct bloodstream infection.[31,32.] Critical illness leads to the rapid colonisation of the oropharynx with potentially pathogenic bacterial adhesins or host surface receptors. It remains contentious whether the aspiration of infected material from the stomach plays an important part in the development of VAP.[33,34,35.] However, alkalinisation of the normally acid environment in the stomach leads to overgrowth with Aerobic Gram negative bacteria, providing a potential pool of infected material.[36] The presence of the cuff on the tracheal tube does not prevent the passage of infected material into the airways. Contaminated secretions pool above the high volume low pressure cuff of the tracheal tube commonly used in ICU, and gain access to the trachea along folds in the cuff. These organisms can then gain

access to and colonise the bio film that rapidly coats the inner surface of the tracheal tube. This is commonly followed by colonisation of the trachea with pathogenic organisms.



The infected material is then propelled into the distal airways by the inspiratory flow provided by the mechanical ventilator. Occasionally, contaminated nebulisers, ventilation circuits or humidifiers may be the source of the infected material.[37,38,39.]

A variety of defence mechanisms exist that protect the lung from infection including non-immune antimicrobial agents in saliva, an intact cough reflex, mucocilliary clearance, and cell mediated and humoral immunity. Indeed, healthy adults frequently aspirate oropharyngeal secretions with impunity because of host defence mechanisms. However immune dysfunction is well reported in the critically ill and many of these host defence mechanisms are ineffective.[40] When infected material reaches the distal airways, the immune mechanisms within the lung attempt to inactivate or kill the offending organisms. Alveolar macrophages, neutrophils, and elements of the humoral immune system interact to mount an inflammatory response. [41,42] If the host's immune system is overwhelmed, then pneumonia develops.



Acute lung injury and acute respiratory distress syndrome are commonplace in the critically ill and are associated with profound changes in the structure and functioning of the alveoli. Martin and colleagues showed that the function of neutrophils obtained from bronchoalveolar lavage fluid of patients with acute respiratory distress syndrome is significantly impaired.[43] These changes impair the ability of the lungs defence mechanisms to deal with a bacterial challenge. Pulmonary oedema and alveolar haemorrhage also provide a favourable environment for the proliferation of bacteria.[44]

RISK FACTORS

Multiple factors have been identified that increase the likelihood of developing VAP.

1. **AGE:**

   Risk of incidence of nosocomial pneumonia increases after 40-50 years.[45]

It is because of the impaired respiratory defence mechanism and because of increased risk of silent aspiration of the respiratory secretions in these patients due to decreased gag and cough reflex[46] and decreased immune mechanism.

2. **SMOKING**:

Cigarette smoke blunts the effectiveness of both nonspecific (phagocytosis, mucocilliary transport system) and specific (immunological) defence system of the lung. This impairment may contribute to the smokers increased susceptibility to pulmonary infection.

3. **ALCOHOL:**

Alcohol is associated with increased risk of nosocomial pneumonia as alcohol impairs pulmonary defence mechanism by depressing mucocilliary transport system,[48] decreasing surfactant production,[49] decreasing alveolar macrophage function[50] and by inhibiting polymorphonuclear migration into the lung.[51] This might contribute to increased incidence of nosocomial pneumonia in alcoholic patients.

4. **SURGERY**:

Surgical patients are at higher risk of developing nosocomial pneumonia. The risk is 58 times greater for combined thoracoabdominal operations than for those not involving either area, 14 times greater for thoracic and 3-4 times greater for abdominal operations.[45,53] Probably the impairment of effective pulmonary toilet and inability to clear airways by coughing and deep breathing are responsible for mechanism for increasing risk of pneumonia in postoperative thoracoabdominal surgical patients.

5. **UNDERLYING DISEASES OR COMORBIDITIES** :

Pierce and Sanford showed increased incidence of gram negative pneumonia in patients with underlying disease condition which included heart disease, alcoholism, renal disease and diabetes mellitus.[54] One study showed that underlying neurological and renal disease, liver disease and collagen vascular disease have increased incidence of nosocomial pneumonia.

6. **IMMUNOCOMPROMISED STATUS**:

Immunocompromised status means underlying disease or therapy that impairs host defence to infection. Nosocomial pneumonia is very common among immunocompromised patients.[56]

Administration of corticosteroids or cytotoxic drugs may alter alveolar macrophages and polymorphonuclear leucocytes number and function and thereby predisposed to infection.

7. **COMA** *:*

Unconscious patients are at high risk of aspiration because of depressed cough and gag reflex and the frequent need for tracheostomy in these patients to keep the tracheobronchial tree free of excess secretion.[59] Patients who remain in one position for a long time develop bronchopneumonia attributed to hydrostatic fluid shift in the lung from hypo ventilation and from atelectasis secondary to elevated diaphragm. These patients are also prone to develop gastric dilatation which makes aspiration more likely[59]

8. **POSITION** *:*

In mechanically ventilated patients supine position promotes the development of nosocomial pneumonia by aspiration of gastric contents. Studies have shown that this aspiration can be decreased by simply placing the patient in semi recumbent position[60] or by periodic lateral rotational therapy.[61]

9. **AIRWAY INTUBATION** *:*

With endotracheal tube intubation there occurs a breach in continuity of mucous membrane and presence of multiple desquamated cells. Bacteria tends to adhere well to these cells thereby increasing risk of nosocomial pneumonia.[47] The endotracheal tube bypasses aerodynamic filtration mechanism (nasal secretions & conchi) thereby leading to direct exposure to ventilatory circuit. Also endotracheal tube impedes coughing and allows leakage around the cuff of oropharyngeal secretion into the tracheobronchial tree.[62] Rigorous suction may dislodge bacteria stuck to the distal end of the endotracheal tube. It is found that the incidence of nosocomial pneumonia increases with more than one intubation.[63] Changing the endotracheal tube may facilitate the aspiration of oropharyngeal secretion accumulated in the posterior oropharyngeal wall.[64] Spray and coworkers found that ventilation with high volume low pressure cuff tube there is decrease incidence of

aspiration.[62] In tracheostomy patients pneumonia is commonly due to break in the sterile technique during care and suctioning of the tube. Reflex glottic closure is interfered by a tracheostomy in place. Inflated cuff partially occlude the oesophagus making it difficult for the patient to swallow the saliva. Moreover periodic deflation of the cuff increases chance of aspiration.

10. **MECHANICAL VENTILATION** *:*

The risk of pneumonia in patients receiving mechanical ventilation increased with time. It is around 5% in patients receiving 1 day of ventilation, to 68.8% in patients receiving ventilation for more than 30 days. Risk of infection is high in the first 8-10 days.[4] Fagon and coworkers found that incidence rises with longer time on ventilator from 6.5% at 10 days to 19% at 20 days and 28% at 30 days. They estimated increasing risk of 1% per day of mechanical ventilation.[10] change of ventilator circuits every 24 hours vs. 48 hours is associated with increased risk.[65] The Centers for Disease Control/Hospital Infection Control Practices Advisory Committee (CDC/HICPAC) guideline recommends that mechanical ventilator breathing circuits be changed no more frequently than every 48 hrs.[65,66] The increased incidence of pneumonia in mechanically ventilated patients is due to increased colonization and subsequent risk of aspiration. Gastric colonization serves as an important source for colonization in trachea. Another factor could be contaminated condensate in ventilator circuits as shown by the study in which there was rapid colonization of the tubings after a circuit change. 33% were colonized at 2 hours, 64% at 12 hours and 80% at 24 hours.[67]

11. INHALATION THERAPY EQUIPMENT:

Inhalation therapy equipment may potentially act as a vector of hospital acquired pneumonia. The major mechanism by which bacteria are disseminated is aerosolisation of organisms that are sufficiently small to be deposited in the terminal lung units. ' Large volume nebulizers are the primary source of aerosolized bacteria.[69,70] There has been reported outbreak of

hospital acquired pneumonia due to medication nebulizers.[70,73] According to Cravin and coworkers nebulizers in line with ventilator circuits have high degree of contamination around 68% and this can be directly deposited into the patients respiratory tract with increased incidence of pneumonia.[74]

12. **NASOGASTRIC TUBE FEEDING** *:*

Nasogastric tube increases the risk of nosocomial pneumonia. The Nasogastric tube disrupts normal oesophagogastric barrier thus allowing small inoculums to reflux and get aspirated Nasogastric tube acts as a conduit for bacteria to ascend from stomach to pharynx. Kingston and workers have found incidence of aspiration in mechanically ventilated patients with nasogastric tube feed to be 21% and 75% of these develop pneumonia.[75] Winterbuer, et al showed that subclinical aspiration in patients with nasogastric tube is about 95%, 32% of these develop respiratory signs.[76] Enteral feeding is a simple non invasive approach to nutritional therapy. Enteral feeding decreases the gastric acidity by neutralization of gastric acid, enabling colonization of stomach which further causes oropharyngeal and tracheal colonization thereby increasing the risk of nosocomial pneumonia. Some investigators have postulated that administration of Enteral feeding with high pH via the oral gastric tube may increase gastric colonization, volume, pressure, reflux and pneumonia. Harkness and coworkers showed the risk of nosocomial pneumonia was 3 fold in patients with nasogastric tube.[46]

13. **HISTAMINE$_2$ RECEPTOR ANTAGONIST***:*

Routine treatment with histamine$_2$ receptor antagonist is associated with increased risk of nosocomial pneumonia as shown by Cravin and coworkers.[77] Antacids and Histamine$_2$ receptor antagonist inhibit peptic activity and decrease acid secretion allowing overgrowth of gram negative bacilli,[78] and retrograde colonization of the oropharynx thereby increasing the risk of nosocomial pneumonia. Torres and coworkers showed a two-fold increase of nosocomial pneumonia in patients treated with antacids or H_2 receptor antagonist.[63] DuMolin et al found the stomach to be the reservoir of organism which causes tracheal colonization in patients receiving antacids or Histamine$_2$ receptor antagonist. Rates of VAP are significantly lower in persons given sucralfate compared to antacids and/or H_2 blockers, as demonstrated by Tryba et al. This may be related to the fact that compared to antacids and H_2 blockers; sucralfate does not have a major effect on gastric pH., thereby decreasing bacterial colonization.

