THE RISK FACTORS, CLNICAL AND BIOLOGICAL PROFILES AND PROGNOSTIC FACTORS IN VENTILATOR ASSOCIATED PNEUMONIA

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A DISSERTATION SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENT FOR THE MD BRANCH XVII (TUBERCULOSIS AND RESPIRATORY MEDICINE) EXAMINATION OF THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY, CHENNAI TO BE HELD IN APRIL 2016.

DEPARTMENT OF PULMONARY MEDICINE

CHRISTIAN MEDICAL COLLEGE

VELLORE

DECLARATION

This is to declare that this dissertation titled "**The risk factors, clinical and microbiological profiles, and prognostic factors in ventilator associated pneumonia**'' is my original work done in partial fulfillment of rules and regulations for MD Tuberculosis and Respiratory Medicine examination of the Tamil Nadu Dr.M.G.R Medical University, Chennai to be held in April 2016.

Dr. Akhil Paul

Postgraduate Student (M D Pulmonary Medicine)

Register Number: 94133

Department of Pulmonary Medicine

Christian Medical College

Vellore.

DEPARTMENT OF PULMONARY MEDICINE
CHRISTIAN MEDICAL COLLEGE
VELLORE

CERTIFICATE

I declare that this dissertation entitled "**The risk factors, clinical and microbiological profiles, and prognostic factors in ventilator associated pneumonia**'' submitted towards fulfillment of the requirements of the Tamil Nadu Dr. M.G.R. Medical University for the MD Pulmonary Medicine examination to be conducted in April 2016, is the bonafide work of Dr. Akhil Paul, postgraduate student in the Department of Pulmonary Medicine, Christian Medical College, Vellore.

GUIDE

Dr. D.J Christopher
Professor and Head,
Department of Pulmonary Medicine
Christian Medical College,
Vellore.

CERTIFICATE

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PRINCIPAL

Dr.Alfred Job Daniel

Professor

Dept of Orthopaedics

Christian Medical College and Hospital,

Vellore – 632002.

Tamil Nadu.

HEAD OF THE DEPARTMENT

Dr. D.J. Christopher

Professor & Head,

Department of Pulmonary Medicine,

Christian Medical College and Hospital,

Vellore – 632002.

Tamil Nadu.

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INTRODUCTION

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Dr. Akhil Paul
PG Registrar
Department of Pulmonary Medicine
Christian Medical College
Vellore 632 004

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Dear Dr. Akhil Paul,

The Institutional Review Board (Blue, Research and Ethics Committee) of the Christian Medical College, Vellore, reviewed and discussed your project entitled "The Incidence, risk factors, clinical and microbiologic profile and prognostic factors of Ventilator Associated Pneumonia in an Indian teaching hospital setting." on December 4th, 2013.

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1. IRB application format
2. Curriculum Vitae' Drs. Akhil Paul, D J Christopher, Balamugesh T, Peter John Victor, K. Subramani.
3. Consent form (English, Tamil, Bengali & Hindi)
4. Information sheet (English, Tamil, Bengali & Hindi)
5. Data sheet
6. No of documents 1-5

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MD., MNAMS., DNB (Endo), FRACP (Endo), FRCP (Edin), FRCP (Glasg)
Deputy Chairperson
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We approve this project to be conducted as presented..The institutional Ethics Committee expects to be informed about the progress of the project, any adverse events occurring in the course of the project , any amendments in the protocol and the patient information / informed consent. On the completion of the study, you are expected to submit the copy of the final report. Respective forms can be downloaded from the following link: htpp://172.16.11.136/research/IRB Policies.html in the CMC intranet and in the CMC website link address: htpp://www.cmch-vellore.edu/static/research/Index.html.

Yours sincerely

Dr. Nihal Thomas
Secretary (Ethics Committee)
Institutional Review Board

Dr. NIHAL THOMAS
MD.,MNAMS.,DNB(Endo),FRACP(Endo),FRCP(Edin),FRCP(Glasg)
SECRETARY - (ETHICS COMMITTEE)
Institutional Review Board,
Christian Medical College, Vellore - 632 002.

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CONTENTS

INTRODUCTION

Ventilator Associated Pneumonia (VAP) is defined as pneumonia that occurs in a patient after 48 hours of intubation. It is associated with high morbidity , mortality, prolonged hospital stay, and cost of treatment. It was said that 3% of the intubated patients get VAP every day in the first 5 days. Late onset VAP , ie VAP that occurs after 5 days of intubation is usually caused by multi-drug resistant pathogens , and it is associated with higher mortality .

The purpose of the study is to determine the clinical profile, microbiological profile, predictive factors of the outcome of VAP and the incidence of VAP. The study consists of collection of demographic details, clinical details, assessment of CPIS score, APACHE-II score, MOD Score, follow up of endotracheal aspirate/ bronchial wash/ bronchoalveolar lavage culture reports and procalcitonin levels of patient who develop VAP in Medical and Surgical ICU and HDUs and Respiratory Medicine HDU. Those patients will be followed up throughout their hospital stay till discharge to analyze the outcome and mortality. The findings in various ICUs will be compared.

AIM

To determine the clinical profile, microbiological profile and the predictive factors of the outcome in Ventilator Associated Pneumonia.

OBJECTIVES

1. To study the clinical profile of VAP in Indian ICUs and HDUs.

2. To describe the microbiologic profile of VAP.

3, To find out the difference in the microbiologic profile amongst different ICUs/HDUs in the same hospital.

4, To find out the prevalence of MDR organisms in VAP.

5, To find out the predictive value of the following at diagnosis towards outcome and prognosis.

- Modified CPIS Score
- APACHE-II Score
- Multiple Organ Dysfunction Score
- Serum Procalcitonin level

REVIEW OF LITERATURE

DEFINITION

Ventilator Associated Pneumonia (VAP) is defined as pneumonia developing 48 hours after intubation, in a patient in whom, there was no signs of symptoms of lung infection at the time of intubation.

VAP is caused by the microbiological invasion of the lower respiratory tract and the lung parenchyma. Endo-tracheal intubation and mechanical ventilation compromises the first line of defence against the microbiological invasion by disrupting the integrity of the oro-pharynx and the airways.

EPIDEMIOLOGY

Ventilator Associated Pneumonia (VAP) is one of the most common adverse event seen in mechanically ventilated patients in ICUs throughout the world. About 28% of the intubated patients get VAP during there intubated days. There are various studies looking at the incidence of VAPs all over the world and it ranges from 3% to 30%. The risk of developing VAP will keep on increasing when the number of intubation days progresses. For the first 5 days, the rate of incidence of VAP is 3% per day. Later

it decreases to 2% per day for the next 5 days, thereafter it is assumed to be 1% per day (1). VAP is considered to be one of the most common infection in ventilated patients in ICUs with an incidence of 6-52 % (2) . VAP is associated with increased hospital and ICU stay. Overall attributable mortality of VAP was estimated to be around 9% (3) . In 1974, studies showed 50% mortality in VAP patients when mortality among other ICU patients was only 4% (4).

In another study, it was showed that VAP will prolong the duration of mechanical ventilation from 10 to 32 days (5). In another study , the median duration of stay in the ICU for the patients with VAP was 21 days and a median of 15 days was observed for paired control subjects (6). A mean prolongation of ICU stay of 20 days was observed in patients with VAP when surviving pairs were compared. Reported mean durations of mechanical ventilation, ICU stay, and hospital stay were, respectively, 12.0, 20.5, and 43.0 days for trauma patients with pneumonia compared with 8.0, 15.0, and 34.0 days for their matched control subjects (7).

Postsurgical patients are at a high risk for VAP. It accounts for about one-third of the pulmonary infiltrates in the ICU patients (8) . In a 1981 study, the VAP rate during the postoperative period was 17% (9). The development of pneumonia was associated with serum markers of severity of the primary disease, like low serum albumin. The history of cigarette smoking, longer hospital stay before surgery, long intra-operative period, and thoracic or upper abdominal interventions were also found to be important risk factors for post-operative pneumonia. Another comparative study on various adult ICUs demonstrated that postsurgical patients had consistently higher rates of

ventilator associated pneumonia than medical ICU patients, with a RR of 2.2 (6).

This throws light to the importance of early detection and adequate management in the intensive care units.

TYPES OF VAP

a, Early VAP

b, Late VAP

VAP which develops within the first 4 days of intubation was called as Early VAP , and those which develop after 4 days was considered as Late VAP. They are found to be different from each other in various aspects, such as mortality, days of hospital stay, microbiological organisms involved, morbidity and other complications. In a prospective study done in JIPMER, Pondichery, following up the patients admitted in various ICUs for a period of 15 months found out that, 36 (18%) out of 200 intubated patients developed VAP. Of these, 41.7% of VAP was early onset and there was a higher incidence of VAP in MICU when compared to CCU (10). Early onset VAP is usually less severe and they are caused by antibiotic sensitive micro organisms. So they have a better prognosis. Late onset VAP is usually caused by Multi drug resistant

organisms and it is associated with high rate of mortality.

RISK FACTORS

There are various risk factors that predispose a patient to develop Ventilator Associated Pneumonia. They can be grossly classified into -

1, Host related

2, Healthcare personnel related

and

3, Device related

HOST RELATED

a, Level of consciousness

b, Underlying immunosuppression

- Infection (eg. HIV)

- Drugs (eg. Chemotherapy)

- Other co-morbidities (eg. Diabetes Mellitus)

c, Chronic obstructive lung disease

d, Acute respiratory distress syndrome

e, Body positioning of the patient

HEALTH PERSONNEL RELATED

a, Poor hand hygiene

b, Not changing gloves after seeing another patient

c, Not wearing aprons and hair cap

d, Not using hand rub

c, Carriers of resistant organisms in the next bed

DEVICE RELATED

a, Unhygienic method of intubation

b, Unhealthy surroundings during intubation

c, Nasogastric and oro-gastric tube

d, Recurrent change of ventilatory circuits

e, Contaminated ventilatory tubings

PATHOGENESIS

Normal defense mechanisms in the human respiratory system

The normal defense mechanism in the human respiratory system consists of

a, Anatomy of the human airway

b, Mucus

c, Basement membrane

d, Cough reflex

e, Muco-ciliary system

f, Lactoferrin

g, Leukocytes

h, Alveolar macrophages

g, Immunoglobulins

h, Complements

Pathway for micro-organisms to reach the lungs

a, Aspiration of the oro-pharyngeal contents

b, Stomach contents reaching the lower respiratory tract by reflux and then getting aspirated

c, Inhalation of the infected chemical fumes and aerosols

d, Direct spread of infection from the pleural space

e, Hematogenous spread of the infection to the lungs

Micro-aspirations are considered to be the most common cause of infection.

The normal flora of our oropharynx consists of Streptococcus viridians, Haemophilus species and anaerobic organisms. When critically ill, a aerobic gram negative bacilli and staphylococcus aureus predominance develop.

Change in the orotracheal mucosa which helps in bacterial adherence in critically ill patients include-

a, Increased protease production

b, Denuded and exposed mucosa

c, Reduced immunoglobulin -A, one of the predominant host defense in the mucosa

d, Elevated pH of the airways

e, Increase in the receptors of the airway for the bacteria

The critical illness as well as the antimicrobial usage play a predominant role in establishment of these changes (11).

The stomach contents reaching the lower airways as a result of reflux mechanism and then getting aspirated to the distal airways is one of the predominant mechanism in the development of VAP. The use of antacids, which is a part of ulcero-prophylaxis in the intubated patients in the Intensive Care Units , can lead to increase in the gastric acid pH and thus the proliferation of the bacteria in the stomach. So once aspirated there is higher chance for this aspirate to cause an active infection in the lower airways in comparison with those who are not on any antacids (12). The immobilization of the patient and absence of gastric feeding will add on to this.

Table A- Source of outbreak and the common organisms found based on various studies

(Adapted *from 'Nasia Safdar CJC. The pathogenesis of ventilator-associated pneumonia: its relevance to developing effective strategies for prevention*.')

Source of Outbreak	Organisms
Reusable electronic ventilator probes and sensors	*Burkholderia cepacia*
	Stenotrophomonas maltophilia
Nebulized medication	*Burkholderia cepacia*
	Pseudomonas aeruginosa
	Mycobacterium tuberculosis
Ventilator circuits and equipment, humidifiers, and respirometers	*Acinetobacter calcoaceticus*
	Burkholderia cereus
	Pseudomonas aeruginosa
Ice and water	*Legionella pneumophila*
	Pseudomonas aeruginosa
	Nontuberculous mycobacteria
Bronchoscopes	*Pseudomonas aeruginosa*
	Mycobacterium tuberculosis
	Nontuberculous mycobacteria
Fingernails and hands of health care workers	*Pseudomonas aeruginosa*
	Klebsiella pneumoniae
Miscellaneous	
Milk bank pasteurizer	*Pseudomonas aeruginosa*
Blood-gas analyzer	*Pseudomonas aeruginosa*
Mouthwash	*Burkholderia cepacia*
Food coloring dye	*Pseudomonas aeruginosa*
	Burkholderia cepacia
Infected patients or health-care workers	SARS human coronavirus
	Influenza A, respiratory syncytial virus
	Mycobacterium tuberculosis
	Methicillin-resistant *Staphylococcus aureus*
Ambient air	Aspergillus, zygomycetes

Biofilms formed inside the endo-tracheal tube can also act as a reservoir of infective organisms. It is resistant to the antibiotics and the various defence mechanisms of our body.