14. **ANTIBIOTICS***:*

Empirical therapy with antibiotics suppresses normal residual bacterial flora of the oropharynx resulting in colonization with gram negative organism. Sprunt and Redman gave penicillin and streptomycin to 10 patients prior to cardiac surgery and found all to be colonized with gram negative rods. Within 10 days of stopping antibiotics most of the flora returned to normal with disappearance of gram negative rods. Antibiotics also have deleterious effects on humoral and cellular immunity increasing the likelihood of nosocomial pneumonia.[79] Steven and workers showed occurrence of enterococcal pneumonia as super infection in patients receiving broad spectrum antibiotics.[80]

15. **PARALYTIC ILEUS***:*

In a study of 10 patients on mechanical ventilation who had paralytic ileus, oropharyngeal colonization occurred in all 10 patients.[42]

16. NUTRITION*:*

In a study by Garibaldi, low serum albumin was taken as a marker for malnutrition was associated with increased risk of hospital acquired pneumonia in postoperative patients.[47] Poor nutritional status has shown to increase risk of colonization by Pseudomonas aeruginosa. In a study by Hanson et al, poor nutrition indicated by serum albumin <3 g/dl was associated with significantly increased risk of nosocomial pneumonia. This increase may be due to increase in tracheal cell binding capacity of the organism in malnourished patients.[83]

PREVENTION

As VAP is associated with considerable mortality and morbidity despite adequate antibiotic therapy, prevention of such infection is mandatory. Many studies suggest different methods by which incidence of VAP can be decreased. Some of the methods are listed below:

1. To classify patients on basis of severity of underlying disease on admission and to keep in mind the increased incidence of nosocomial pneumonia in such patients.[96]

2. Use of disposable respiratory therapy equipment, small dose medication vials, proper and frequent cleaning of non disposable equipment decreases the risk considerably.[8]
3. Decontamination of respiratory therapy equipment should be carried out at least once every 24 hours while the equipment is in use.[73] In line nebulizers used along with mechanical ventilation should be cleaned after each treatment rather than after 24 hours.[74]
4. Simple measures like checking the potency of nasogastric tube, controlling the rate of tube feed, proper positioning of patient in bed, suctioning of mouth and pharynx in patients with tracheostomy, cleaning mouth of any vomitus that might have occurred and paying proper attention to suctioning techniques can significantly decrease risk of pneumonia in the ventilated patients.[47,59] Periodic changes of endotracheal tube should be discouraged. In addition, careful oral or nasotracheal suctioning above the cuff before removing the tube should be routinely followed.[63]
5. Sucralfate when used as a prophylactic agent for stress ulcer as compared to antacids or Histamine$_2$ receptor antagonist decreases incidence of nosocomial pneumonia by maintaining acidity of the stomach and preventing colonization.[97,116,117] Some evidence suggest it may also have some antibacterial action.[99]
6. Strict hand washing technique has shown to decrease incidence of pneumonia and they should be followed even on minimum contact with the patient.[100,101]
7. Enteral feed contains many organisms that might cause nosocomial pneumonia. Hence enteral feeding for patients in intensive care unit should be prepared under strict aseptic precautions.[102]
8. Positioning the patient on one side with the foot end of the bed raised by 6-9 inches on wooden blocks, a pillow between the legs and against the back and nothing under the head decreases oropharyngeal secretions and prevents aspiration.[59]
9. Various decontamination procedures using medications has been tried, both local and systemic.
    i. Instillation of polymyxin used as aerosol substantially decrease the incidence of nosocomial pneumonia caused by Pseudomonas aeruginosa.[103,104,105] These studies showed there was no substantial increase in colonization of the pharynx with resistant organisms following polymyxin aerosol. Some studies show that this form of prophylaxis lead to emergence of polymyxin resistant organisms which have a high mortality rate of about 64%.

ii. Instillation of Gentamicin through the endotracheal tube has also shown to decrease the incidence of pneumonia, but at the cost of emergence of resistant strains.[106]

iii. Many studies have shown selective decontamination of the digestive tract (SDD) to decrease incidence of respiratory tract infection.[101,108,109,110] SDD showed significant reduction after decontamination of the oropharynx and pharynx with polymyxin, Gentamicin and Nystatin of colonization of the oropharynx and stomach with no increase in resistant strains.[109] SDD was tried on one study to control outbreaks of Klebsiella and was found to be effective. In this, SDD consisted of tobramycin, amphotericin and colistin as gel applied to oropharynx, nose and rectum and a suspension via the nasogastric tube into the stomach.[101]

iv. One study had shown that oropharyngeal decontamination decrease incidence of nosocomial pneumonia by a factor of 5. [111] On the contrary Castenne and co-workers showed that SDD does not improve survival in mechanical ventilated patients in intensive care units. It only substantially increases the cost of their care.[112]

10. Vaccines have been tried to decrease incidence of pneumonia in high risk patients. Immunization of patients against Pseudomonas aeruginosa was quite effective in reducing the incidence of infection with that organism.[113] Pneumococcal vaccine decreases the incidence of pneumonia in high risk patients, elderly patients with underlying disease and Immunocompromised patients.[114,115]

MICROBIOLOGICAL DIAGNOSIS

A number of specialized microbiologic methods and also several invasive methods for obtaining specimens have been described as potentially useful for improving diagnostic specificity for VAP.

Noninvasive modalities

The concentration of organisms necessary to cause pneumonia varies in relation to the virulence of the bacteria and the competence of the host defenses. Once bacterial infection of the lung are manifest clinically, they ordinarily contain at least 10^4 CFU/g of tissue (colony forming unit) and 10^5 or more bacteria/ml in patients without antibiotic.[129,136] Quantitative culture with a low colony count in patients not receiving antibiotic treatment is likely to indicate contamination or colonization. A colony count greater than or equal

to 10^5 CFU/ml was seen in the majority of patients with pneumonia but also in 40% of patients without pulmonary infection.[90] The presence of elastin fibers in the endotracheal aspirate was highly specific for the presence of necrotizing pneumonia[90] (100%), however was not very sensitive (52%).

Endotracheal aspirate is the simplest method of obtaining secretions in patient on mechanical ventilation.

Invasive methods

Because of the well known inaccuracy of routine sputum cultures in diagnosing pneumonia, physicians have been researching new techniques to obtain samples from the lower respiratory tract free from contamination by upper respiratory tract bacteria.

Bronchoscopy provides direct access to the lowest airways for sampling bronchial and parenchymal tissue. To reach the bronchial tree, however the bronchoscope must traverse the endotracheal tube and proximal airways where contamination is likely to occur. Therefore distal secretions directly aspirated through the bronchoscope suction channel are frequently contaminated, thereby limiting their clinical specificity. To reduce contamination of lower airway rates collected by Bronchoscopy, Wimberley and colleagues[129,136] developed the ***protected specimen brush (PSB)*** technique. It consists of a special double catheter brush system with a distal occluding plug to reduce contamination of lower airway aspirates, and concentration of $>10^3$ CFU/ml in PSB specimen indicates significant infection of the lung.[136] The clinical utility of PSB has been studied by Fagon et al, in a large group of intubated patients, most ventilated for respiratory insufficiency after cardiac surgery.[129] The predictive value of a positive PSB culture ($>10^3$ CFU/ml) was greater than 75%.

Recently two modifications of the PSB technique were proposed, nonbronchoscopic method to perform protected brushing, using a metras catheter through an endotracheal tube, second is plugged telescoping catheter used with or without fibreoptic bronchoscopy.

Bronchoalveolar lavage (BAL) is useful in establishing the diagnosis of bacterial pneumonia. Lavage is a safe and practical method for obtaining cells and secretions from the lower respiratory tract. The technique obtains samples from a relatively large area of the lung, and the cells and liquid recovered can be examined microscopically immediately after the procedure and are also suitable for culture using quantitative techniques.

ETIOLOGIES

Microbiology of nosocomial pneumonia differs from that of community acquired pneumonia. Although bacteria are most commonly isolated, diagnostic cultures for viruses, legionella, anaerobes and fungi are not routinely performed.

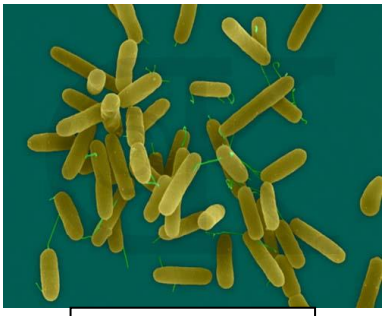
According to the National Nosocomial Infection Surveillance System Data of 1984, aerobic gram negative organisms account for 50-60% of all nosocomial pneumonia with Pseudomonas aeruginosa and Klebsiella being the most frequently recovered gram negative bacilli. Staphylococcus aureus is the most frequent gram positive organism. Streptococcus pneumoniae accounted for <3% of isolates.[119]

Fagon and coworkers showed that in patients receiving mechanical ventilation, Pseudomonas aeruginosa, acinetobacter and proteus species were the predominant gram negative bacilli isolates. At least one gram positive organism was isolated in 52% of episodes; approximately 40% of infections were polymicrobial.[125]

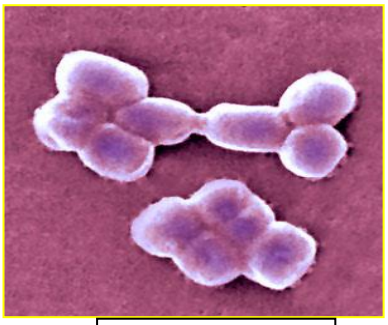
Study by Rello et al revealed the impact of previous antimicrobial therapy on the etiology and outcome of VAP. The rate of VAP caused by gram positive cocci or Haemophilus influenzae was statistically lower in the patients who had received antibiotics previously, while the rate of VAP caused by Pseudomonas aeruginosa was statistically higher.[85]

Fagon et al in a study showed prior antibiotic therapy increased the rate of pneumonia caused by Pseudomonas aeruginosa or acinetobacter species which was 65% in the group received antibiotic compared to 18% in the group which did not receive prior antibiotic.[125]

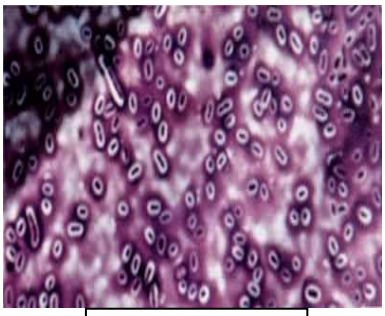
MICRO-ORGANISMS COMMONLY INVOLVED IN PATHOGENESIS OF VAP



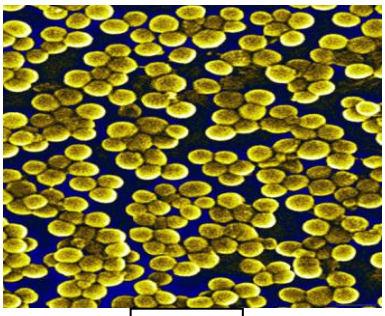
Pseudomonas aeruginosa



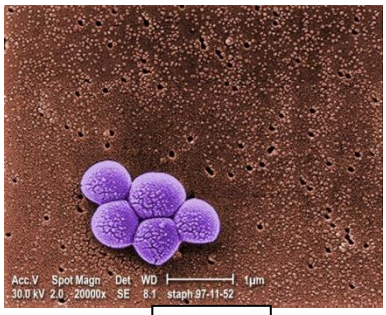
Acinetobacter baumannii



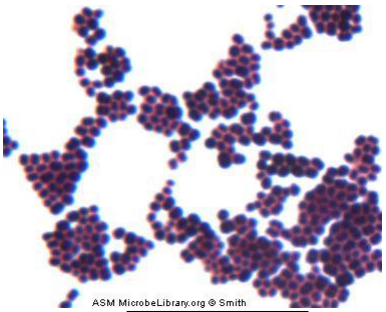
Klebsiella pneumonia



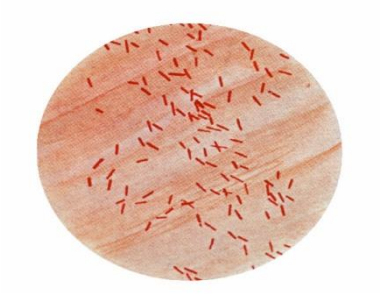
MRSA



MRSA



Staph. epidermis



E. coli

Candida albicans

METHODOLOGY

DESIGN : - Prospective study

SOURCE OF DATA

Patients who were admitted to Intensive care unit of R.L.Jalappa Hospital and Research Center, Tamaka, Kolar attached to Sri Devaraj Urs Medical College.

DURATION

Data collection 20 months (January 2009 to August 2010) Data analysis 2 months (September 2010 to October 2010).

INCLUSION CRITERIA

- Age greater than 18 years.
- Those on mechanical ventilation for more than 48 hours.

EXCLUSION CRITERIA

- Pre-existing pneumonia at the beginning of the ventilation.
- Developing VAP within 48 hours of ventilation**.**
- Age less than 18 years.

DIAGNOSTIC CRITERIA

VAP was diagnosed in patients when new and persistent pulmonary infiltrates (not otherwise explained) appeared on chest radiograph after 48hrs of ventilation and any two of the three criteria were met.[3,4,7,8,9,10.]

4. Fever with temperature more than $38^{o}C$ ($100.4^{0}F$) or hypothermia with temperature of less than $35^{o}C$ (95^{0} F).

5. Increased peripheral total leukocyte count (more than 16000/mm^3) or leukopenia (less than 3000/mm^3).

6. Positive endotracheal tube aspirates (ETA) culture.

METHOD OF COLLECTION OF DATA

All relevant data including gender, age, and admission diagnosis were noted. History of pre-existing diseases like Diabetes Mellitus, Hypertension, COPD, Ischaemic Heart Disease and previous admission to hospital and present symptomatology was listed and detailed physical examination was done. Details of medical interventions were recorded.

The diagnosis of VAP was made according to clinical and laboratory findings (as per the diagnostic criteria)

Investigations comprising complete blood count, biochemical tests including blood sugar, creatinine, liver function tests, Chest X Ray Sputum Grams stain and culture, blood and Endotracheal Tube Aspirate culture were listed and analysed, as per proforma.

SPECIFIC SAMPLING PROCEDURES EMPLOYED IN THE STUDY

Endotracheal Tube Aspirate Culture: - On making a diagnosis of ventilator associated pneumonia ETA was obtained for microbiological semi quantitative assay. After hand washing with soap and water for two minutes and wearing sterile gloves, the intracath was introduced through the ET and advanced beyond the carina, to collect the lower respiratory tract secretions into a mucus trapper. In the laboratory 0.001 ml of collected sample was directly inoculated on the blood agar, chocolate agar and Mc Coney's agar. Following overnight incubation at 37^0C, the media were examined for any growth and subsequently at 24,48,72,96 hours and 7 days. A quantitative count of greater than 10^5 cfu/ml was labelled [as] infection[138]. Colonisation was defined as isolation of microorganism where CFU was < 10^5 cfu/ml.

The sensitivity pattern was studied by 'modified Stroke's disc diffusion method'. The tip of the ET was also sent for microbiological assay as and when the patients were extubated as per clinical need.

RISK FACTORS FOR VAP STUDIED

Duration of intubation, duration of mechanical ventilation, tracheostomy, use of nasogastric tube feeding, use of sedative drugs, co morbid conditions like DM, COPD, HIV, sepsis were studied.

FOLLOW UPS

The patients were followed up for a minimum duration of 7 days after developing VAP.

STATISTICAL METHODS [152,153,154,155.]

Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups. 95% Confidence Interval has been computed to find the significant features. Confidence Interval with lower limit more than 50% is associated with statistical significance.

- **Fisher Exact test**

Let there exist two such variables X and Y, with m and n observed states, respectively. Now form an $m \times n$ matrix in which the entries a_{ij} represent the number of observations in which $x = i$ and $y = j$. Calculate the row and column sums R_i and C_j, respectively, and the total sum

$$N = \sum_i R_i = \sum_j C_j$$

of the matrix. Then calculate the conditional probability of getting the actual matrix given the particular row and column sums, given by

$$P_{\text{cutoff}} = \frac{(R_1!\, R_2! \cdots R_m!)\,(C_1!\, C_2! \cdots C_n!)}{N! \prod_{i,j} a_{ij}!},$$

which is a multivariate generalization of the hypergeometric probability function.

- **Chi-Square Test**

$\chi^2 = \frac{\sum(Oi - Ei)^2}{Ei}$, Where Oi is observed frequency and Ei is Expected frequency

$Z = \frac{(!\, p - p_0 !) - 1/2n}{\sqrt{p_0 q_0 / n}}$

- **95% Confidence Interval**

$P \pm 1.96^*$ SE(P), Where SE(P) is the Standard error of proportion = P*Q/√n

- **Significant figures**

+ Suggestive significance (P value: 0.05<P<0.10)

* Moderately significant (P value: 0.01<P ≤ 0.05)

** Strongly significant (P value: P≤0.01)

STATISTICAL SOFTWARE

The Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1 ,Systat 12.0 and R environment ver.2.11.1 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc**.**

The proforma used in the study is shown in the appendix…. A.

RESULTS

A Prospective clinical non-controlled study with 50 patients of ventilator Associated Pneumonia was undertaken to study the Clinical features, organisms and outcome. 50 cases of VAP were studied and the patients were selected from ICU of R. L. Jalappa hospital kolar attached to Sri Devaraj Urs Medical College between January 2009 and October 2010. The results of the study are as follows. :-

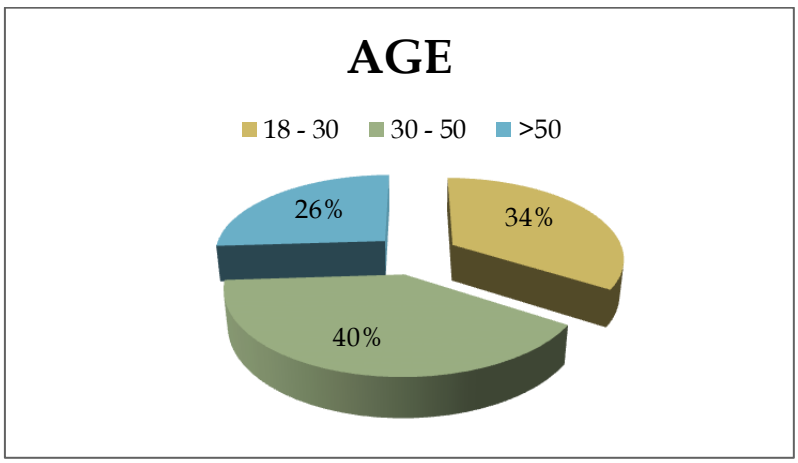
1. AGE DISTRIBUTION OF PATIENTS STUDIED

Majority of the patients with VAP were in age group 30-50 years. Minimum age found in the study group was 18 years.

TABLE - 1

Age in years	Number of patients	%
18-30	17	34.0
30-50	20	40.0
>50	13	26.0
Total	50	100.0

GRAPH - 1



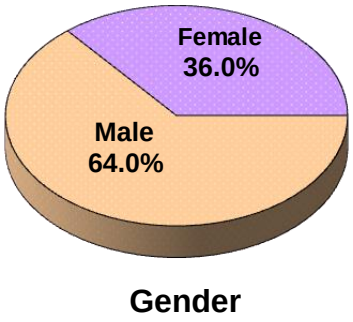
2. GENDER DISTRIBUTION OF PATIENTS STUDIED

In the study group males were more affected than females. The male: female ratio was 1.78: 1.

TABLE – 2

Gender	Number of patients	%
Male	32	64.0
Female	18	36.0
Total	50	100.0

GRAPH – 2



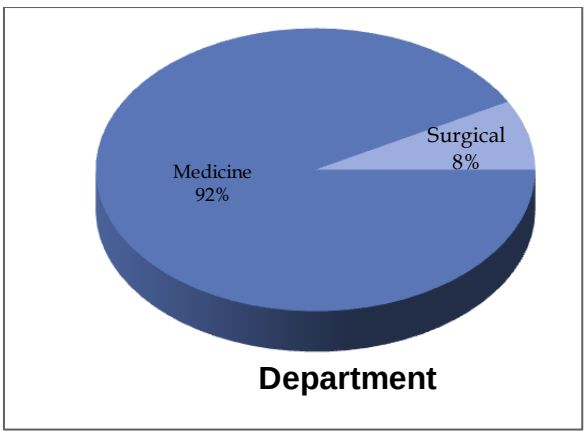
3. DISTRIBUTION OF DEPARTMENTS

Most of the patients selected were medical cases. i.e. 92 %.

TABLE – 3

Department	Number of patients	%
Medicine	46	92.0
Surgical	4	8.0
Total	50	100.0

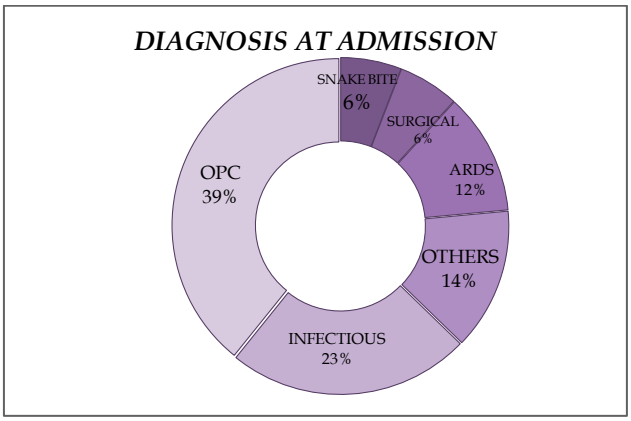
GRAPH – 3



4. DIAGNOSIS AT ADMISSION

The provisional diagnosis of the patients taken up for the study is shown in the graph and the table provided. Most common diagnosis being organophosphosous poisoning (40%) and least being snake bite and surgical patients (6% each).

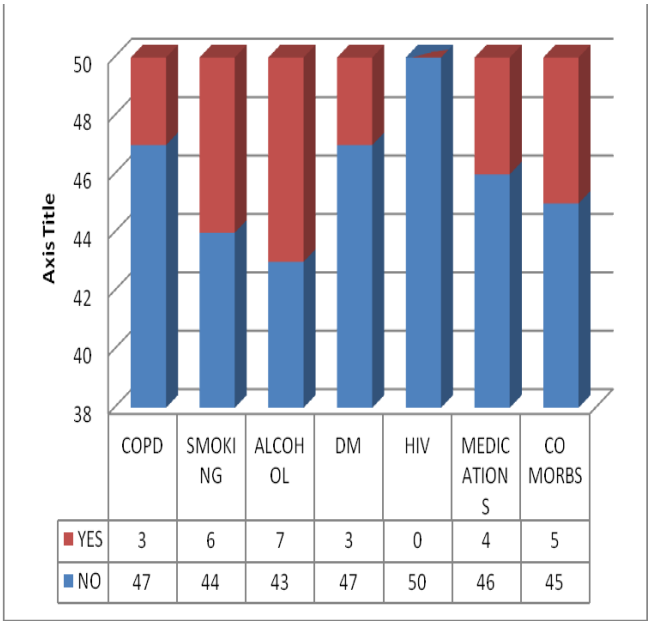
GRAPH – 4



5. ASSOCIATED COMORBIDITIES

The comorbities associated in the patient studied were as follows. 6% of the patients had COPD, where as 12% were smokers. 14% were alcoholics. 6% were diabetics and none of the patient studied was HIV positive.

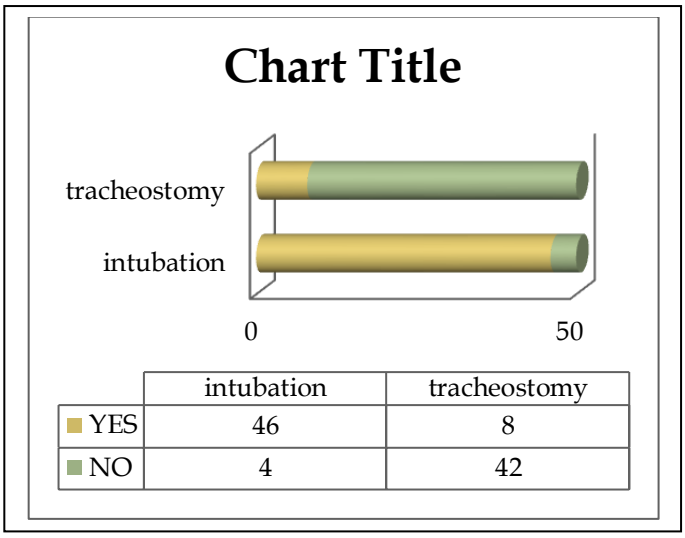
GRAPH – 5



6. INTUBATION VS TRACHEOSTOMY

At the time of examination 46 out of 50 patients were intubated. Out of 50 patients 8 eventually required tracheostomy.

GRAPH – 6



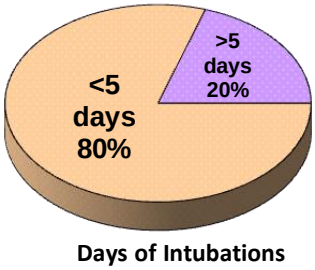
7. DURATION OF INTUBATION PRIOR TO ONSET OF VAP

Majority of the patients developed VAP within 5 days of intubation. i.e. 80 %.