- **CLINICAL SYMPTOMS**

VAP characterisrically presents with -

A, A new or worsening lung opacities in the chest x ray

B, Fever

C, Purulent tracheobronchial secretions

D, Leukocytosis

E, Tachypnoea

F, Decreased tidal volume

G, Increased minute ventilation

H, Hypoxia (13)

On respiratory system examination, following findings can be observed

- Asymmetric ronchi (due to the secretions)
- Crackles
- Decreased breathsounds
- Bronchospasm
- Hemoptysis

Deterioration in the patient's condition in terms of the oxygenation and ventilator requirements can be the first sign of development of Ventilator Associated Pneumonia.

EVALUATION AND DIAGNOSIS

There are various criteria used in the diagnosis of VAP. European literature uses HELICS criteria for the diagnosis of VAP.

A, Hospitals in Europe Link for Infection Control through Surveillance **(HELICS)** criteria (14)

- Positive radiology

2 or more serial chest X-rays or CT scans with a image of pneumonia for patients those who have an underlying cardiac or pulmonary disease. In patients those who have underlying cardiac or pulmonary disease, only one definitive chest X-ray or CT-scan is enough.

• Fever > 38 ˚C and no other causes for the fever

• Leukopenia (<4000 WBC/mm3) or leucocytosis (≥ 12 000 WBC/mm3)

and at least anyone of the following (or at least two if clinical pneumonia only = PN 4 and PN 5)

• New onset of purulent sputum, or change in character of sputum (colour, odour, quantity, consistency)

• Cough or dyspnoea or tachypnoea

• Suggestive auscultation (rales or bronchial breath sounds), rhonchi, wheezing

• Worsening gas exchange (e.g., O2 desaturation or increased oxygen requirements or increased ventilation demand)

a – Bacteriologic diagnostic performed by:

Positive quantitative culture from minimally contaminated LRT1

specimen

• Broncho-alveolar lavage (BAL) with a threshold of ≥ 104 cfu/mL or ≥ 5 % of BAL obtained cells contains intracellular bacteria on direct microscopic exam (classified on diagnostic category BAL).

• Protected brush (PB Wimberley) with a threshold of ≥ 103 cfu/mL

• Distal protected aspirate (DPA) with a threshold of ≥ 103 cfu/mL - PN1

Positive quantitative culture from possibly contaminated LRT specimen

Quantitative culture of LRT specimen (e.g., endotracheal aspirate) with a threshold of 106 cfu/mL - PN2

b- Alternative microbiology methods

• Positive blood culture not related to another source of infection

• Positive growth in culture of pleural fluid

• Pleural or pulmonary exam shows evidence of pneumonia

• Positive exams for pneumonia with virus or particular germs (Legionella, Aspergillus, mycobacteria,

Mycoplasma, Pneumocystis carinii)

• Positive detection of viral antigen or antibody from respiratory secretions (e.g., EIA, FAMA,

shell vial assay, PCR)

• Positive direct exam or positive culture from bronchial secretions or tissue

• Seroconversion (ex: influenza viruses, Legionella, Chlamydia)

• Detection of antigens in urine (Legionella) - PN3

c-Others

Positive sputum culture or non-quantitative LRT specimen culture - PN4

No positive microbiology - PN5

B, **Modified CDC criteria for diagnosis of VAP** (15)

RADIOLOGICAL -

Two or more serial chest radiographs with at least one of the following:

• New or progressive and persistent infiltrate

• Consolidation

• Cavitation

In patients without underlying pulmonary or cardiac disease (e.g., respiratory distress syndrome, bronchopulmonary dysplasia, pulmonary edema, or chronic obstructive pulmonary disease), one definitive chest radiograph is acceptable

SIGNS/ SYMPTOMS/ LABORATORY -

For ANY PATIENT, at least one of the following:

• Fever (>38°C or >100.4°F)

• Leukopenia (<4000 WBC/mm3) or leukocytosis (>12,000 WBC/mm3)

• For adults >70 years old, altered mental status with no other recognized cause

and at least two of the following:

• New onset of purulent sputum, or change in character of sputum, or increased respiratory secretions, or increased suctioning requirements

• New onset or worsening cough, or dyspnea, or tachypnea

• Rales or bronchial breath sounds

• Worsening gas exchange (e.g., O2 desaturations (e.g., PaO2/FiO2 <240)7, increased oxygen requirements, or increased ventilator demand)

As the Modified CDC criteria is simpler and most of our lab culture reports are qualitative and not quanitative, It is preferred to HELICS criteria and thus used in this study.

C, **Modified CPIS scoring**

Clinical Pulmonary Infection Score is based on multiple variables including temperature, WBC count, tracheal secretion, oxygenation, radiography and culture. Inclusion of 'culture' in the diagnostic criteria can delay the diagnosis of VAP. Modified CPIS scoring system is introduced by excluding the 'culture' from the variables considered.

Table B- CPIS score calculation (adapted *from 'Ventilator-Associated Pneumonia: The Clinical Pulmonary Infection Score as a Surrogate for Diagnostics and Outcome'- Marya D. Zilberberg and Andrew F. Shorr)*(16)

Parameter	Points
Temperature, °C	
36.5–38.4	0
38.5–38.9	1
⩾39.0 and ⩽36.0	2
Blood leukocyte level, leukocytes/mm^{-3}	
4000–11,000	0
<4000 or >11000	1
Plus band forms ⩾500	2
Tracheal secretions	
<14+	0
⩾14+	1
Plus purulence	2
Oxygenation, PaO_2:FiO_2, mm Hg	
>240 or ARDS	0
⩽240 and no ARDS	2
Pulmonary radiograph finding	
No infiltrate	0
Diffuse or patchy infiltrate	1
Localized infiltrate	2
Culture of tracheal aspirate specimen (semiquantitative: 0–1, −2, or 3+)	
Pathogenic bacteria cultured ⩽1 or no growth	0
Pathogenic bacteria cultured >1+	1
Plus same pathogenic bacteria on Gram stain >1+	2

NOTE. ARDS, acute respiratory distress syndrome; PaO_2:FiO_2, ratio of partial pressure of arterial oxygen to the fraction of inspired oxygen.

A score of 7 or more in modified CPIS is considered as ' high probability' for Ventilator Associated Pneumonia.

As there is no gold standard for the diagnosis of VAP so far, a combination of clinical, radiological and microbiological assessment have to be applied for an early detection of VAP. Clinical suspicion of VAP arises if there is a fever of >38.3degree celsius, purulent tracheal secretions, leukocytosis> 10,000/mm3 or leukopenia<

4000/mm3 and the presence of a new radiological opacity in the chest X-ray. But there can be many other causes for these clinical presentations apart from VAP. It decreases the specificity of the diagnosis of VAP by using clinical criteria alone. According to a study conducted by Fagon et al, clinical criteria in diagnosis of VAP has false positivity of 20-25% and a false negativity of 30-35% (6).

MICROBIOLOGICAL SPECIMENS

A, Non-quantitative or semi-quantitative samples :-

It includes Gram stain and the culture of tracheal aspirate. It has the advantage of that there is no need of technical expertise or special equipment or technology, but it is reproducible. But the specificity and sensitivity of these tests to a diagnosis of VAP is low. The growth can be a mere colonisation. In a study were 48 patients having respiratory failure are investigated and followed up, the non-quantitative tracheal culture and open lung biopsy had a concordance of only 40% (17). These cultures are more sensitive and specific, when the sample is adequate and there is no change or addition of antibiotic in the previous 72 hours.

Poor positive predictive value of these cultures will result in over diagnosis and over treatment of VAP. Depending more on the clinical signs and symptoms will have an opposite effect .

B, Quantitative culture samples :-

Various methods to get good samples include-

1, Quantitative ET Aspirate

2, Samples from distal airway through an endobronchial catheter

3, Blind bronchial sampling

4, Sampling by a protected telescoping catheter

5, Bronchoscopic Broncho-alveolar lavage

6, Protected BAL (mini-BAL)

7, Bronchoscopic Protected Specimen Brush

'Where to sample?' is decided based on the site of the opacities in the radiological evaluation. Oropharyngeal colonization in the sample is suggested by

- more than 1% epithelial cells

- 10 or more epithelial cells per low-power

.

Threshold values for each and every type of quantitative culture samples has been decided and they are expressed as Colony Forming Units per milliliter. If the CFU/ml of a particular sample is more than the threshold value for that particular sample, then a diagnosis of Ventilator Associated Pneumonia s made. Threshold values of various sampling methods are mentioned below :-

1, Quantitative culture of ET aspirate - $\geq 10^5$ to 10^6 CFU/ml

2, Bronchoscopic BAL - $\geq 10^4$ CFU/ml

3, Bronchoscopic Protected Specimen Brush $\geq 10^3$ CFU/ml (18)

COMMON ORGANISMS

1, *Pseudomonas* species

2, Other highly resistant Gram-negative bacilli

3, Staphylococci

4, E*nterobacteriaceae*

5, Streptococci

6, H*aemophilus* species (19)

Resistant organisms such as *Pseudomonas*, *Acinetobacter* species and methicillin-resistant *Staphylococcus aureus (MRSA) are commonly seen after* -

a, Prior antibiotic treatment

b, Prolonged mechanical ventiation

Atypical bacteria, fungi and viruses can also cause VAP, but such pneumonias are not studied in detail.

The micro-organism that causes the VAP varies depending on

- The patient profile
- In which ICU he was admitted
- Country
- The day of occurence of VAP (post intubation) (20)

Early onset VAP is usually caused by

- Staphylococcus aureus
- Strpetococcus pneumonia
- Haemophilus influenzae

Late onset VAP is generally caused by

- Pseudomonas aeruginosa
- Acinetobacter
- Enterobacter
- MRSA (21)

In a study conducted by Varun Goel et al in a medical college in Karnataka showed that out of 53 cases they followed up 3.77% were polymicrobial, 49.09% was due to Acinetobacter baumannii and 30.9% was due to Pseudomonas aeroginosa, which were multi-drug-resistant (22). The background knowledge of the microbiological profile and sensitivity pattern of organisms causing VAP helps the physician to initiate the appropriate anti-microbial therapy at the earliest.

Patients with VAP caused by Staphylococcus aureus and Pseudomonas aeroginosa are at high risk, due to their resistance to drugs and high mortality(23). Most of the resistant organisms occur in late VAP. Pseudomonas are commonly seen in those who are on steroids, previously received antibiotics or having structural lung disease.

ANTI- MICROBIAL THERAPY

Once the samples for microbiological evaluation was obtained, it is advisable to start on an empiric regimen. Delay in initiating the treatment will result in increased morbidity and mortality. In a study were 430 patients who developed VAP was followed up, 34% of those who did not receive immediate empiric antimicrobial therapy, incidence of shock was 28.8% , whereas those who received was 17.1% and attributable mortality was 24.7% , where as it was 16.2%, in those who received appropriate antibiotic therapy (24). Appropriate and immediate empiric therapy should be initiated in patients whom a diagnosis of VAP is suspected. In a study where outcomes in patients whom empiric antibiotic therapy was initiated within 24 hours of the diagnosis was compared to those who received antibiotic therapy after 24 hours (25). Rates of bacteremia and mortality were significantly increased in those who received delayed treatment.

The American Thoracic Society recommends aggressive management with empiric anti-microbial treatment in late VAPs and in those who are at risk in getting infected with drug resistant organisms. The recommended empiric regimen in such patients include

a, Anti-pseudomonal betalactem - betalactamase inhibitor / anti-pseudomonal cephalosporins/ anti-pseudomonal carbapenems plus

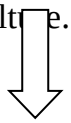
b, Anti-pseudomonal fluoroquinolone or aminoglycoside plus

c, Vancomycin or Linezolid (26).

-A FLOW CHART FOR THE ANTIMICROBIAL THERAPY

If clinical suspicion of VAP is high with a modified CPIS score of more than 6, initiate on empiric therapy after sending ET aspirate for culture and sensitivity.

Re-assess after day-3, if the modified CPIS score is less than 7 and culture did not show any growth, discontinue the antibiotic. If the modified CPIS score is equal to or more than 7, optimize the antibiotic according to the culture and sensitivity of the organism isolated in the ET aspirate culture.



Re- assess the patient on day-7 for clinical improvement. If there is complete resolution of signs and symptoms, stop the antibiotic. If there is no resolution or there is worsening of the clinical signs and symptoms, thoughts are

a, Non-Fermenting Gram Negative Bacilli requires a longer duration of therapy.

b, Complicating issues like abscess or empyema should be excluded.

c, Re-evaluation should be done for secondary infection with a drug resistant organism.

PREDICTORS OF POOR OUTCOME

The Clinical Pulmonary Infection Score (CPIS) was proposed by Pugin et al. They showed that CPIS has a good correlation with bronchial lavage culture bacterial index and that it can be as good a diagnostic predictor of VAP, as bronchial lavage quantitative culture (27). In a prospective study done in Beijing, it was found that there is a significant relation between CPIS score and duration of mechanical ventilation ($r = 0.526$, $P = 0.00$), duration of ICU stay ($r = 0.449$, $P = 0.00$) and the duration of total hospital stay ($r = 0.519$, $P = 0.00$) (28).

A high APACHE-II score also was found to be having a significant correlation with the diagnosis and outcome of VAP (18). In a retrospective cohort study, APACHE II score >27 at onset of VAP was found to be an independent predictor of the mortality (ROC AUC: 0.841: Sensitivity: 70%; Specificity: 90.6%; p=0.001) (29) .

Multi Organ Dysfunction Score was developed by Marshall et al, which includes evaluation of failure of 6 organs- Respiratory, hematologic, hepatic, cardiovascular, neuronal and renal. Each one is given a score from 0-4 based on extend of damage. Study show that , for a total points of 9 to 12 the mortality rate is about 25% and it gradually increases with the increase in total points. 75% mortality for a total point of 17- 20 and 100% for >20 (30). MOD score at diagnosis of VAP and the comparison

with the outcome will help us to understand the influence of other organ damage in the outcome of VAP patients.

Many biomarkers were considered and studied in association with VAP, as early indicators, treatment response markers and outcome predictors. Midregional pro-atrial natriuretic peptide- MR proANP, C-terminal provasopressin-copeptin- CT-proAVP and procalcitonin were found to be indicators of sepsis and predictors of mortality (31)(32)(33). In a prospective observational study done by Ashraf Abd El Halim et al in Egypt, a significant statistical difference (*p* value < 0.001) was found in the serum Procalcitonin levels among VAP patients, non VAP-ICU patients and healthy controls (1.54 ± 0.5 ng/ml , 0.06 ± 0.03 ng/ml and 0.04 ± 0.02 ng/ml respectively) (34). In a study done by Charles Edouard et al, they found out that on Day 1, serum procalcitonin > 1 ng/ml is the strongest indicator of poor outcome (odds ratio of 12.3). On Day 3, a P/F ratio < 210 mm Hg and serum procalcitonin of > 1.5 ng/ml were more strongly associated with poor outcome. On Day 7, serum procalcitonin > 0.5 ng/ml was the strongest independent predictor of poor outcome,(odds ratio of 64.2) (9). There are multiple studies which show that rate of fall of procalcitonin levels can be used as a prognostic factor to predict the outcome in VAP patients. But multiple procalcitonin level estimation is not economically practical in our setting as the cost requirement is high. In this study, we'll be trying to correlate the initial procalcitonin level at the time of diagnosis of VAP to the prediction of outcome.

PREVENTION

Prevention is better and easier than cure. Strategies for preventing VAP are described in detail by The Society for Healthcare Epidemiology of America, in their 2014 update on VAP. Some prevention strategies are :-

a, Preventing aspiration

Aspiration is an important risk factor for both hospital and ventilator acquired pneumonia. Important modalities for aspiration prevention are-

1, Positioning of the patient

Supine position of a ventilated patient predisposes to aspiration. Head end should be elevated by 30 to 45° (35). Supine position will pre-dispose a patient to microaspiration of the gastric contents when compared to other positions (36)(37). Even if there is no difference in the mortality detected, it is advisable to keep the ventilated patient in the semi-recumbent position, if there is no contraindication.

2, Subglottic drainage

Subglottic secretion drainage lessen the chance of aspiration and thus the incidence of VAP. Modified endo-tracheal tubes are available which will help in continuous or intermittent drainage of the subglottic secretions. But cost is of concern.

A meta-analysis showed that the drainage of the subglottic secretions will reduced the length of the ICU stay, days of mechanical ventilation and prolongs the time to the

onset of VAP. But this strategy also does not show any improvement in the mortality (38).

b, Gastric volume monitoring

It is a standard practice to monitor the gastric residual volume prior to increase in the gastric feed volume. It was thought to be helpful in preventing the accumulation of the gastric content leading to vomiting and thus aspiration. But several studies had shown that there is no correlation between the gastric volume monitoring and incidence of VAP, instead it was noticed that such monitoring will lead to unnecessary reduction in the calorie provided to the patient (39).

c, Decontamination of the digestive tract

Decontamination of the digestive tract using antiseptics or non-absorbable antibiotics in the oropharynx is done with an intention to decrease the colonization in the upper respiratory tract. Poor oral hygiene in ventilated patient, in whom the normal mechanical methods of oral hygiene is inhibited will lead to colonization of the dental and the gingival plaques by aerobic pathogens.

In a meta-analysis done in 2007, which included 11 trials, showed that the incidence of VAP was reduced significantly in those who received oral application of antiseptics/ antibiotics (40).

d,Probiotics

Probiotics are microorganisms from humans that can persist in the lower intestinal tract and provide a benefit to the host in terms of health (41). Various studies had shown benefit in preventing VAP, but no advantage in mortality prevention was noticed.

e, Silver-coated endotracheal tube

NASCENT, a single blinded randomized trial, in 2003, compared silver coated ETT with an uncoated ETT in ventilated patients ventilation (42). This study showed that incidence of microbiologically confirmed VAP was lower in those who had Silver coated ETT, in comparison with those who normal ETT. A retrospective analysis in the same cohort later showed a reduced mortality in the silver coated ETT group.

f, Glucocorticoids

Use of glucocorticoids was not shown to decrease the incidence of Hospital Acquired Pneumonia (HAP) in Traumatic brain injury patients (43), but it had shown benefit in reducing HAP in Acute Respiratory Distress Syndrome patients (44). Further studies are required to establish the benefit of steroids in ventilated patients.

g, Others

1, Glove and gown for the nursing staff
2, Endotracheal tube cuff pressure >20 cm H_20
3, Orogastric rather than nasogastric feeding tubes
4, Avoiding nonessential tracheal suctioning

In 2007, a meta-analysis was done to compare the closed endotracheal suctioning with open endotracheal suctioning in preventing Ventilator Associated Pneumonia (45) . Nine randomized control trials were included in the same. This analysis showed that there is no superiority for closed endotracheal suctioning above open method in decreasing the incidence of VAP or ICU mortality.

Mortality rate in VAP ranges between 20% - 76% (46). Other than significant mortality, it also causes significant morbidity and indirect expenditure in terms of loss of pay , expenses of the bystander and miscellaneous expenses, due to the prolonged hospital stay. In a retrospective study the cost of treatment of a VAP was found to be five times more than a non-infected patient who was treated in ICU (47). Thus it is important to detect VAP and initiate adequate and appropriate therapy as early as possible. And it is also important to understand and explain the outcome of therapy and prognosis of the patient based on the clinical scores and biomarkers available.

Even if multiple studies had happened before on different aspects of VAP, it is important to have a significant study analyzing all these data in a single cohort, in a teaching institute in South India. In CMC.Vellore Medical ICU, about 300-350 patients get admitted every year. About 70% of them undergo invasive ventilation. From August2013-November2013, 12 patients got VAP. But there was 28 VAPs reported in MHDU in the same period. Focus of this study is to get detailed

information on the clinical profile of VAP, microbiological profile, prognosis predictors that can be assessed at the time of diagnosis itself from a single cohort of patients (intubated patients in medical and surgical ICUs and HDUs, and AICU in CMC,Vellore over 12 months of study period). The incidence of VAP also will be looked at.

MATERIAL AND METHODS

This prospective observational study was conducted in the various Intensive Care Units in Christian Medical College, Vellore which is a tertiary referral centre in Tamil Nadu. Approval of the Institutional Review Board at Christian Medical College was obtained in October 2013 (IRB Min No. 8449).

STUDY DESIGN

Observational study.

STUDY PERIOD

February 15th 2013 to February 15th 2015.

SETTING

The study was conducted in the Medical, Surgical and A-Block Intensive Care Units in Christian Medical College and Hospital, Vellore.

PARTICIPANTS

Among the patients admitted in the Medical, Surgical and A- Block Intensive Care Units in Christian Medical College, Vellore, during the study period, those who developed Ventilator Associated Pneumonia as per the Modified CDC criteria.

Inclusion criteria:

- Intubated patients admitted in ICU - MICU/MHDU, SICU/SHDU, AICU in Christian Medical College, Vellore
- Clinico-radiological evidence of pneumonia

Exclusion criteria:

- Pneumonia before intubation or within 48hrs post intubation
- Intubated outside
- Any abnormal opacity on chest x ray at the time of intubation

SAMPLE SIZE

This is a descriptive study where all the intubated patients admitted in MICU/MHDU,SICU/SHDU,AICU,KHDU of CMC, Vellore within a period of 12 months from the beginning of the study who develops VAP will be evaluated and followed up

METHODOLOGY-

Patients admitted in Medical, Surgical and Respiratory medicine ICUs and HDUs in CMC, Vellore for a period of 12 months will be followed up. Any patient with a new onset fever, purulent secretions, leukocytosis, decline in oxygenation will be investigated with a Chest X-ray. If a physician diagnosis of Hospital Acquired Pneumonia is made, the patient will be included. The diagnosis will be based on the Modified CDC Criteria based on 2014 guidelines.

CPIS score, MOD Score and APACHE-II score will be calculated, Procalcitonin levels and microbiologic results of any respiratory and blood sample cultures will be obtained. They will be followed up for the rest of the ICU/HDU and hospital stay till the discharge (or death in hospital).

'Resistant organisms' were defined as per the recommendations by the Centers for Disease Control and Prevention (CDC) and the European Centre for Disease Prevention and Control (ECDC) , which was published in Clinical Microbiology and Infectious disease in 2011.

A difference of 2 ICU days and 4 hospital days are considered as clinically significant difference in this study.

MAIN OUTCOME MEASURES-

-Clinico-radiological features will be analyzed

-The microbiological profile of organisms causing VAP in various ICU/HDUs will be analyzed

-The correlation between CPIS Score, MOD Score, APACHE-II Score and Procalcitonin levels at the diagnosis of VAP and outcome in terms of number of days of ICU/HDU stay, number of days of hospital stay and mortality will be analyzed separately.

VARIABLES

- The ICU/HDU where the patient is admitted
- Microbiological profile of organisms
- Early and late VAP
- CPIS score
- APACHE-II score
- MOD Score
- Procalcitonin levels
- Number of days of ICU/HDU and hospital stay
- Discharged/died

DATA SOURCES/MEASUREMENT:

All the intubated patients in MICU/MHDU, SICU/SHDU, AICU and KHDU for 12months will be considered. The ICU registrars will be well informed when to suspect VAP. When VAP is suspected in a patient Chest x-ray will be done, and ET-aspirate and Procalcitonin levels will be sent for that patient and the principal investigator will be informed about the patient. The patient will be seen by the Principal investigator on the same day and the CPIS score, MOD Score and APACHE-II score of that patient will be calculated .

The patient will be followed up throughout his stay in the hospital. His number of days of ICU/HDU stay , hospital stay and the final outcome (discharged/ death) will be noted.

STATISTICAL METHODS:

Logistic regression analysis was done to determine the association between the continuous variables -Procalcitonin, Modified CPIS Score, MOD Score and APACHE-II Score at the time of diagnosis, and the final outcome in VAP (Death/ discharged). A survival analysis was done to calculate the mean/ median survival period in VAP patients (ICU stay and Hospital stay) and the association with the Procalcitonin, Modified CPIS score, MOD Score and APACHE-II Score at the time of diagnosis. Ranksum Test was used to compare the median values of a variable among 2 groups, and Kruskal Wallis test is

used to compare the median values of a variable among the three ICUs. T-Test is applied to compare the mean value of a variable among 2 different groups and ANOVA test is used to compare the mean values of various variables among the different ICUs.

COMPLETE BUDGET PLAN –

The tests included in this study is usually done in the ICUs as a part of the protocol for the infections. Therefore extra expenditure was not estimated for the study.

RESULTS

3005 intubated patients were managed in the Medical, Surgical and A-block ICUs during the study period from 15th february 2014 to 15th february 2015. 200 patients were evaluated due to the clinical suspicion of Ventilator Associated Pneumonia. Of which 78 patients fulfilled the Modified CDC criteria and the Inclusion criteria of the study, and they were followed up during the stay in the hospital, till discharge/ death. Patients who had any lung opacities at the time of admission were excluded, even if they had fulfilled the Modified CDC criteria for the diagnosis of Ventilator Associated Pneumonia. It was done so, to avoid any contamination of the data as the objective was to find out the clinical and biological profile of the VAP in our ICUs.