TABLE – 4

Days of Intubations	Number of patients	%
Less than 5 days	40	80.0
More than 5 days	10	20.0
Total	50	100.0

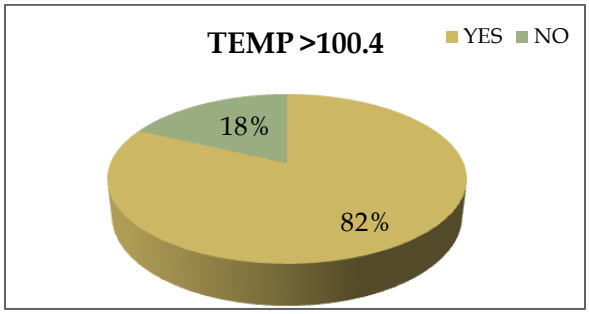
GRAPH – 7



8. TEMPERATURE (FEVER > 100.4^{0}F)

During the course of illness 82% of the patients developed fever and there temperature was more than 100.4^{0}F at one or more occasions.

GRAPH – 8



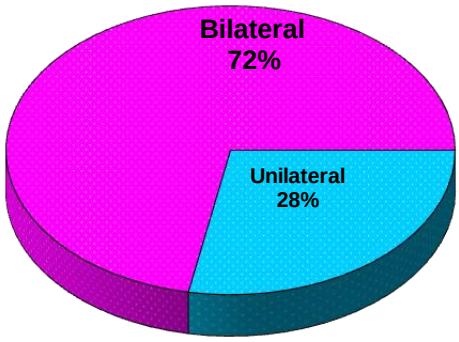
9. LATERALITY OF THE PNEUMONIA IN CHEST X-RAY

In 72% of the patients VAP was bilateral where as in 28% of the patients it was unilateral.

TABLE – 5

Laterality	Number of patients	%
Unilateral	14	28.0
Bilateral	36	72.0
Total	50	100.0

GRAPH – 9



Laterality

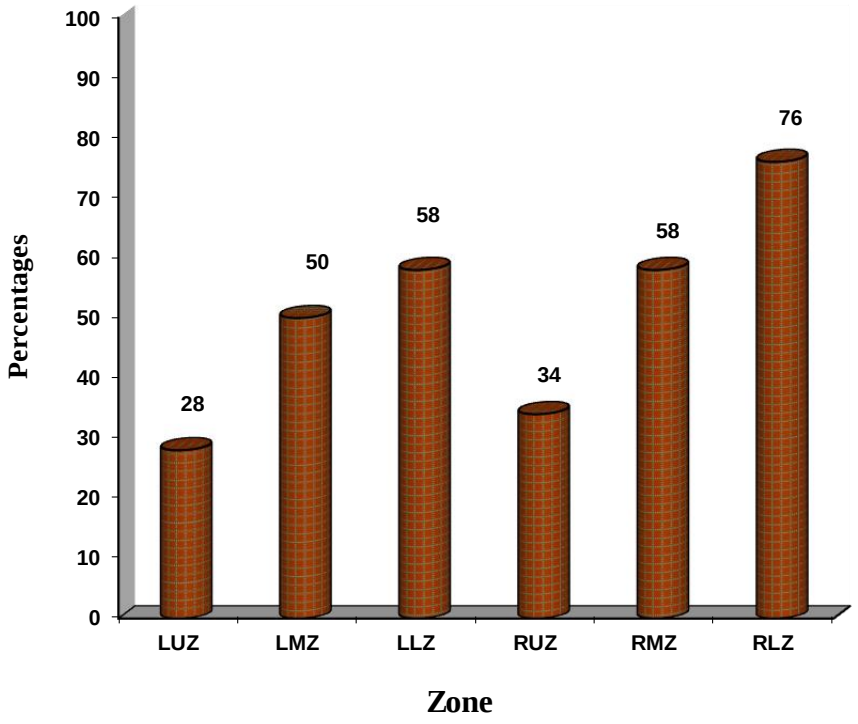
10.CHEST X –RAY ZONAL INVOLVEMENT

Right lower Zone was involved most commonly in about 76% of the patients followed by left lower zone and right middle zone. Least commonly involved zone was left upper zone.

TABLE – 6

Zone	Number of patients (n=50)	%
Left Upper Zone (LUZ)	14	28.0
Left Middle Zone (LMZ)	25	50.0
Left Lower Zone (LLZ)	29	58.0
Right Upper zone (RUZ)	17	34.0
Right Middle Zone (RMZ)	29	58.0
Right Lower Zone. (RLZ)	38	76.0

GRAPH – 10



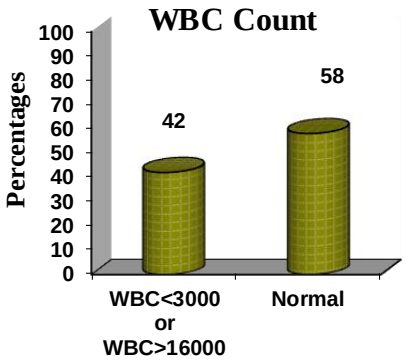
11.LEUKOCYTOSIS VS. LEUCKOPENIA

42% of the patients had an elevated WBC counts more than 16000 cells/dl. None of the patients in the study group had a count less than 3000 cells/dl.

TABLE – 7

WBC count	Number of patients (n=50)	%
WBC<3000 or WBC >16000	21	42.0
Normal	29	58.0

GRAPH – 11



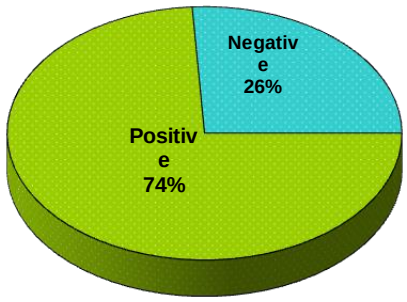
12. ENDO TRACHEAL ASPIRATE (ETA) CULTURE POSITIVITY

Among the study group 74% of the patient's endotracheal aspirate was positive for one or more organisms.

TABLE – 8

ET culture	Number of patients (n=50)	%
Positive	37	74.0
Negative	13	26.0

GRAPH – 12



ETA culture

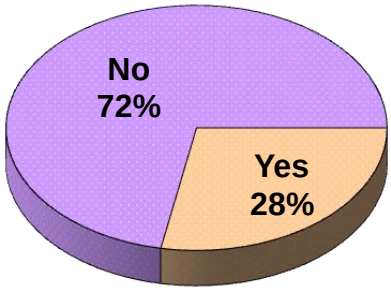
13.MULTIPLE INFECTION VS. SINGLE INFECTION

Of the 50 VAP cases studied 14 patients had multiple infection that is more than one organism was grown in ETA culture.

TABLE – 9

Multiple Infection	Number of patients (n=50)	%
Yes	14	28.0
No	36	72.0

GRAPH – 13



MULTIPLE INFECTION

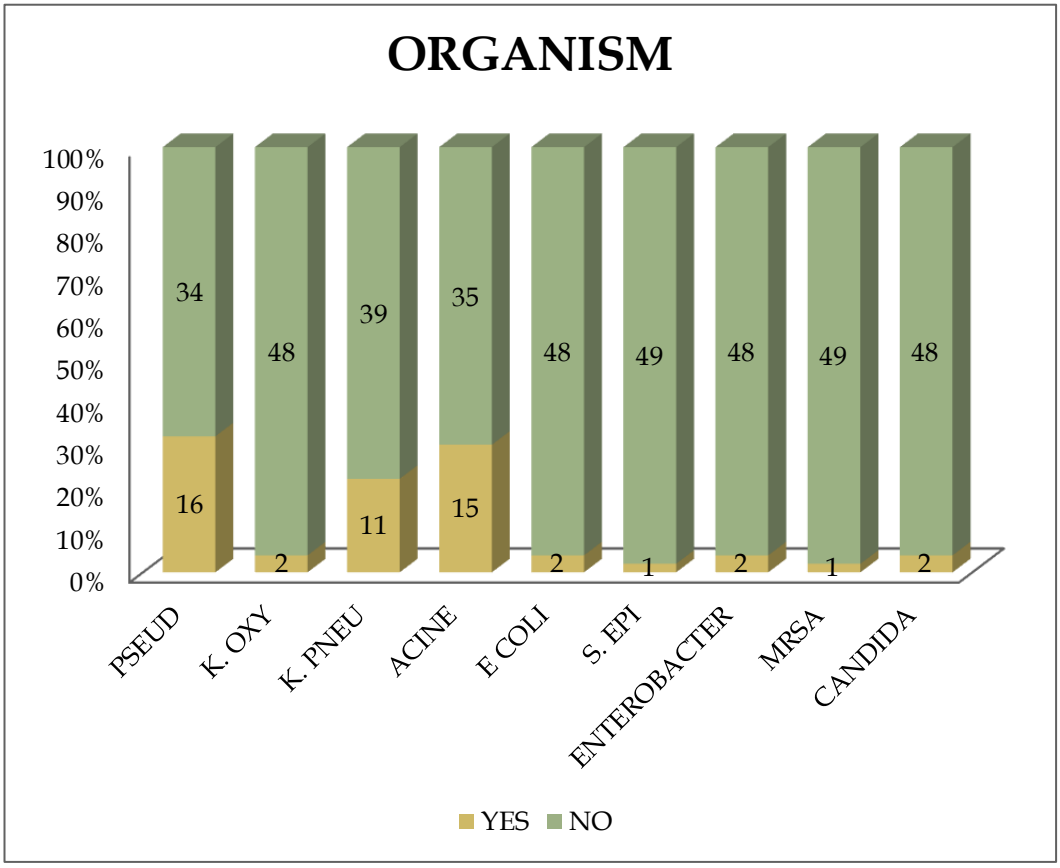
14. ORGANISMS ISOLATED

TABLE – 10

Organisms isolated	Number of patients (n=50)	%
1.PSEUDOMONAS AERUGINOSA	16	32.0
2. KLEBSIELLA OXYTOCEA	2	4.0
3. KLEBSIELLA PNEUMONIA	11	22.0
4. ACINETOBACTER BAUMANII	15	30.0
5. E COLI	2	4.0
6 .STAPH. EPIDERMIDIS	1	2.0
7.ENTERO-BACTER SPP.	2	4.0
8.MRSA	1	2.0
9.CANDIDA ALBICANS	2	4.0

The most common organism grown was *Pseudomonas aeruginosa* . It was cultured in 32% of the endotracheal aspirate. Other organisms cultured were *Acinetobacter baumanii, Klebsiella pneumonia, Klebsiella oxytocea, E.coli, Enterobacter spp., Candida albicans, MRSA, and Staph. Epidermis*.