DEMOGRAPHIC AND CLINICAL DATA OF THE COHORT

TABLE- 1. A, Demography of the cohort B, Demography of the AICU arm C, Demography of the Medical ICU arm D, Demography of the Surgical ICU arm

A,

OVERALL

Variable	n	Mean	S.D.	Min	0.25	Mdn	0.75	Max
age	78	45.47	17.96	18	28	45	62	87
vapday	78	7.04	4.82	3	4	6	8	28
map	78	84.76	15.37	54	71	81	96	125
cvp	78	10.31	0.86	8	10	10	11	12
hr	78	109.38	16.95	56	100	110	120	142
temp	78	100.93	1.17	98	100	101	101	104
rr	78	23.91	5.97	12	20	24	28	49
gcst15	78	7.03	2.92	2	5	8	10	10
output	78	1843.29	1005.95	0	1200	1787.5	2400	5800
ph	78	7.41	0.1	7.07	7.35	7.43	7.47	7.68
aagradien	78	137.12	113.97	-7.8	79.8	103.58	163.4	589.5
fio2	78	39.67	19.23	21	30	31	40	100
pao2	78	92.64	37.51	45	70	85.5	108	263
pfratio	78	258.92	111.18	46	193	242.5	287	623
pc02	78	38.29	10.39	23	31.6	35.85	43	75
hematocrit	78	28.19	6.13	15	24	27.65	31	46
platelets	78	160000	120000	3000	70000	140000	190000	490000
wbc	78	14983.72	8690.04	100	8300	13900	20600	41600
sodium	78	138.62	6.36	125	134	138.5	143	158
potassium	78	3.87	0.58	2.3	3.5	3.8	4.2	5.7
creatinine	78	1.79	1.96	0.2	0.54	0.92	2.37	10.27
bilirubin	78	2.59	4.85	0.14	0.48	0.94	2	30.47
urea	78	76.72	64.42	12	28	53.5	111	303
glucose	78	146.38	32.05	83	120	140	167	250
albumin	78	2.4	0.58	0.9	2	2.45	2.7	4.1
cpis	77	5.35	1.38	3	4	5	6	9
mod	77	8.05	3.45	3	5	8	10	16
apache3	77	79.01	26.16	28	59	76	97	146
procalcitonin	59	24.75	41.06	0.06	1.56	7.85	23.45	159.7
icustay	77	14.34	15.88	1	5	10	19	103
hospstay	77	22.79	22.67	1	9	15	30	103

B,

AICU

Variable	n	Mean	S.D.	Min	0.25	Mdn	0.75	Max
age	6	47.17	22.28	24	27	43.5	66	79
vapday	6	11.67	8.52	4	6	8	18	26
map	6	77	11.78	68	70	73	78	100
cvp	6	10.33	0.52	10	10	10	11	11
hr	6	94.67	23.62	56	82	100	110	120
temp	6	101.17	1.17	99	101	101.5	102	102
rr	6	22.17	5.08	15	20	22	24	30
gcst15	6	4.17	3.37	2	2	2	8	9
output	6	1626.33	1252.79	190	404	1715	2120	3614
ph	6	7.36	0.11	7.2	7.32	7.34	7.48	7.5
agradien	6	147.88	56.58	58	97.7	171.75	192.1	196
fio2	6	40.33	8.16	30	35	38.5	50	50
pao2	6	94.33	22.11	54	87.4	99.5	111.1	114.5
pfratio	6	237	88.81	135	175	217.5	295	382
pc02	6	45.6	9.62	36.1	38.4	44.2	48.8	61.9
hematocrit	6	27.85	4.86	24	25	26.05	28.8	37.2
platelets	6	44833.33	59891.29	3000	8000	14500	74000	160000
wbc	6	7650	8614.58	100	2200	6050	7200	24300
sodium	6	141	8.44	130	134	140.5	150	151
potassium	6	4.4	0.38	3.8	4.3	4.35	4.7	4.9
creatinine	6	2.03	1.4	0.48	0.85	1.81	3.55	3.66
bilirubin	6	6.05	9.03	0.4	1	1.35	8.93	23.3
urea	6	157.33	104.98	45	67	151.5	226	303
glucose	6	147	32.88	120	120	134	174	200
albumin	6	2.53	0.42	1.9	2.4	2.5	2.7	3.2
cpis	6	6	1.1	5	5	6	6	8
mod	6	11.83	4.4	4	11	12	16	16
apache3	6	112.17	19.75	95	97	108	119	146
procalcitonin	6	33.99	56.88	1.25	3.43	13.86	22.56	149
icustay	6	8.67	5.96	3	5	7.5	9	20
hospstay	6	15.17	16.69	3	5	8	20	47

C,

MICU

Variable	n	Mean	S.D.	Min	0.25	Mdn	0.75	Max
age	41	45.78	18.53	18	28	45	64	87
vapday	41	6.49	4.58	3	4	5	7	28
map	41	84.65	12.83	60	75	85	95	118
cvp	41	10.32	0.88	8	10	10	11	12
hr	41	111.98	14.02	83	100	110	120	142
temp	41	101.27	1.16	98	101	101	102	104
rr	41	24.44	5.78	12	20	25	28	42
gcst15	41	6.85	2.82	2	5	7	10	10
output	41	2024.24	1132.12	0	1322	1800	2533	5800
ph	41	7.42	0.11	7.07	7.36	7.43	7.48	7.68
aagradien	41	140.17	138.65	-7.8	69	100.65	146	589.5
fio2	41	41.15	24.4	21	30	30	40	100
pao2	41	96.15	47.71	45	69	79	111	263
pfratio	41	268.45	127.48	46	210	243.3	287	623
pc02	41	37.66	12.51	23	29	34	43	75
hematocrit	41	28.32	7.25	15	23	28.2	32	46
platelets	41	170000	100000	22000	100000	170000	230000	490000
wbc	41	16555.37	9633.98	1900	9600	13400	23600	41600
sodium	41	138.85	6.03	125	135	138	142	158
potassium	41	3.82	0.52	3.1	3.5	3.7	4.1	5.1
creatinine	41	1.72	2.21	0.22	0.5	0.86	1.55	10.27
bilirubin	41	1.82	2.99	0.14	0.4	0.7	1.2	12.5
urea	41	65.66	62.58	12	22	42	80	289
glucose	41	149.83	38.08	83	120	151	174	250
albumin	41	2.44	0.61	0.9	2	2.4	2.8	4.1
cpis	40	5.63	1.41	3	4.5	6	6.5	9
mod	40	7.58	2.93	3	5	7	9	14
apache3	40	76.47	23.03	38	59	72.5	92.5	132
procalcitonin	23	6.65	10.85	0.06	0.92	3.11	7.64	51.74
icustay	40	15.03	18.98	1	5	10	16.5	103
hospstay	40	24.5	27.01	1	8	13.5	29.5	103

D,

SICU

Variable	n	Mean	S.D.	Min	0.25	Mdn	0.75	Max
age	31	44.74	16.92	21	29	47	60	77
vapday	31	6.87	3.85	3	4	5	11	15
map	31	86.4	18.67	54	71	81	100	125
cvp	31	10.29	0.9	8	10	10	11	12
hr	31	108.81	18.16	63	98	110	120	142
temp	31	100.45	1.02	98	100	101	101	103
rr	31	23.55	6.43	14	20	22	26	49
gcst15	31	7.81	2.66	2	7	9	10	10
output	31	1645.97	729.63	260	1000	1770	2300	2945
ph	31	7.41	0.09	7.08	7.39	7.43	7.46	7.56
aagradien	31	130.99	84.27	13.5	79.8	112	167.8	436.2
fio2	31	37.58	11.7	21	30	35	40	80
pao2	31	87.68	21.29	58	71.9	87.2	103	139
pfratio	31	250.55	91.93	76.9	189	243	287	479
pc02	31	37.71	6.41	28.1	32.8	37.6	42.3	53
hematocrit	31	28.07	4.72	18.1	25	27.4	31	39.6
platelets	31	160000	130000	19000	63000	120000	190000	480000
wbc	31	14324.52	6566.97	900	8500	15000	17900	34000
sodium	31	137.84	6.45	127	132	138	143	153
potassium	31	3.83	0.64	2.3	3.4	3.8	4.2	5.7
creatinine	31	1.83	1.75	0.2	0.55	0.98	2.47	7.14
bilirubin	31	2.93	5.61	0.19	0.5	1.2	2.9	30.47
urea	31	75.74	46.1	16	40	63	123	167
glucose	31	141.71	21.99	107	130	140	150	194
albumin	31	2.32	0.57	1	1.6	2.5	2.7	3.5
cpis	31	4.87	1.28	3	4	5	6	7
mod	31	7.94	3.54	3	5	8	11	16
apache3	31	75.87	27.21	28	54	71	92	137
procalcitonin	30	36.77	47.93	0.08	1.72	14.37	45.61	159.7
icustay	31	14.55	12.54	1	5	11	19	58
hospstay	31	22.06	17.07	1	11	18	32	71

The mean age of the patients included in the study was 45years. Mean day of development of Ventilator associated pneumonia (VAP) was 7 days post intubation. They had an average of 14 days of hospital stay and 23 days of total number of days in the hospital. Only 59 patients had Procalcitonin levels analyzed. One patient was discharged at request from the ICU itself, before completion of the treatment. So he was not included in the analysis for the primary objective of 'prognostic factors towards the outcome'.

Patients from the Surgical ICU had a mean age of 45 years. Mean days to development of VAP was 7 days. Average number of ICU stay was 15 days and that of total hospital days was 22 days. Patients from Medical ICU had an average age of 46 years , mean days to development of VAP was 6 days, ICU stay for 15 days and hospital stay for 25 days. AICU patients had an average age of 47 years, mean days to development of VAP was 12 days, ICU stay of 9 days and Hospital stay of 15 days.

CLINICAL PROFILE

Table 2 Significant features of the Cohort

	AICU	MICU	SICU	TOTAL	P VALUE
Mean AGE(yrs)	47.17 (22.28)	45.78 (18.53)	44.74 (16.92)	45.47	0.95
Median Hosp Days	8 (3-47)	13.5 (1-103)	18 (1-71)	15	0.43
Median ICU Days	7.5 (3-20)	10 (1-103)	11 (1-58)	10	0.50
Median Day of developing VAP	8 (4-26)	5 (3-28)	5 (3-15)	6	0.16
Median APACHE III	108* (95-146)	72.5 (38-132)	71 (28-137)	76	0.009
MODS	12 (4-16)	7 (3-14)	8 (3-16)	8	0.07
Mod CPIS	6 (5-8)	6 (3-9)	5 (3-7)	5	0.05
Procalcitonin (ng/dl)	13.86 (1.25-149)	3.11* (0.06-51,74)	14.37 (0.08-159.7)	7.85	0.012

Age is represented as mean age and standard deviation is mentioned in closed bracket below the mean value. Rest of the variables including Hospital days, ICU days, Day of developing VAP, APCHE-III, MODS, Modified CPIS and Procalcitonin levels were taken as the median, as there was a wide range of values. The minimum and maximum values are mentioned in the closed brackets below the median value.

ANOVA test was used to compare the mean age between the three ICUs and Kruskal Wallis test was used to compare the median of the rest of the variables from the three ICUs.

*-- APACHE-III score was significantly high in the AICU arm, when compared to the rest of the cohort. The median score was 108 in AICU arm, where as average of all the median values were 76. (p=0.009). The Procalcitonin level was significantly low in the Medical ICU arm- 3.11ng/dl , in comparison to 13.86 ng/dl and 14.87 ng/dl in AICU and Surgical ICU respectively (p=0.012). There was no significant difference among the 3 different arms in respect to the variables such as age, median APACHE III, modified CPIS, MOD score and Procalcitonin levels.

EARLY AND LATE VAPS- PROPORTION

Table 3. Early and Late VAP - Comparison among the 3 ICUs

	EARLY VAP	LATE VAP
AICU	1/6 (16.67%)	5/6 (83.33%)
MICU	17/41 (41.46%)	24/41 (58.54%)
SICU	11/31 (35.48%)	20/31 (64.51%)
TOTAL	29/78 (37.18%)	49/78 (62.82%)

p=0.486

37.18% had early VAPs. Incidence of early VAP (within 4 days of intubation) was much lesser than the incidence of late VAP (after 4 days of intubation) in all the ICUs.

ANOVA test was used to compare the values from the various ICUs. There was no significant statistical difference noticed between the three ICU on the incidence of the Early and the Late VAP.