GRAPH – 14



15. **DRUG SENSITIVITY PATTERN OF THE VARIOUS ORGANISMS ISOLATED**

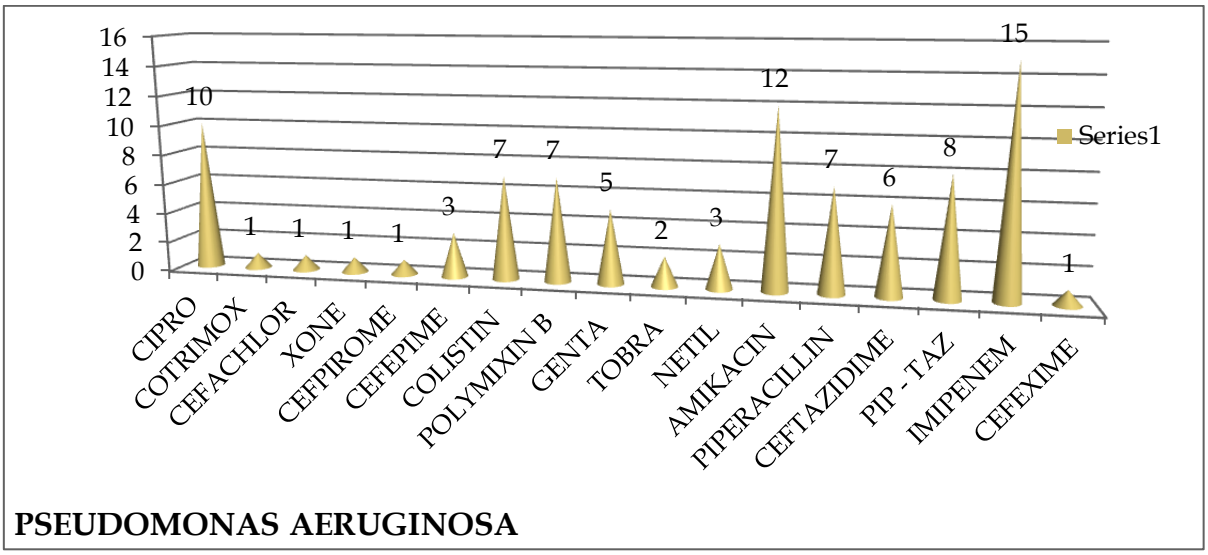
TABLE - 11

	ORGANISM	ACIN. BAU	E. COLI	ENTERO	KLEB. PNEU	KLEB. OXY	PSEUD	MRSA	STAPH EPIDERMIS
	SENSITIVE DRUG								
1	CHLORAMPHE	0	0	0	1	0	0	1	1
2	CIPRO	0	0	2	3	1	10	0	0
3	COTRIMOX	1	1	0	2	1	1	0	0
4	CEFAZOLIN	0	0	0	0	0	0	0	0
5	CEFACHLOR	0	0	0	1	0	1	0	0
6	TAXIM	0	0	0	1	0	0	0	0
7	XONE	0	0	0	1	0	1	0	0
8	CEFPIROME	0	0	0	1	0	1	0	0
9	CEFEPIME	0	0	0	0	1	3	0	0
10	COLISTIN	1	0	0	1	0	7	0	0
11	POLYMIXIN B	0	0	0	0	0	7	0	0
12	NORFLOX	0	0	1	0	0	0	0	0
13	TETRA	2	0	0	2	0	0	1	0
14	DOXY	0	0	0	1	0	0	0	0
15	GENTA	1	0	0	2	1	5	1	0
16	TOBRA	0	0	0	1	0	2	0	0
17	NETIL	4	1	1	2	1	3	0	0
18	VANCO	0	0	0	0	0	0	1	1
19	AMIKACIN	2	1	1	6	0	12	0	0
20	PIPERACILLIN	0	0	0	2	0	7	0	0
21	MAGNAMYCIN	0	0	0	0	0	0	0	0
22	MOXCLAV	1	0	0	0	0	0	0	0
23	CEFTAZIDIME	0	0	0	0	0	6	0	0
24	PIP - TAZ	4	0	0	2	1	8	0	0
25	MEROPENEM	0	0	0	1	0	0	0	0
26	IMIPENEM	11	2	1	11	2	15	0	0
27	LEVOFLOX	0	0	0	1	0	0	0	0
28	CEFEXIME	0	0	0	0	0	1	0	0
	TOTAL	27	5	6	40	8	90	4	2

1) PSEUDOMONAS AERUGINOSA

Pseudomonas aeruginosa was the most commonly grown organism. Imipenam was the most effective antibiotics. Out of the 16 positive cultures, 15 were sensitive to Imipenam. Next effective drugs were Amikacin and Ciprofloxacin.

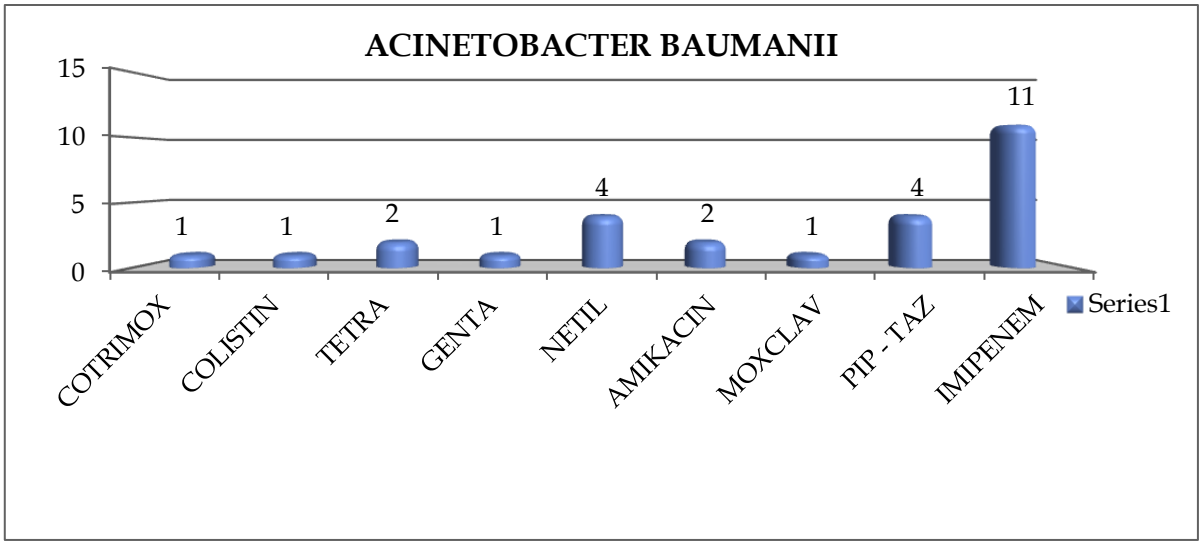
GRAPH – 15



2) ACINETOBACTER BAUMANII

This organism was most sensitive to Imipenam. Of the 15 cultures 11 were sensitive to it. . Other effective antibiotics were piperacillin-tazobactum and Netilmicin.

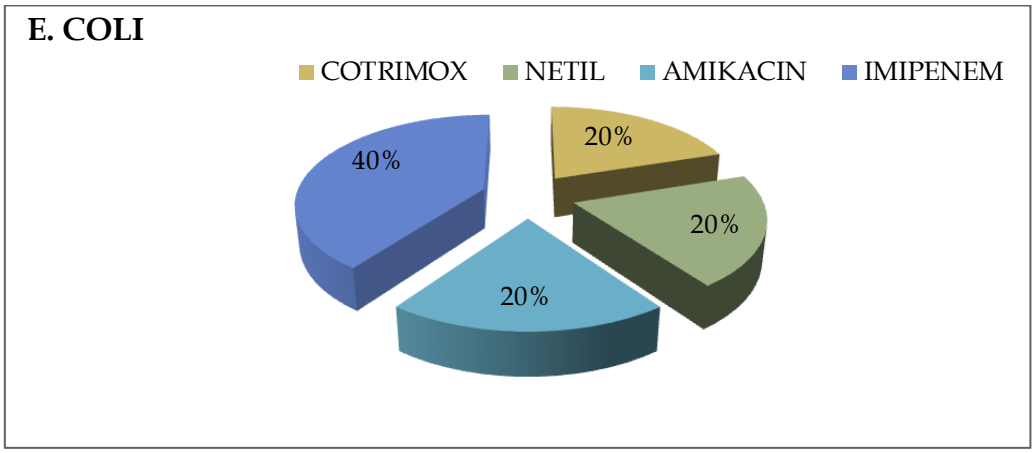
GRAPH – 16



3) E. COLI

This organism was most sensitive to cotrimoxazole; other effective antibiotics included Netilmicin, Amikacin and Imipenam.

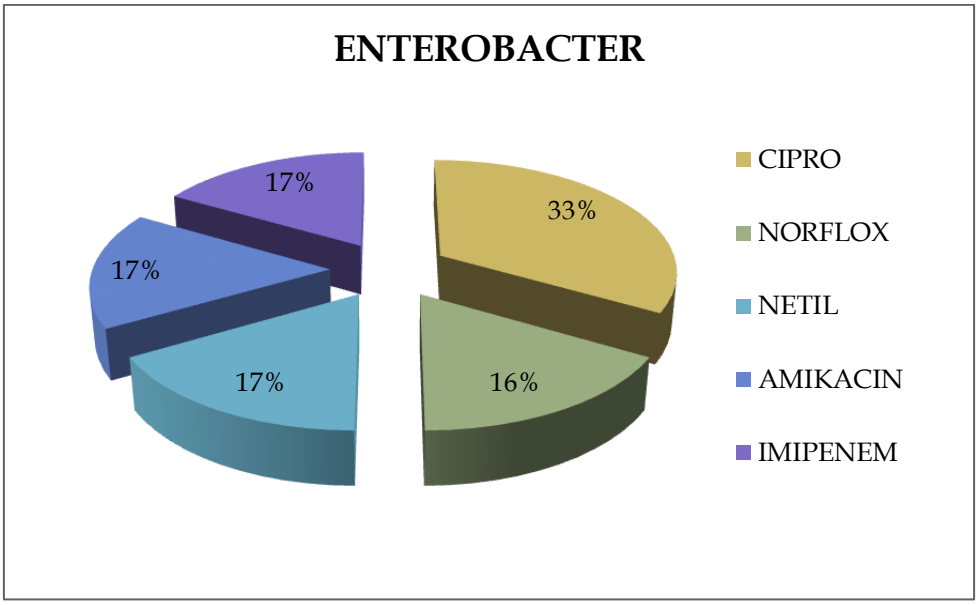
GRAPH – 17



4) ENTEROBACTER

This organism was most sensitive to ciprofloxacin (33%). Other effective antibiotics were Norfloxacin, Netilmicin, Amikacin, and Imipenam.

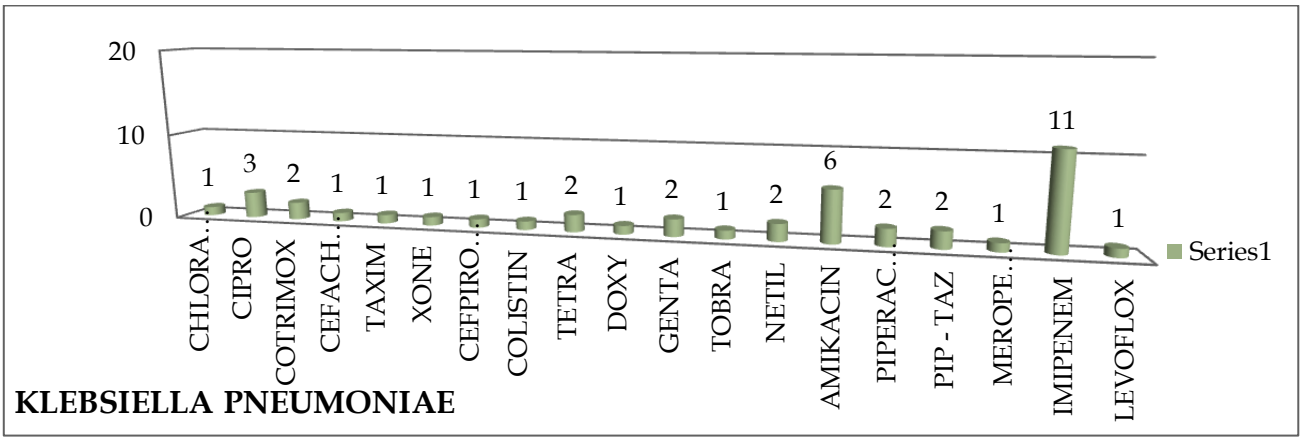
GRAPH – 18



5) KLEBSIELLA PNEUMONIAE

Meropenam and Imipenam were effective against all the 11 cultures of this organism. The second effective drug being Netilmicin.