SEX DISTRIBUTION

Figure 1 Sex distribution of the cohort in the various arms

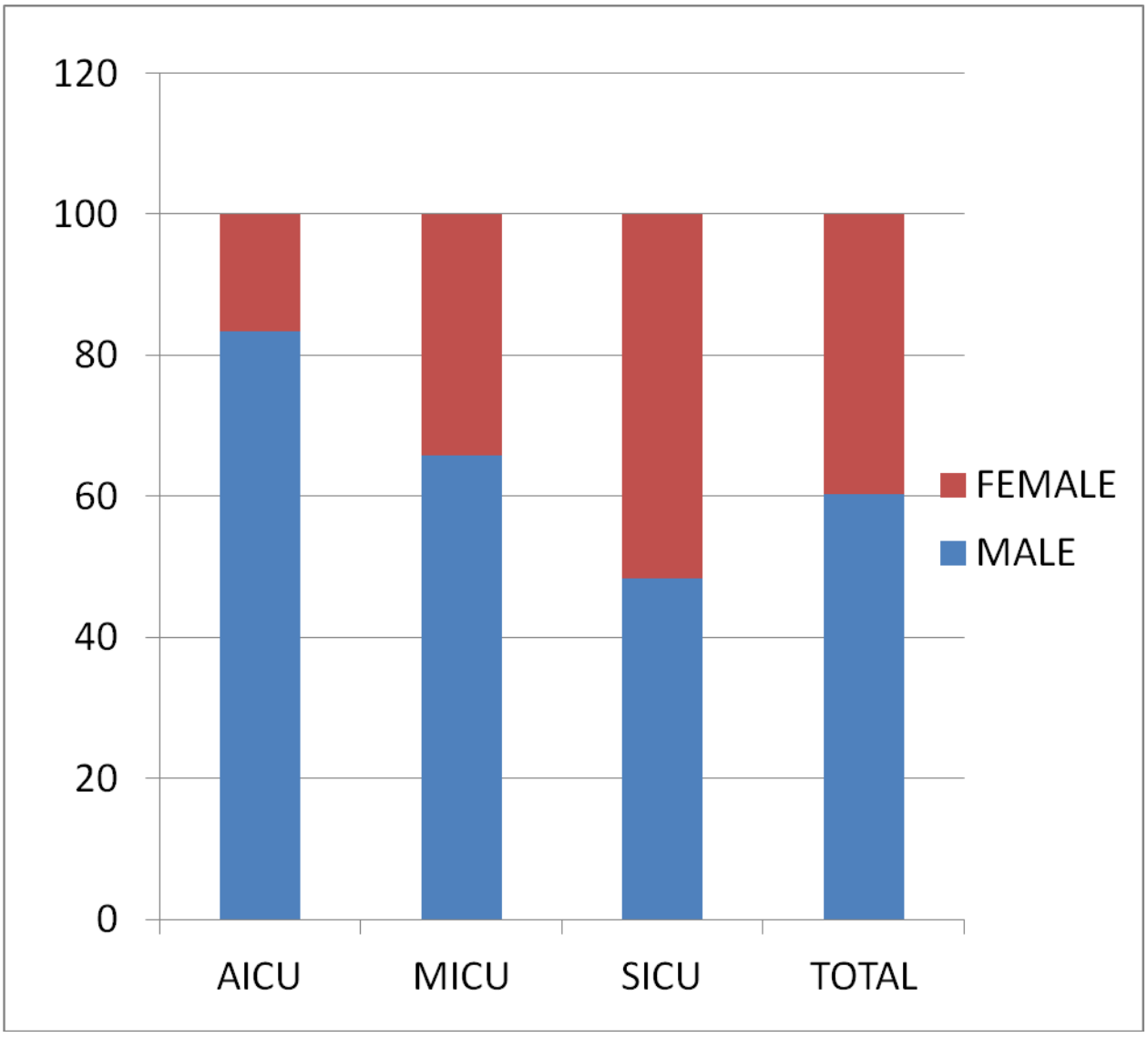


Table 4 Sex distribution of the cohort in the various arms

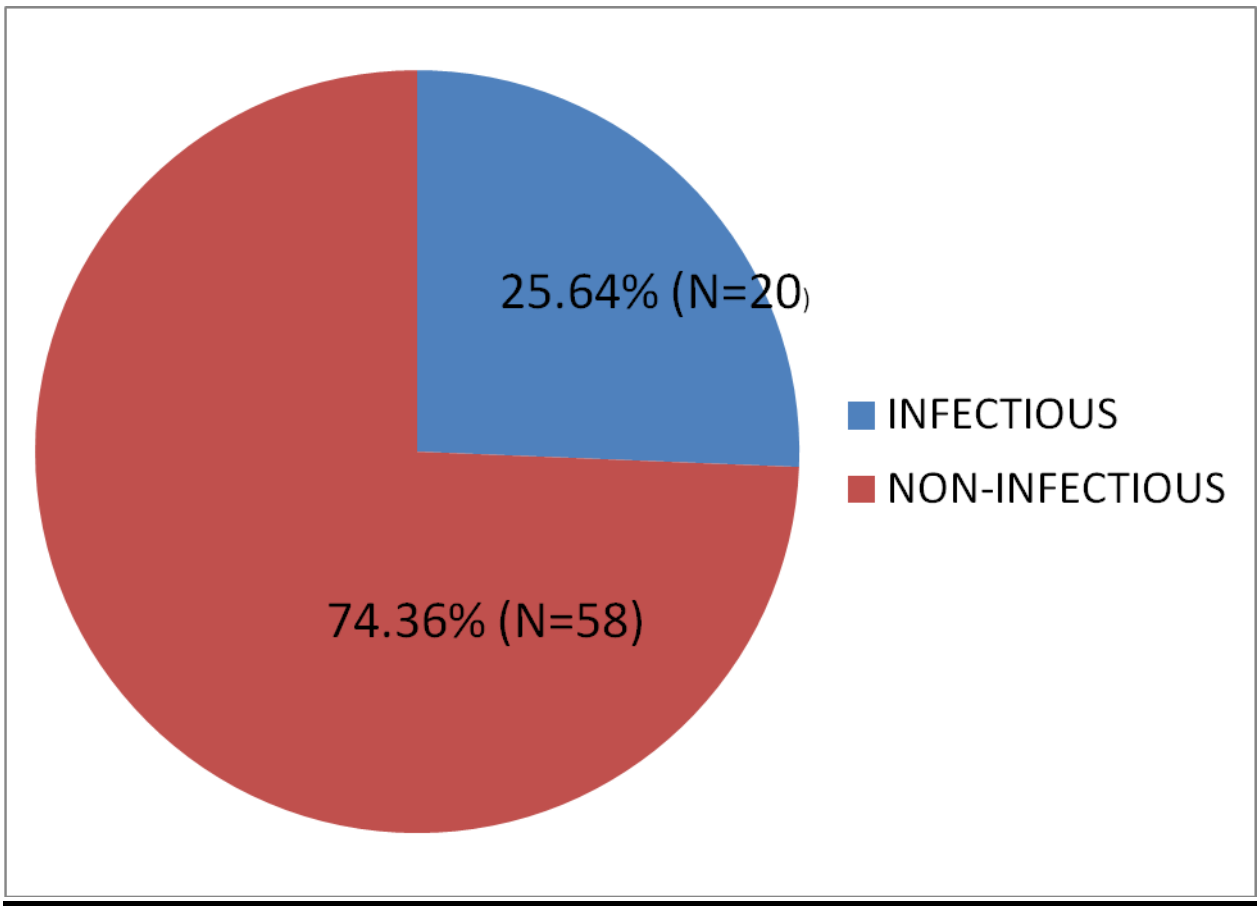
SEX	AICU	MICU	SICU	TOTAL
FEMALE % (n)	16.67 (1)	34.15 (14)	51.61 (16)	39.74 (31)
MALE % (n)	83.33 (5)	65.85 (27)	48.39 (15)	60.26 (47)

p=0.158

ANOVA test was used to compare the sex distribution among the three arms and there was no significant difference noticed. There were 31 females (39.74%) and 47 males (60.26%) in the cohort.

PATIENTS ADMITTED IN ICU WITH A PRIMIARY DIAGNOSIS OF INFECTIOUS ORIGIN

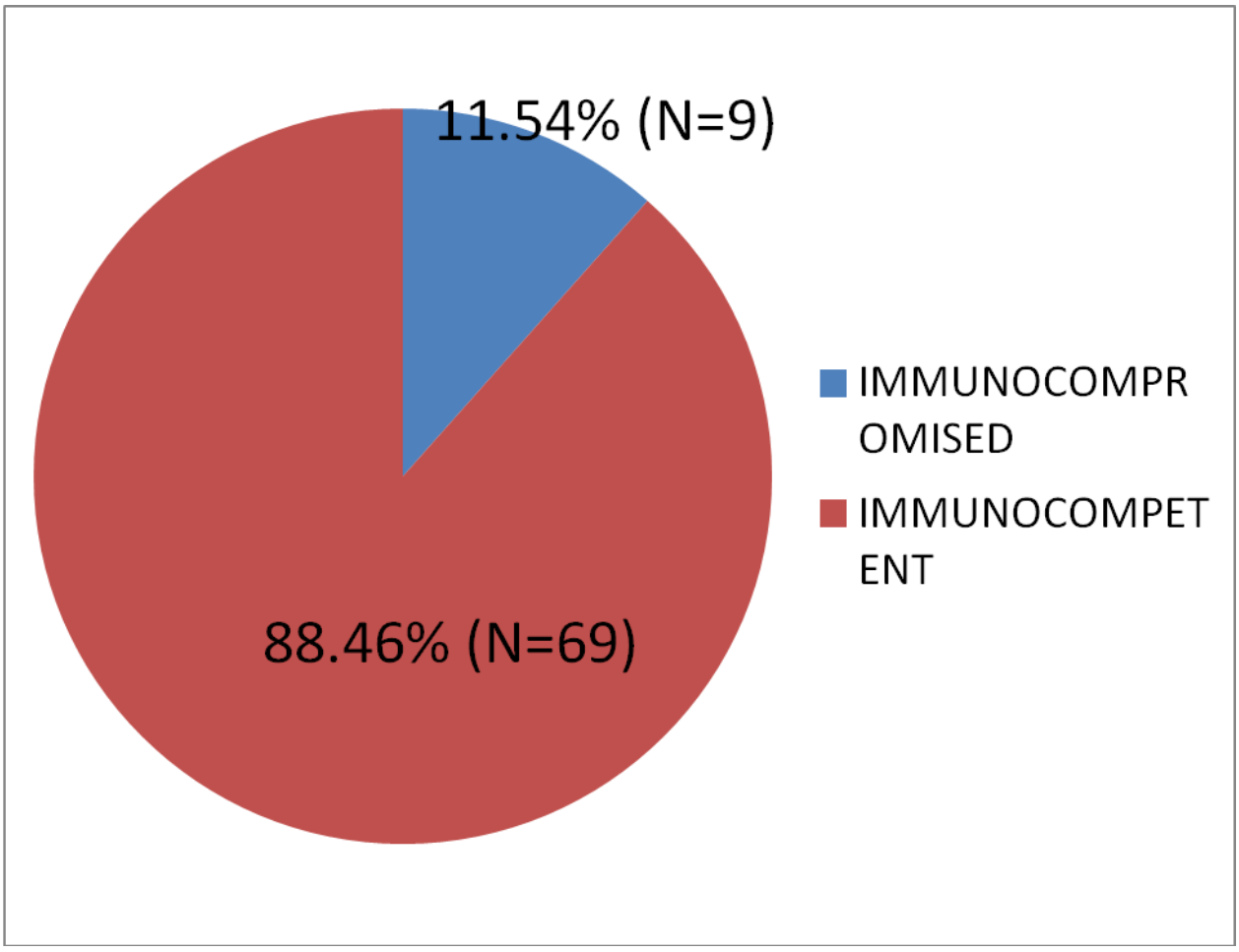
Figure 2 Proportion of patients admitted in ICU primarily with a infectious disease.



25.64% of all VAP patients had primarily infectious diseases as a reason for the ICU admission.

PROPORTION OF IMMUNOCOMPROMISED PATIENTS

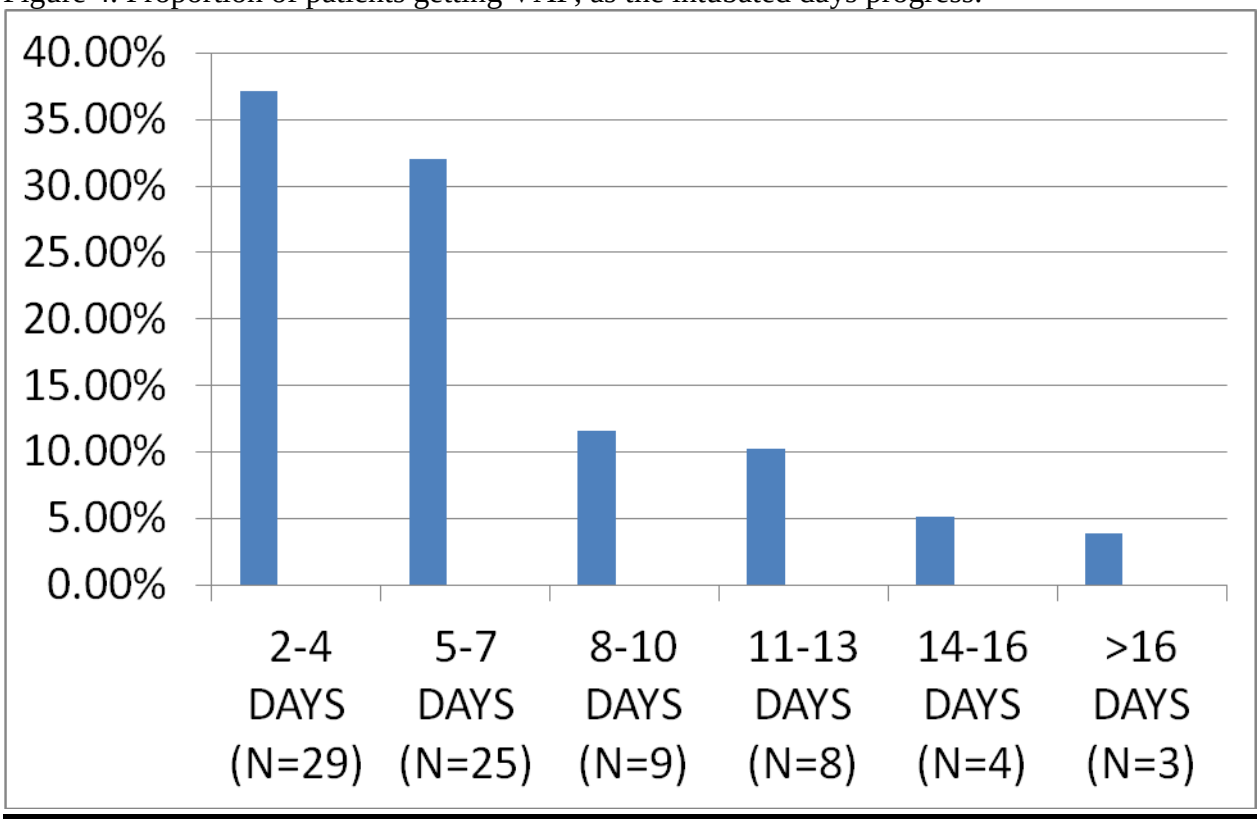
Figure 3 Proportion of the patients in the cohort with a immune compromised status.



Majority of the patients under this study were immunocompetent. 11.54% of the study population were immunocompromised. Haematological malignancies, disseminated malignancies on chemotherapy, liver and renal cell failure were the causes of immunosuppression.

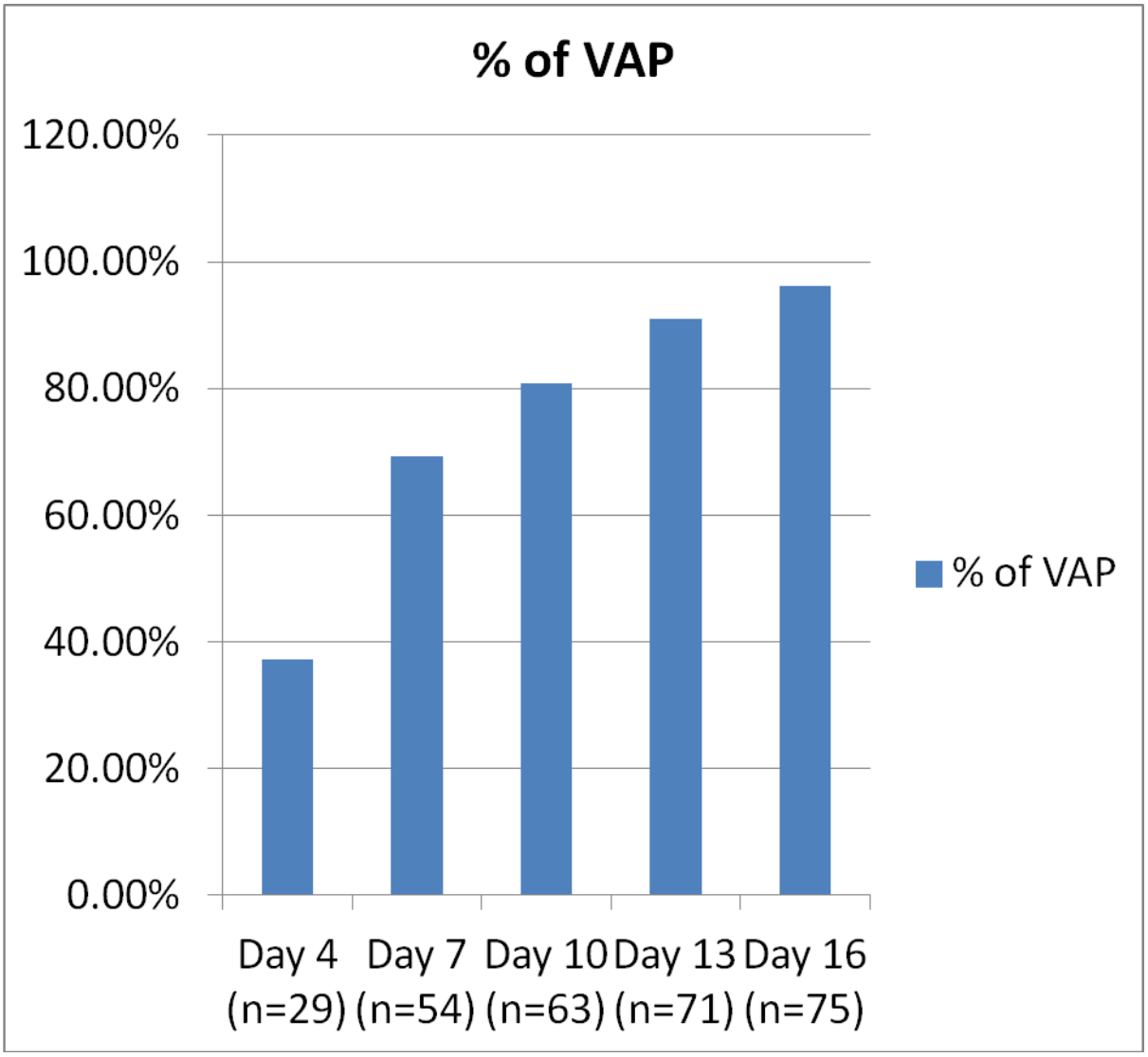
DAY OF ONSET OF VAP

Figure 4. Proportion of patients getting VAP, as the intubated days progress.



37.18% of the patients developed VAP in the first 4 days. 32.05% developed VAP between the 5th and the 7th day of post intubation. 11.54% developed VAP between 8th and 10th day, 10.26% between 11th and 13th day, 5.13% between 14th and 16th day, 3.85% developed VAP after 16th day of post intubation.

Figure 5 Development of VAP as the intubated days progress



37.18% of the cohort developed VAP by day 4 of intubation. It increased to 69.23% by day 7 and 80.77% by Day 10. 96.15% developed VAP by day 16 of intubation.

MORTALITY

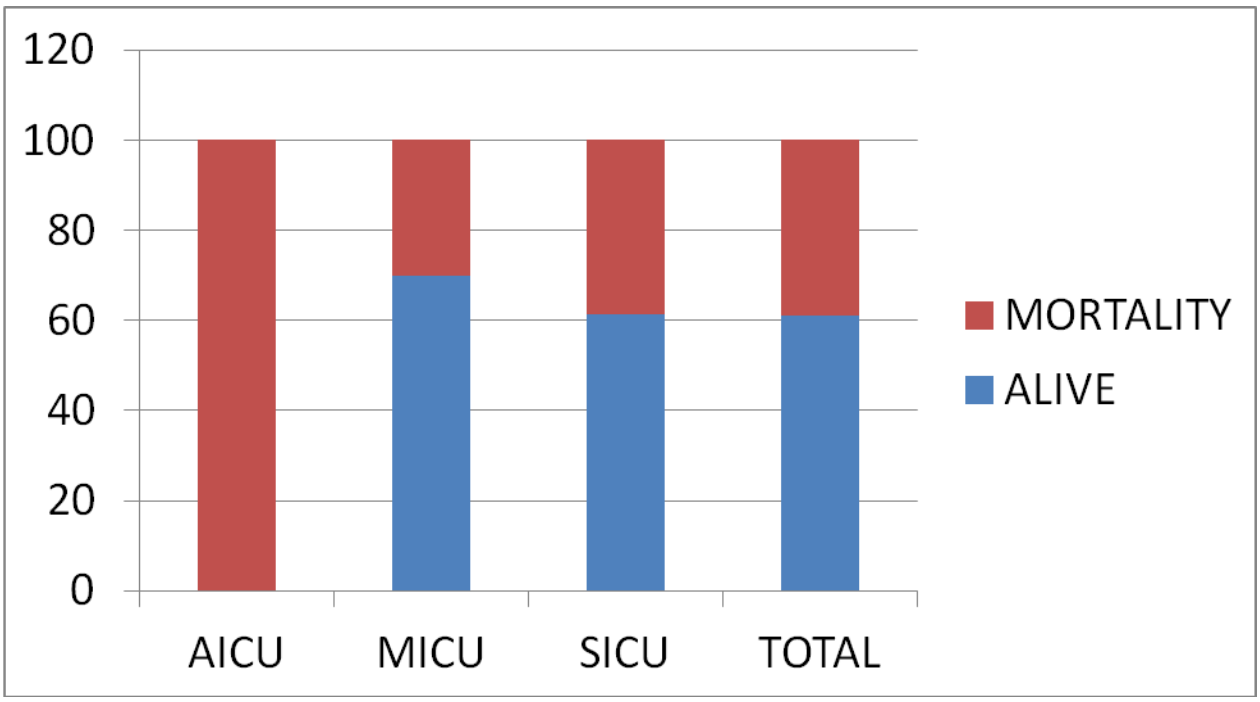
Table 5 Mortality in various ICUs

MORTALITY	AICU	MICU	SICU	TOTAL
DEATH (n)	100 (6)*	30 (12)	38.71 (12)	38.96 (30)
ALIVE (n)	0	70 (28)	61.29 (19)	61.04 (47)

p=.005

ANOVA test was used to compare the mortality among the patients who had developed VAP in various ICUs. *In AICU the mortality was 100% (case fatality of VAP) which was significant in comparison with the mortality rates in medical and surgical ICU.

Figure 6 Mortality in various ICUs



There was an overall mortality of 38.96%.

BACTERIOLOGICAL PROFILE

45 of 78 patients (57.69%) had multiple organisms grown in the ET aspirate culture in significant amount.

Table 6. Common organisms in various ICUs

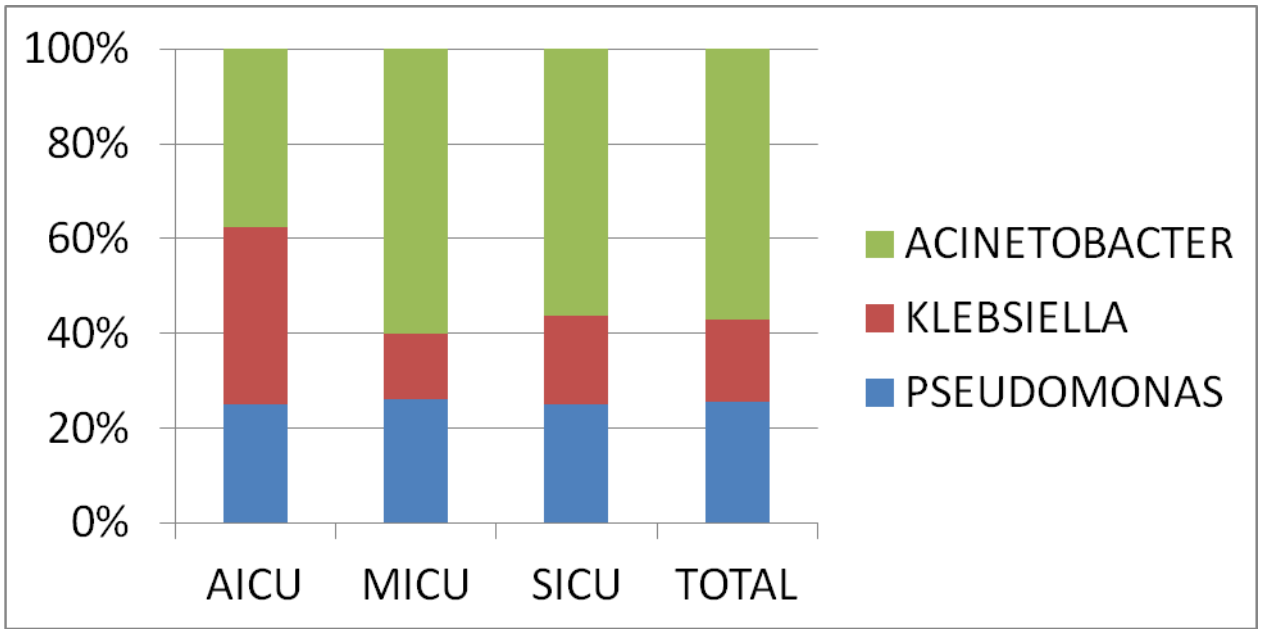
	PSEUDOMONAS	KLEBSIELLA	ACINETOBACTER
AICU	2/8 (25%)	3/8 (37.5%)	3/8 (37.5%)
MICU	13/63 (20.63%)	7/63 (11.1%)	30/63 (47.62%)
SICU	8/43 (18.6%)	6/43 (13.95%)	18/43 (41.86%)
TOTAL	22/121 (18.18%)	15/121 (12.39%)	49/121 (40.5%)

The bacteriological profile was almost the same in all the ICU , irrespective of the cases being surgical or medical. Ainetobacter sp was the most commom organism, followed by pseudomonas and the klebsiella. There was no difference noticed in the bacteriological profile , between the early and late VAP.