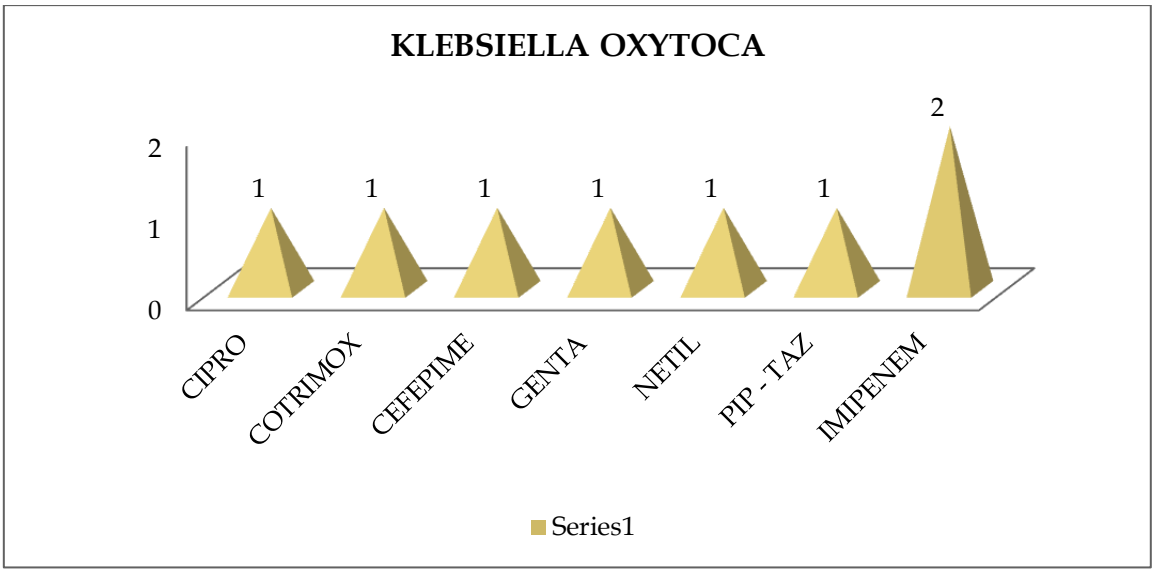
GRAPH – 19



6) KLEBSIELLA OXYTOCA

This organism was cultured in two of the specimens. Against both of them Imipenam was effective. Other effective antibiotics were ciprofloxacin, cotrimoxazole, cefepime, Gentamicin, Netilmicin, piperacillin-tazobactum.

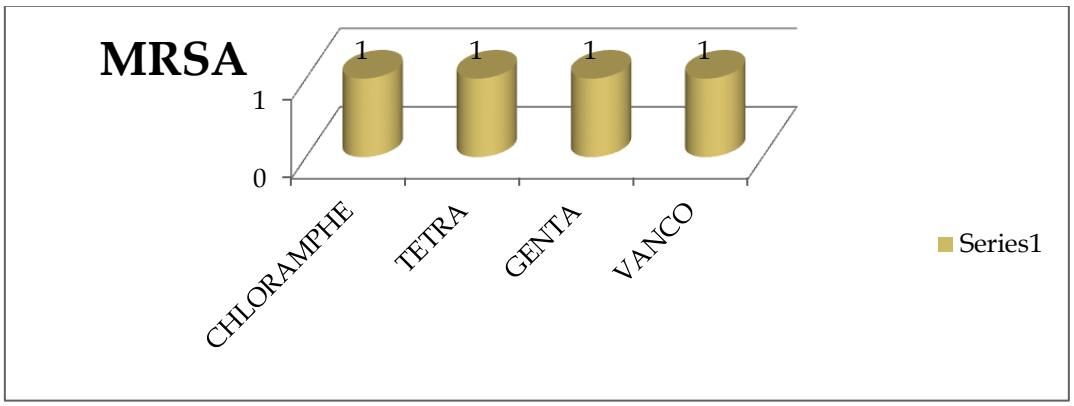
GRAPH - 20



7) METHICILLIN RESISTANT STAPH AUREUS (MRSA)

MRSA was grown in one of the cultures. And it was sensitive to the following antibiotics Chloramphenicol, Tetracycline, Gentamicin, and Vancomicin.

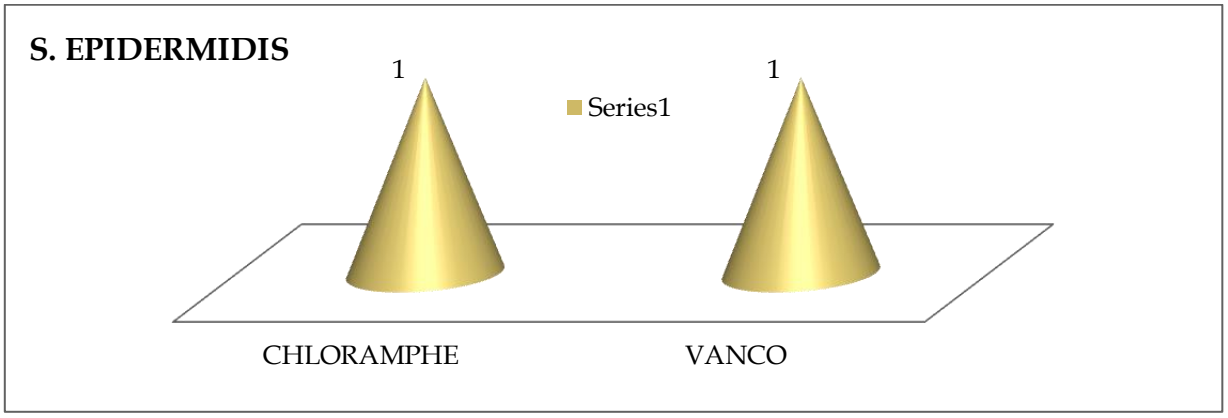
GRAPH – 21



8) S.EPIDERMIS

This organism was grown in one of the cultures and it was sensitive to chloramphenicol and Vancomicin.

GRAPH – 22



COMPLETE RESISTANCE WAS SEEN FOR THE FOLLOWING ANTIBIOTICS IN THE ORGANISMS ISOLATED.

TABLE – 12

AMPICILLIN	CEFUROXIME	LINCOMYCIN	CLOXACILLIN
AZITHROMYCIN	LINEZOLID	NALIDIXIC ACID	NITROFURANTOIN
OFLOXACIN	LOMEFLOXACIN	PENICILLIN	TEICOPLANIN
TICARCILLIN	PEFLOXACIN	CLINDAMYCIN	ERYTHROMYCIN

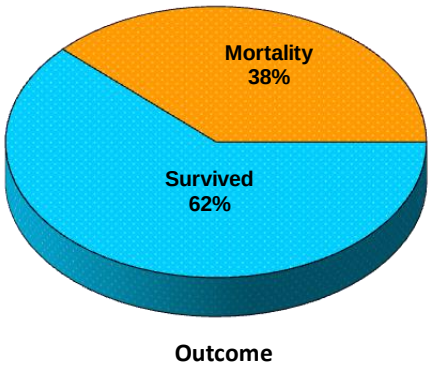
16.OUTCOME

62 % of the patients who developed VAP survived. Whereas the mortality rate was 38% in this study group.

TABLE – 13

Outcome	Number of patients (n=50)	%	95% CI
Survived	31	62.0	48.15-74.14
Mortality	19	38.0	25.86-51.85

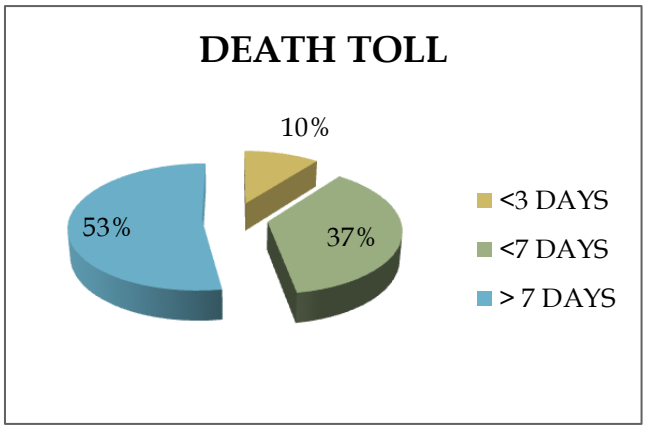
GRAPH – 23



17.NUMBER OF DAYS AFTER WHICH DEATH OCCURRED.

Of the 19 patient who died 10% of the death occurred within first 3 days, whereas 47% of the patient died within 7 days of the development of the VAP. More patients (53%) died after 7 days of the Development of VAP.

GRAPH – 24



STATISTICAL ANALYSIS

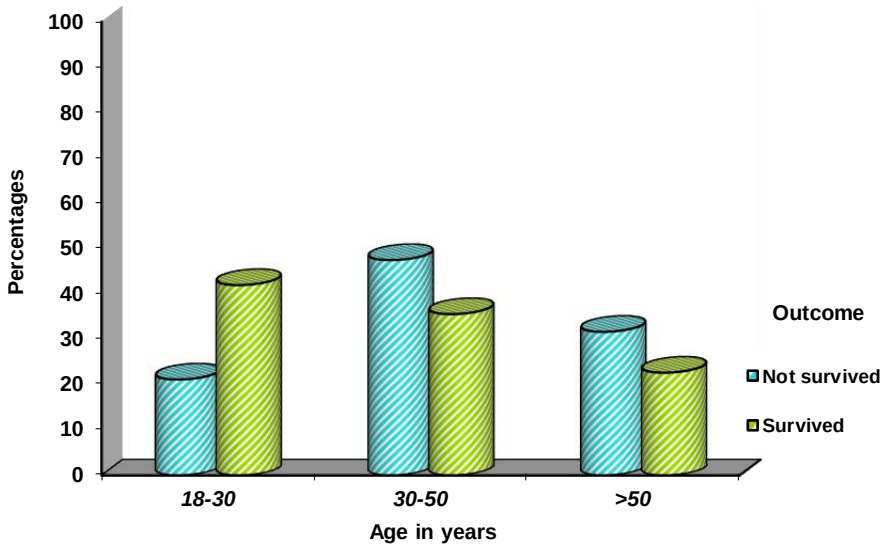
ASSOCIATION OF CLINICAL VARIABLES WITH OUTCOME

TABLE – 14

Clinical variables	Outcome		P value
	Not Survived	Survived	
Age in years			
• 18-30	4 (21.1%)	13 (41.9%)	0.354
• 30-50	9 (47.4%)	11 (35.5%)	
• >50	6 (31.6%)	7 (22.6%)	
Gender			
• Male	11 (57.9%)	21 (67.7%)	0.481
• Female	8 (42.1%)	10 (32.3%)	
Department			
• Medicine	18 (94.7%)	28 (90.3%)	1.000
• Surgical	1 (5.3%)	3 (9.7%)	
Days of Intubations			
• Less than 5 days	17 (89.5%)	23 (74.2%)	0.282
• More than 5 days	2 (10.5%)	8 (25.8%)	
Laterality			
• Unilateral	4 (21.1%)	10 (32.3%)	0.392
• Bilateral	15 (78.9%)	21 (67.7%)	
ZONE			
• LUZ	6 (31.6%)	8 (25.8%)	0.659
• LMZ	11 (57.9%)	14 (45.2%)	0.382
• LLZ	12 (63.2%)	17 (54.8%)	0.563
• RUZ	6 (31.6%)	11 (35.5%)	0.777
• RMZ	12 (63.2%)	17 (54.8%)	0.563
• RLZ	17 (89.5%)	21 (67.7%)	0.100
WBC count			
• WBC<3000 or WBC >16000	8 (42.1%)	13 (41.9%)	0.991
• Normal	11 (57.9%)	18 (58.1%)	
TOTAL	**19 (100%)**	**31 (100%)**	

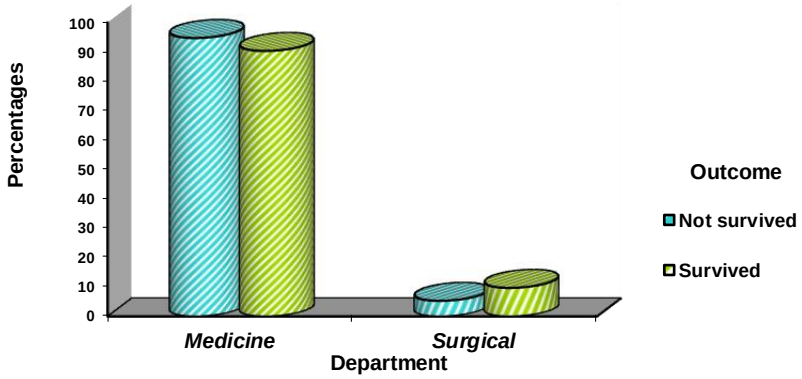
A. The age group associated with maximum death was 30-50 years. In 18-30 years age group the mortality was least.

GRAPH – 25



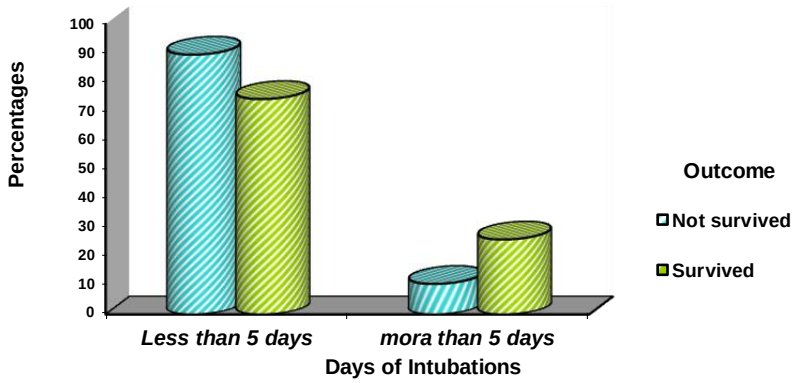
B. The mortality rate did not vary much with respect to the department under which patients were admitted.

GRAPH – 26



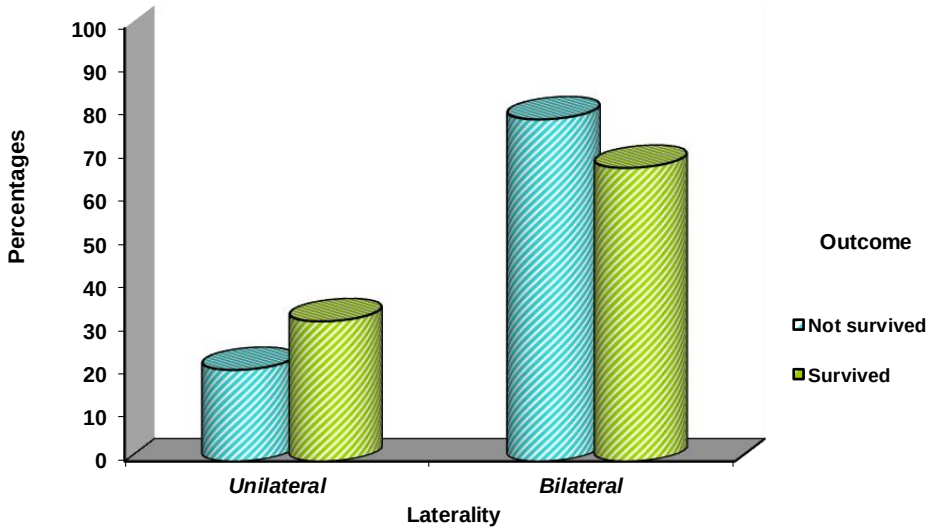
C. If the patient was intubated for more than 5 days the mortality was more as compared to the mortality associated with in 5 days of intubation.

GRAPH – 27



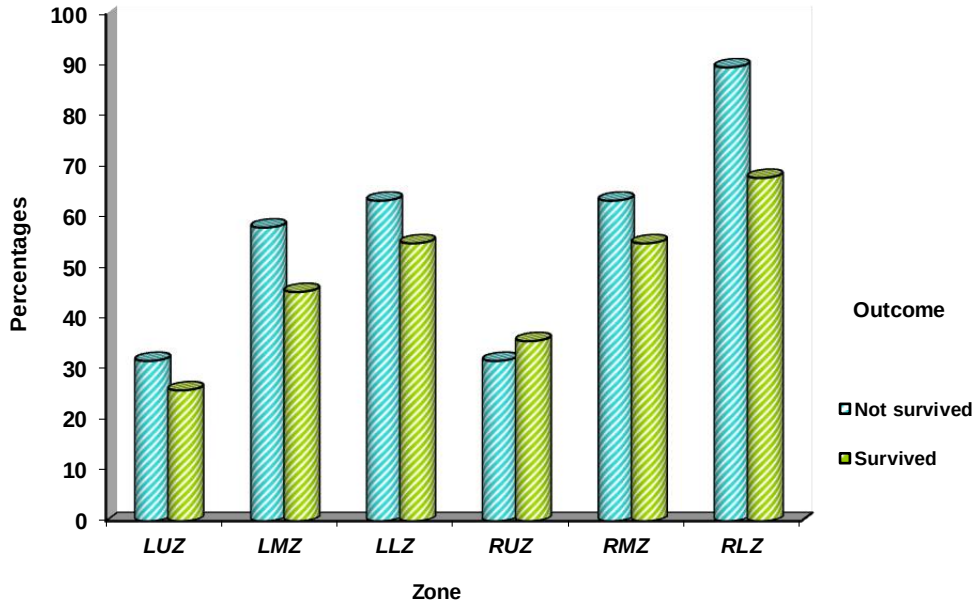
D. Bilateral involvement of the lung was associated with the higher mortality as compared to the unilateral involvement.

GRAPH – 28



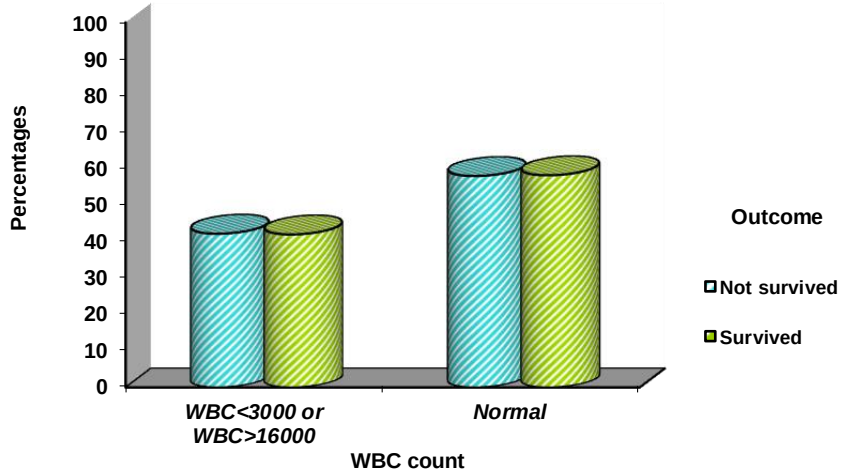
E. Right lower zone involvement was associated with the maximum mortality. Whereas right upper zone involvement had least mortality.

GRAPH – 29



F. The death rate was not affected by the presence or absence of leukocytosis in this study group.

GRAPH – 30



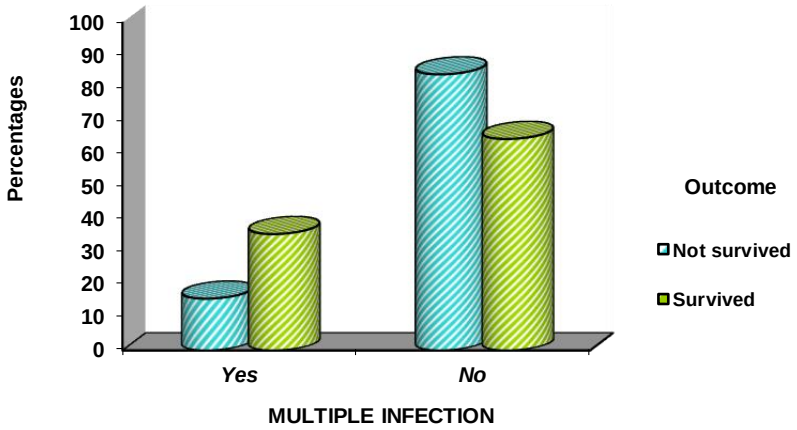
ASSOCIATION OF ENDOTRACHEAL ASPIRATION CULTURE AND MULTIPLE INFECTIONS WITH OUTCOME

TABLE – 15

	Outcome		P value
	Not Survived	**Survived**	
ET CULTURE			
• Positive	12 (63.2%)	25 (80.6%)	0.199
• Negative	7 (36.8%)	6 (19.4%)	
MULTIPLE INFECTION			
• YES	3 (15.8%)	11 (35.5%)	0.132
• NO	16 (84.2%)	20 (64.5%)	
TOTAL	19 (100%)	31 (100%)	-

G. Multiple infections did not affect the survival of the patients and survival rate was better in the patients with multiple infections in this study group.

GRAPH - 31



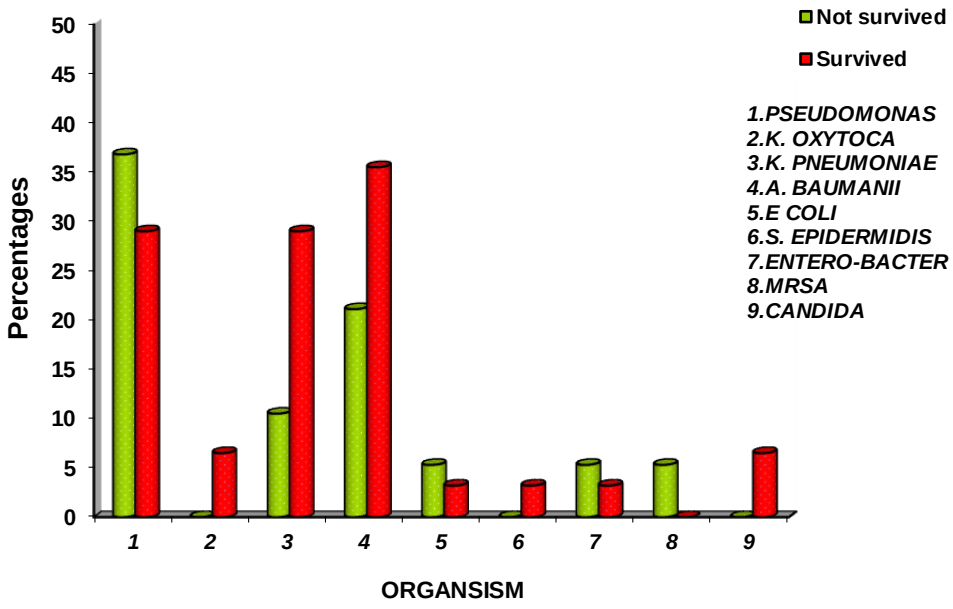
ASSOCIATION OF CLINICAL VARIABLES WITH OUTCOME

TABLE – 16

ORGANSISM	Outcome		P value
	Not Survived (n=19)	Survived (n=31)	
1.PSEUDOMONAS	7 (36.8%)	9 (29%)	0.619
2.K. OXYTOCA	0 (0%)	2 (6.5%)	0.519
3.K. PNEUMONIAE	2 (10.5%)	9 (29%)	0.170
4.A. BAUMANII	4 (21.1%)	11 (35.5%)	0.280
5.E COLI	1 (5.3%)	1 (3.2%)	1.000
6.S. EPIDERMIDIS	0 (0%)	1 (3.2%)	1.000
7.ENTERO-BACTER	1 (5.3%)	1 (3.2%)	1.000
8.MRSA	1 (5.3%)	0 (0%)	0.380
9.CANDIDA	0 (0%)	2 (6.5%)	0.519

H. Comparing the organisms and survival rate MRSA had worst prognosis and *Klebsiella oxytocea, S. epidermis* and *Candida albicans* had the best.