Other organisms which were detected in this cohort were-

- Serratia
- Staphylococcus aureus
- E.coli
- Proteus sp
- Sterotrophomonas
- NFGNB
- Enterobacter
- Providencia
- Citrobacter
- Chrysobacterium indolgeis

Figure 7. Common organisms in various ICUs



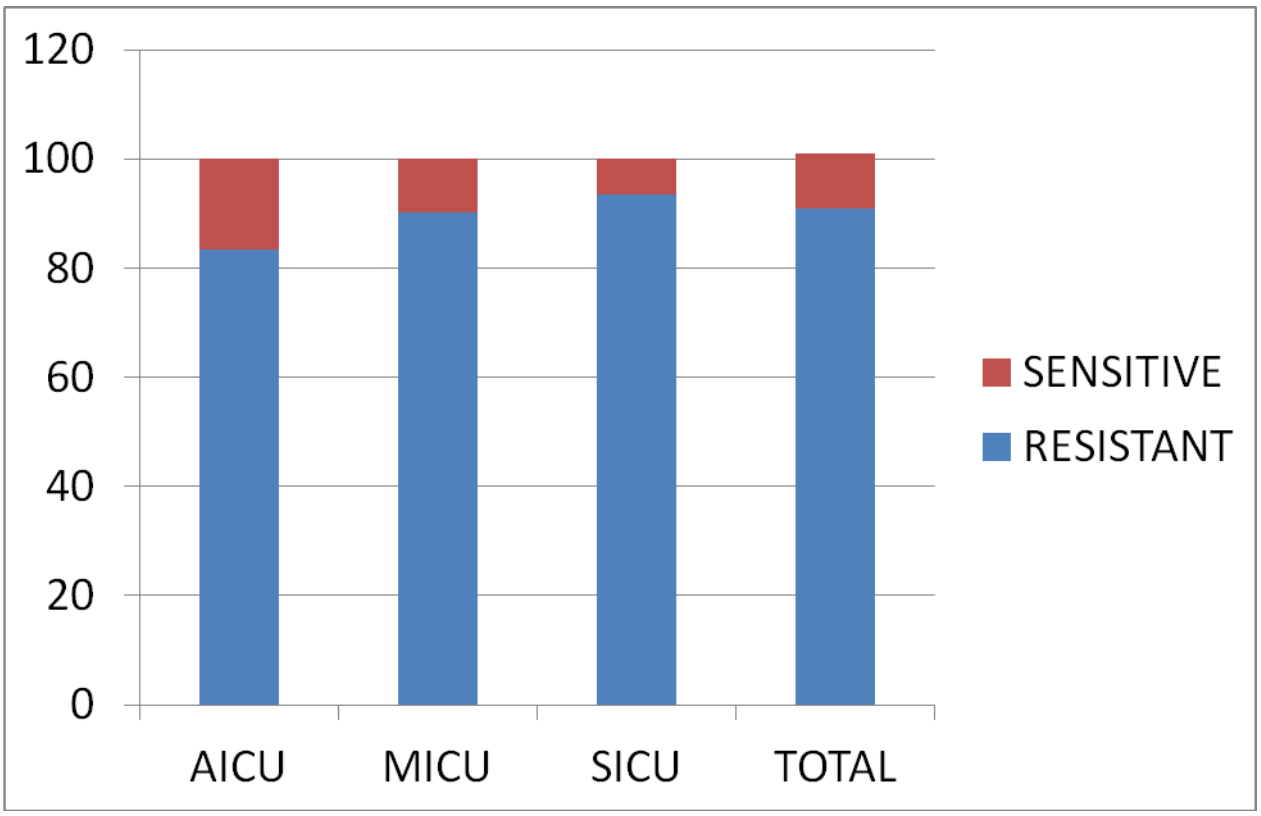
PROPORTION OF RESISTANT ORGANISMS

Resistant organisms-

- **AICU- 5/6 (83.33%)**
- **MICU- 37/41 (90.24%)**
- **SICU- 29/31 (93.55%)**

- **TOTAL- 71/78 (91.03%)**

Figure 8 Proportion of resistant organisms in various ICUs



p=0.702

Proportion of resistant organisms grown in the ET Aspirate from the cohort was 91.03%. ANOVA test was used to compare the proportion of resistant organisms in various ICUs and there was no statistically significant difference noticed.

OUTCOME

MORTALITY, ICU AND HOSPITAL STAY

Table 7. Mortality Predictors

	MORTALITY	ALIVE	p- VALUE
Procalcitonin (ng/dl)	10.54 (0.31-157)	6.36 (0.06-159.7)	0.15
APACHE III	96.00 (52-146)	66.00 (28-132)	<0.001
Mod CPIS	5.50 (3-9)	5.00 (3-9)	0.44
MODS	10.00 (4-16)	7.00 (3-14)	0.004
AGE (yrs)	47.00 (19.08)	45.00 (17.56)	0.57

Age is represented as mean age and standard deviation is mentioned in closed bracket below the mean value. Rest of the variables including APCHE-III, MODS, Modified CPIS and Procalcitonin levels were taken as the median, as there was a wide range of values. The minimum and maximum values are mentioned in the closed brackets below the median value.

Ranksum Test was used to compare the median values of different scores and procalcitonin levels, and T-test was used to compare the mean 'age' among those who succumbed to their illness and those who survived. Median APACHE-III score among those who died was 96, where as the score among those who survived was 66. Median MOD score among those who died was 10 and the score among the survivors was 7. The difference in both APACHE-III score and the MOD score between the two groups were statistically significant. There was no significant difference noticed in relation to modified CPIS score and the Procalcitonin levels.

PROCALCITONIN

Table 8. Mean procalcitonin in the survivors and those who died.

	MEAN	95% CI
MORTALITY (n=24)	35.36	14.14 - 56.57
ALIVE (n=35)	17.47	6.42 - 28.52

p= 0.1007

Mean Procalcitonin level among those who survived was 17.47 and those who succumbed to their illness was 35.36. But there was no statistical significance noticed.

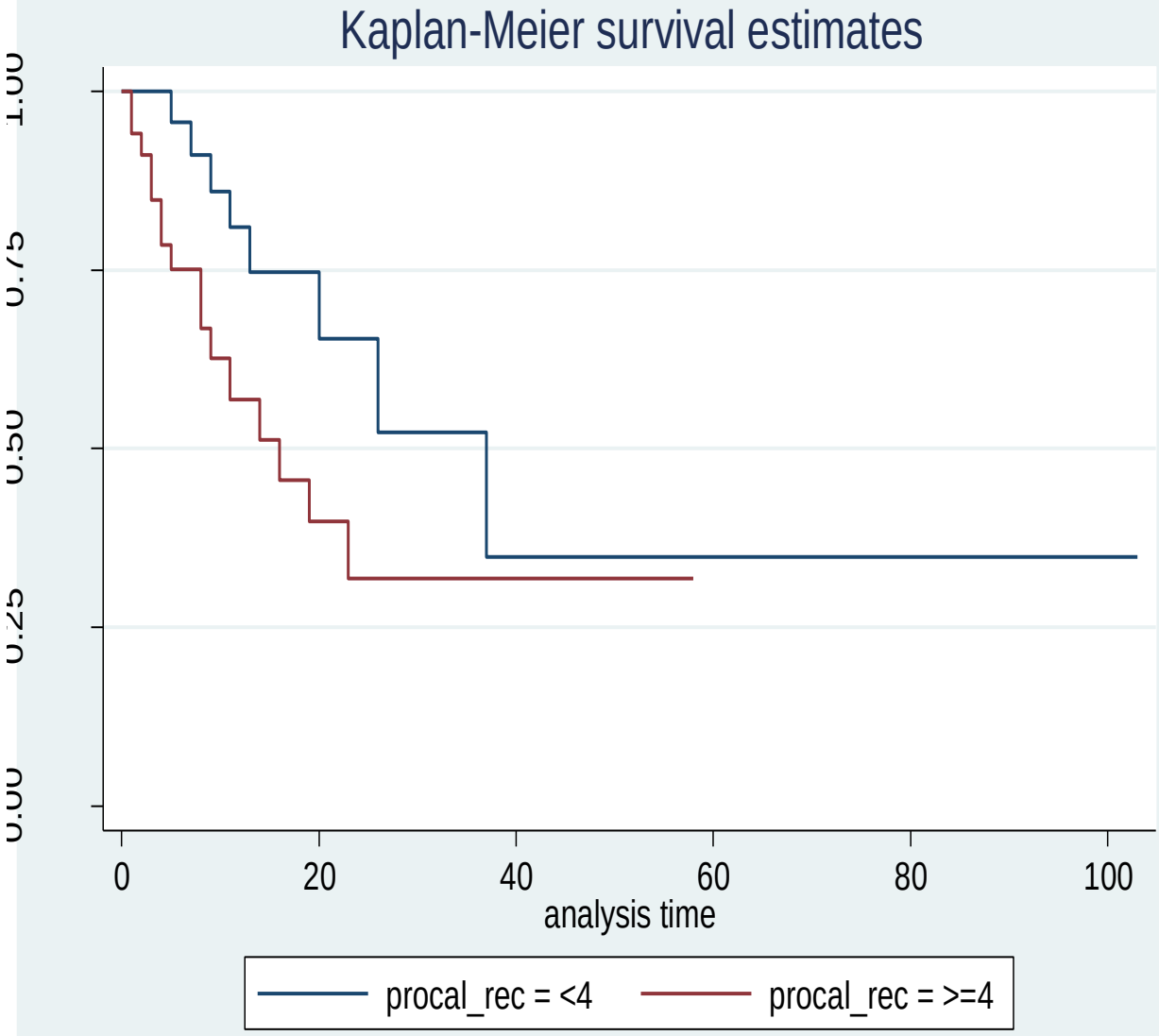
Table 9. Procalcitonin level of 4ng/dl as a predictor of mortality

Procalcitonin (ng/dl)	Mortality	Alive	Total
<4 (%)	8 (33.33)	17 (48.57)	25 (42.37)
>4 (%)	16 (66.67)	18 (51.43)	34 (57.63)
Total	24	35	59

p= 0.245

A procalcitonin level of 4 ng/dl was taken to see whether a high level like that can be considered as a predictor of mortality. But there was no significance noticed. Procalcitonin failed to stand as an independent predictor of mortality.

Figure 9 Median survival analysis -Procalcitonin



The median survival for patients with Procalcitonin <4 ng/dl was 37 ICU days, whereas those who had Procalcitonin level more than or equal to 4 ng/dl had only 16 ICU days (p=.06). But the difference fell short of statistical significance.

ICU AND HOPSITAL DAYS

Table 10. Correlation of Procalcitonin and ICU days

PROCALCITONIN	Median ICU days	Min-Max
< 4ng/dl	13	1 - 103
>/=4ng/dl	9.5	1 - 58

p=0.261

Patients with a procalcitonin level of less than 4ng/dl at the time of diagnosis had a median of 13 ICU days and those with a procalcitonin level equal to or more than 4ng/dl had 9.5 days, the difference was not statistically significant.

Table 11. Correlation of Procalcitonin and Hospital days

Procalcitonin	Median Hospital days	Min - Max
<4ng/dl	26	5 - 103
>/=4ng/dl	17	7 - 71

p= 0.181

Patients with a procalcitonin level of less than 4ng/dl at the time of diagnosis had a

median of 26 hospital days and those with a procalcitonin level equal to or more than 4ng/dl had 17 days, the difference was not statistically significant.

APACHE-III

Table 12 Mean APACHE -III score among the survivors and those who died

	MEAN	95% CI
MORTALITY (n=30)	94.07	84.33 - 103.81
ALIVE (n=47)	69.40	63.11 - 75.7

$p < 0.001$

Mean APACHE III score of those who survived was 69.40 and those who succumbed to illness was 94.07 and it was statistically significant.

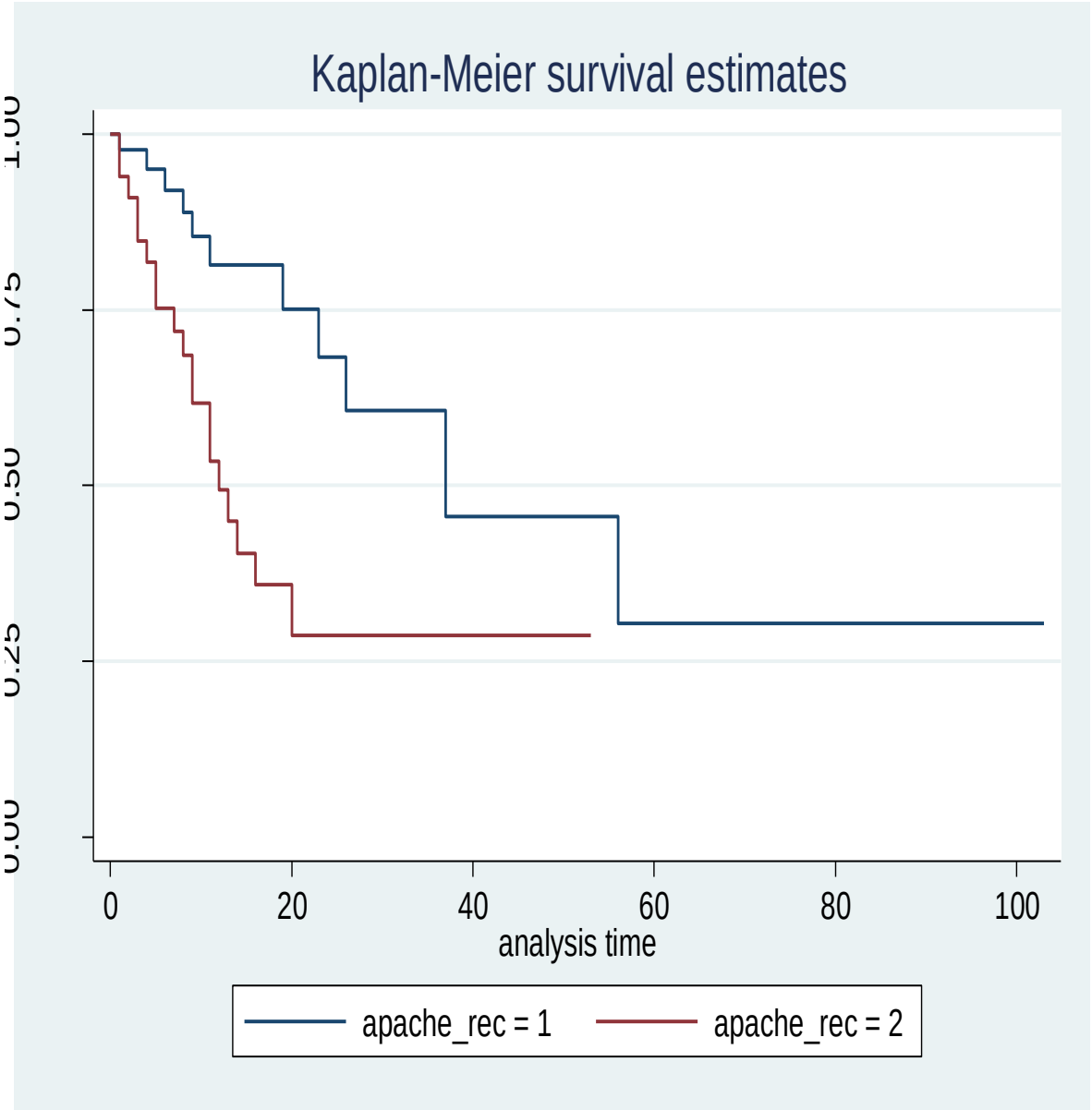
Table 13 APACHE -III Score of 80 as a predictor of mortality

APACHE III	MORTALITY	ALIVE	TOTAL
<80 (%)	11 (36.67%)	33 (70.21%)	44 (57.14%)
>/=80 (%)	19 (63.33%)	14 (29.79%)	33 (42.86%)
TOTAL	30	47	77

P= 0.004

APACHE-III score of 80 or more has a 63.33% sensitivity and 70.21% specificity in predicting mortality in patients with ventilator associated pneumonia.