GRAPH – 32



DISCUSSION

Nosocomial pneumonia is the second most common nosocomial infection overall and the most common nosocomial infection in an intensive care unit,[3,4,7,8,118,129] additionally pneumonia is associated with highest mortality amongst nosocomial infections and with substantial increase in cost of care.[120] Mechanical ventilation has been associated with 4-21 fold increased risk for nosocomial pneumonia[9,10] ; we undertook this study to find out the clinical profile of VAP, its morbidity and mortality in our set up.

In this study during the study period of nearly 20 months 50 cases of VAP which occurred in the Intensive Care Unit of R. L. Jalappa Hospital attached to Sri Devaraj Urs Medical College were studied.

Various aspects of VAP including risk factors, microorganism involved, clinical findings, lab findings and there association and affect on the outcome of VAP was meticulously studied.

The crude mortality rate in the Study group was 38%. This value was slightly higher than the values obtained in other studies for example in a study done by Marin H. Kollef in 2006 VAP was associated with a crude mortality rate of approximately 30%.[8,9.] Whereas in the studies done at Virginia in 2006 by Steven M. Koenig and Jonathon D. Truwit[10] the mortality in patients with VAP ranged between 0 – 50 %.

Most of the patients under study were in the age group of 30 – 50 years. In this age group maximum mortality was there. Young patient between 18 – 30 years had best survival rate probably because of better immunity and minimal co morbidity.

The study group was male dominant in numbers as well as in the rate of survival.

There was no effect on the outcome whether the patient was admitted to medical side or surgical side. The majority of patients had consumed Organophosphorus poison. These patients stayed for a longer time on ventilators and probably developed pneumonia.

Patients with chronic obstructive pulmonary disease have impaired clearance of bronchial mucosal secretion and loss of mucosal integrity. This significantly increases the risk of nosocomial pneumonia in ICU patients with COPD, especially when these patients undergo tracheal intubation and mechanical ventilation. 6% of the patients were suffering from COPD in our study.

The risk of pneumonia in patients receiving mechanical ventilation increases with time. Fagon et al found that incidence of VAP rises with number of days of mechanical ventilation, incidence being 6.5% at 10 days to 19% at 20 days and 28% at 30 days.[125] They estimated the risk of 1% per day of mechanical ventilation.

All of the study group patients had nasogastric tube and were receiving nasogastric tube feeding. At least 2 studies have shown that the presence of nasogastric tube results in a six fold increase in the risk of pulmonary infection.[47,125.]

The risk of pneumonia is further increased by Enteral feeding by the nasogastric tube, mainly due to increased gastric and pharyngeal colonization by pathogenic gram negative bacilli.[147]

In our country however, economic considerations make it mandatory to initiate and continue nasogastric tube feeding in intensive care unit patients because of high cost of parenteral alimentation.

As far as onset of VAP is considered. Early onset VAP occupied most of the study group i.e. VAP occurring within 5 days. Almost 80% of the patient developed VAP

Within first 5 days. Mortality was more in the study group who developed VAP later

i.e. after 5 days of intubation. This is probably because this was the group whose general condition was not good and they required prolonged ventilatory support and had more co morbidities.

Chest X – ray findings were more prevalent bilaterally. Probably because the factors which led to VAP were systemic and general rather than local. More over Bilateral involvement was associated with higher mortality rate.

Right lower zone involvement was commonest and left upper zone was least involved. This finding corresponds well with the pattern of aspiration and indicating aspiration as one of the important modality of transport of micro organism to the lungs. Moreover a higher rate of mortality was associated with the patient who developed pneumonia in the lower zone and this value was statistically significant ($p = 0.100$).

ETA culture positivity was present in good number of the patient and was associated with higher rate of mortality but the data is not statistically significant. Heyland et al.[8] found that the use of bronchoalveolar lavage did not influence in-hospital mortality or length of stay as compared with endotracheal aspiration.

However, the main potential effect of bronchoalveolar lavage is to permit the de-escalation or cessation of unnecessary antimicrobial therapy on the basis of microbiologic findings, especially when initial broad-spectrum antimicrobial agents are prescribed for patients at risk for infection with resistant bacteria. These findings suggest that clinicians caring for patients with suspected ventilator-associated pneumonia should use antimicrobial treatment strategies that minimize the prolonged and potentially unnecessary administration of antibiotics, in order to curtail resistance.

Multiple infections in a single patient or multiple ETA cultures positivity was fairly common but contrary to normal expectation the patient did well and the mortality was less in this group of patients.

Pseudomonas aeruginosa was the most common organism grown in ETA culture next common being *Acinetobacter baumannii*. These results were consistent with the study done at Kasturba Medical College, Manipal, India in 2007.[4]

The organism specific death rate was statistically insignificant and no particular organism was responsible for higher mortality. Mostly because the sensitivity pattern for the antibiotics was worked out and respective antibiotic was started.

Coming to the sensitivity pattern of the Individual organisms there was complete resistance for the commonly used antibiotics like Ampicillin , Cefuroxime, Cloxacillin, Azithromycin, Nalidixic acid, Ofloxacin, Lomefloxacin, Penicillin, Clindamycin and Erythromycin.

Imipenam was the antibiotic for which most of the time most of the organism were sensitive. For pseudomonas aeruginosa best antibiotics were Imipenam and Amikacin where as Acinetobacter baumannii was sensitive to Imipenam and piperacillin – tazobactum combination. Other organisms also showed similar sensitivity patterns as discussed in results section. In a study done by SM Ahmed and others at JN Medical College, AMU, Aligarh, India[3] in 2007 showed that Cefepime-Levofloxacin combination is an effective alternative to piperacillin-tazobactam-amikacin for empirical treatment of VAP.

Our study has its limitations in that the patients could not be subjected to Bronchoalveolar lavage. Anaerobic cultures could not be done because it required specific CDC recommended anaerobic plates for culture. Fungal culture also could not be done.

Simple and effective preventive measures can be instituted easily and at minimal costs. Such measures might include Non Invasive Ventilation, diligent respiratory care, hand hygiene, elevation of head, oral and not nasal cannulation, minimization of sedation, institution of weaning protocols, judicious use and de-escalation of antibiotics administered. More costly interventions should be reserved for appropriate situations.

Utilizing the preventive, diagnostic, and treatment recommendations outlined in this study should allow for improved outcomes for a common and serious medical complication seen in ICU mechanically ventilated patients.

CONCLUSIONS

1. The mortality associated with the patient with VAP was 38 %. Mortality rate of VAP in our ICU population correlates well with other studies in the literature.

2. VAP was more common in early (<5days) than late phase (>5days) of ventilation. But death rate was higher in late phase of ventilation.

3. Right lower zone on chest X – ray was most commonly involved with statistically significant mortality rate.

4. ETA culture was positive in 74% of the patients and multiple infections did not affect the outcome.

5. The most frequently isolated microorganisms were *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, *Klebsiella pneumonia* and *E.Coli*.

SUMMARY

A prospective non-controlled study was done to analyze the clinical presentations, organisms involved and outcome of patient with Ventilator Associated pneumonia in the ICU setup of R. L. Jalappa Hospital and Research Center Tamaka, Kolar attached to Sri Devaraj Urs Medical College during January 2009 to October 2010.

A total of 50 patients of VAP were evaluated during the study period and different parameters analyzed.

It was found that crude mortality rate was 38%. Most of the patients were in age group of 30 – 50 years with male dominance. Right lower zone was most commonly involved and had statistically significant mortality rate. *Pseudomonas aeruginosa* was the commonest organism cultured in the Endo Tracheal Aspirate and mortality associated with it was higher although not statistically significant. Most effective antibiotic overall was Imipenam in the study group. The data obtained in the given study were comparable to the contemporary studies done.

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APPENDIX A

"VENTILATOR ASSOCIATED PNEUMONIA: STUDY OF CLINICAL PRESENTATIONS, ORGANISMS INVOLVED AND OUTCOME."

PROFORMA

IDENTIFICATION DETAILS

NAME:
AGE/SEX: IP NO. : SERIAL NO:
ADDRESS:

DATE OF ADMISSION:

DEPARTMENT (UNDER WHICH PATIENT IS ADMITTED):

PROVISIONAL DIAGNOSIS:

GENERAL INFORMATION:

- COPD YES/NO
- SMOKING YES/NO
- ALCOHOL YES/NO
- DIABETES: YES/NO
- HIV YES/NO
- DRUGS
- DISEASE
- INTUBAION PRESENT/ABSENT
- IF PRESENT NO OF DAYS
- TRACHEOSTOMY PRESENT/ABSENT
- IF PRESENT NO OF DAYS
- PARALYTIC ILEOUS PRESENT/ABSENT
- NASOGASTRIC TUBE PRESENT/ABSENT

- PNEUMONIA(AT ADMISSION) PRESENT / ABSENT

- ANTIBIOTICS GIVEN AT ADMISSION YES/NO
- IF YES WHICH ONE(S)

ON EXAMINATION

VITALS:

PULSE	B.P.	RESP. RATE	TEMP.		

LEVEL OF CONCIOUSNESS (GLASSGO COMA SCALE)

EYE OPENING(4)	VERBAL(5)	MOTOR(6)	TOTAL(15)

GENERAL SURVEY:

PALLOR	ICTERUS	CLUB.	CYANOSIS	L.N.	EDEMA	JVP		

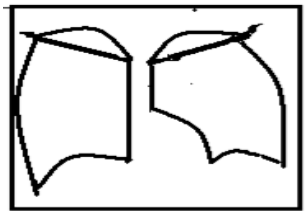
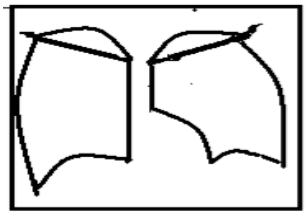
RESPIRATORY SYSTEM.

CENTRAL NERVOUS SYSTEM

CARDIOVASCULAR SYSTEM

GASTROINTESTINAL SYSTEM

DIAGNOSTIC CRITERIA

CHEST X-RAY  AT  THE TIME

AFTER 48 HRS OR MORE OF ADMISSION OF INTUBATION

FEVER(>38 0R <35 ^{0} C)

DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 7	

WBC COUNTS(>16000 OR <3000)		

ENDOTRACHEAL TUBE CULTURE: POSITIVE / NEGATIVE

IF POSITIVE WHICH ORGANISMS WERE GROWN

SL. NO	NAME	SENSITIVITY

BASIC INVESTIGATIONS

TEST	VALUE	DATE	TEST	VALUE	DATE
HB			TOTAL BR		
TC			DIRECT		
DC(N,L,E)			SGOT		
ESR			SGPT		
PLATELET			ALK.PHOSPHATE		
CT			TOTAL ALB.		
BT			SR. ALBUMIN		
PT/APTT			BLOOD UREA		
INR			SR. CREATININE		
SODIUM			URINE ALB		
POTASIUM			URINE SUGAR		
CALCIUM			URINE WBC		
MAGNESIUM			URINE RBC		
HIV			SPUTUM AFB		
OTHERS					

BLOOD CULTURE: POSITIVE/NEGATIVE

IF POSITIVE WHICH ORGANISMS WERE GROWN

SL. NO.	NAME	SENSITIVITY

ECG

CT SCAN (IF DONE)

USG (IF DONE)

OTHER TESTS

WHETHER PNEUMONIA DEVELOPED AFTER 48 HRS ON VENTILATOR YES/NO

ANY CHANGE IN THE ANTIBIOTICS DURING THE COURSE OF TREATMENT

OUTCOME (TILL DAY 7)

SURVIVAL

DEATH

REMARKS