Figure 10 Median survival analysis- APACHE -III



The median survival for patients with APACHE-III score <80 was 37 ICU days, whereas those who had APACHE-III score more than or equal to 80 had only 12 ICU days (p=.0038). The difference was both clinically and statistically significant.

ICU AND HOPSITAL DAYS

Table 14. Correlation of APACHE III and ICU days

APACHE III	Median ICU days	Min-Max
< 80	9	1 - 103
>/=80	14.5	4 - 53

p=0.196

Patients with a APACHE III score of less than 80 at the time of diagnosis had a median of 9 hospital days and those with a APACHE III score equal to or more than 80 had 14.5 days, the difference was not statistically, but clinically significant.

Table 15. Correlation of APACHE III and hospital days

APACHE-111	Median Hospital days	Min - Max
<80	19	4 - 103
>/=80	28.50	10 - 67

p= 0.55

Patients with a APACHE III score of less than 80 at the time of diagnosis had a median of 19 hospital days and those with a APACHE III score equal to or more than 80 had 28.5 days, the difference did not reach statistical significance, but could be clinically significant.

Mod. CPIS

Table 16. Mean Modified CPIS score among the survivors and those who died

	MEAN	95% CI
MORTALITY (n=30)	5.5	4.98 - 6.02
ALIVE (n=47)	5.26	4.85 - 5.66

p = 0.4529

The mean mod CPIS score was 5.5 in the patients who succumbed to their illness and 5.26 among those who survived. There was no significant difference among the both groups.

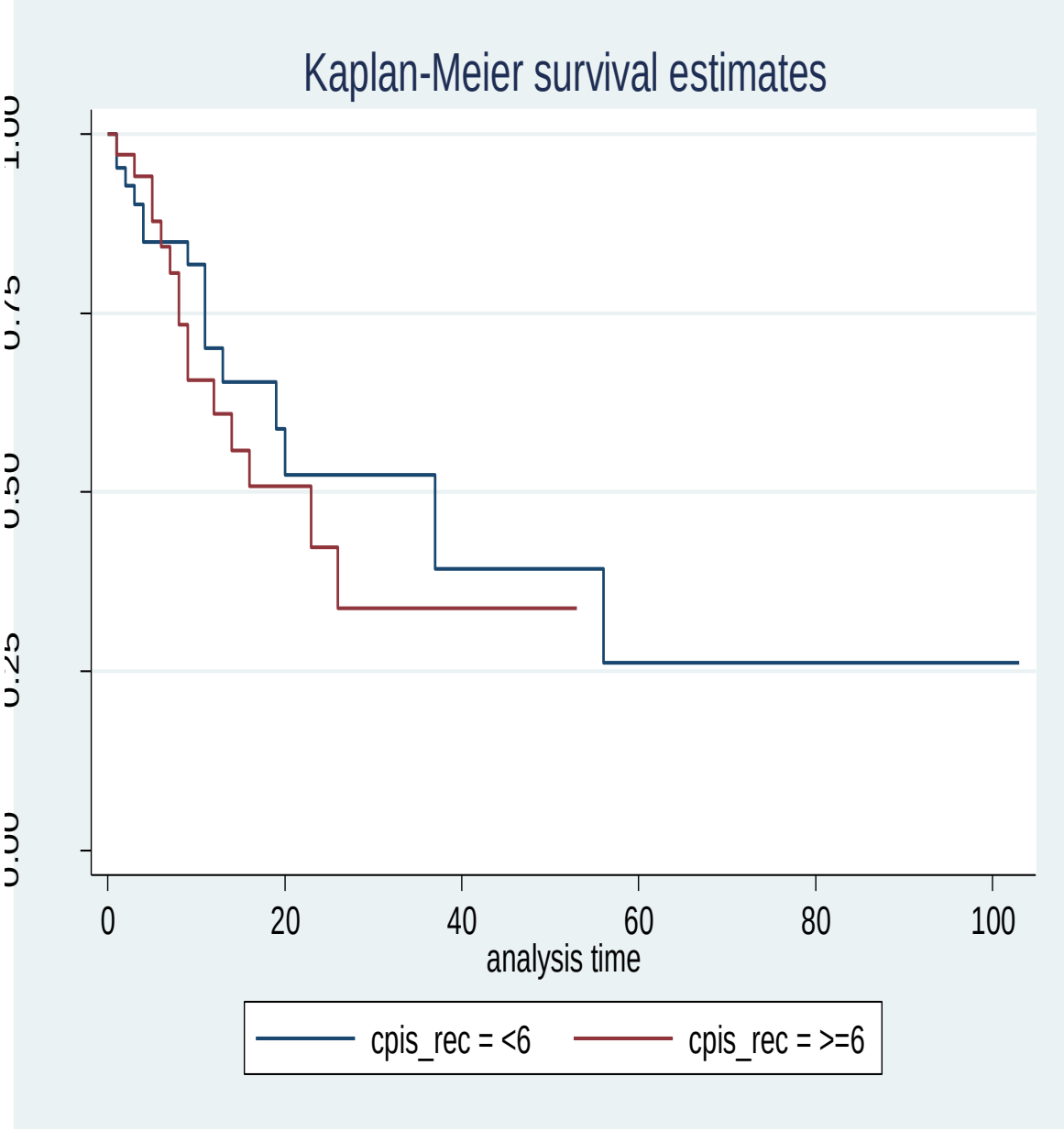
Table 17. Modified CPIS score of 6 or more as a predictor of mortality

Mod CPIS	MORTALITY	ALIVE	TOTAL
<6 (%)	15 (50%)	27 (57.45%)	42 (54.55%)
>/=6 (%)	15 (50%)	20 (42.55%)	35 (45.45%)
TOTAL	30	47	77

p= 0.522

Analysis was done to see whether a modified CPIS score of 6 or more can be used as a predictor of mortality. But there was no significant correlation noticed.

Figure 11 Median survival analysis- Modified CPIS Score



The median survival for patients with modified CPIS score <6 was 37 ICU days, whereas those who had modified CPIS score more than or equal to 6 had only 23 ICU days (p=.4182). The difference was clinically significant.

ICU AND HOPSITAL DAYS

Table 18. Correlation between Modified CPIS score and ICU days

Mod.CPIS	Median ICU days	Min-Max
< 6	10	1 - 103
>/=6	10.5	1 - 53

p=0.9313

Patients with a mod.CPIS score of less than 6 at the time of diagnosis had a median of 10 ICU days and those with a mod.CPIS score equal to or more than 6 had 10.5 days, the difference was not statistically or clinically significant.

Table 19, Correlation between Modified CPIS score and Hospital days

Mod.CPIS	Median Hospital days	Min - Max
<6	19	4 - 103
>/=6	22	4 - 67

p= 0.6824

Patients with a mod. CPIS score of less than 6 at the time of diagnosis had a median of 19 hospital days and those with a mod.CPIS score equal to or more than 6 had 22 days, the difference was not statistically significant, but it could be clinically significant.

MOD SCORE

Table 20. Mean MOD score among the survivors and those who died

	MEAN	95% CI
MORTALITY (n=30)	9.63	8.16 - 11.10
ALIVE (n=47)	7.04	6.26 - 7.83

p = 0.0010

The mean MOD Score among those who survived was 7.0 and among those who succumbed to illness was 9.6, and it was statistically significant.

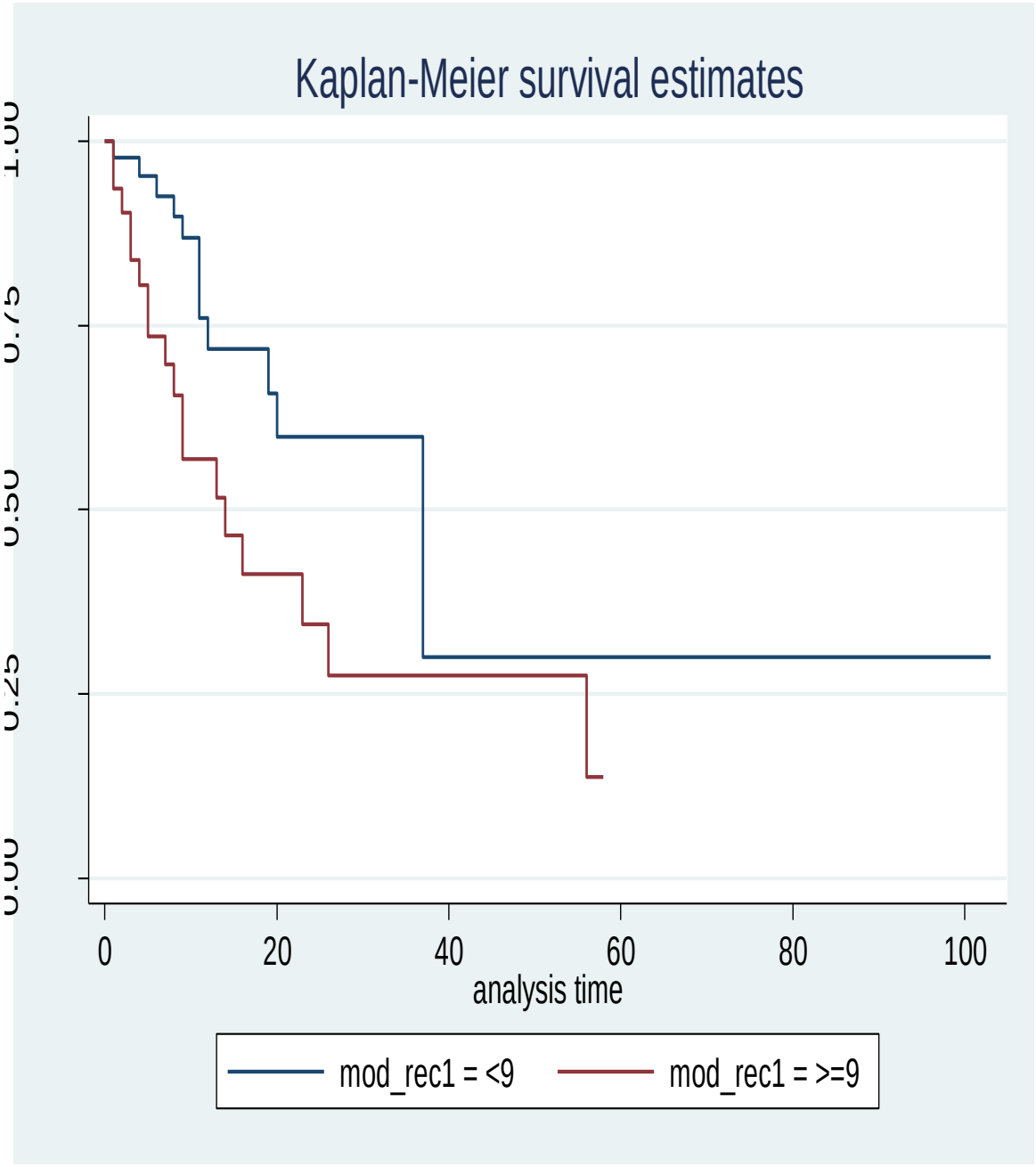
Table 21. MOD score as a predictor of mortality

MODS	MORTALITY	ALIVE	TOTAL
1-4 (%)	4 (13.33%)	10 (21.28%)	14 (18.18%)
5-8 (%)	8 (26.67%)	24 (51.06%)	32 (41.56%)
9-12 (%)*	10 (33.33%)	12 (25.53%)	22 (28.57%)
>/=13 (%)	8 (26.67%)	1 (2.13%)	9 (11.69%)
TOTAL	30	47	77

P=.004

*33.33% of the patients who died had a MOD score between 9 and 12. Specificity of a MOD score between 9 and 12 in predicting mortality was 74.47%. This finding was statistically significant as well.

Figure 12. Median survival analysis- MOD score



The median survival for patients with MOD score <9 was 37 ICU days, whereas those who had MOD score more than or equal to 9 had only 14 ICU days (p=.019). The difference was both clinically and statistically significant.

ICU AND HOSPITAL DAYS

Table 22. Correlation between MODS sore and ICU days

MODS	MEDIAN ICU DAYS	MIN - MAX
1-4	9	1 - 103
5-8	11	1 - 34
9-12	11	3 - 58
>/=13	7	7 - 7

p= 0.8112

There was no significant correlation noticed between the MODS score at the time of diagnosis of VAP and the median days of ICU stay.

Table 23. Correlation between MODS score and hospital days

MODS	MEDIAN HOSPITAL DAYS	MIN - MAX
1-4	18.5	5 - 103
5-8	24	4 - 103
9-12	24.5	11 - 71
>/=13	11	11 - 11

p= 0.5949

There was no significant correlation noticed between the MODS score at the time of diagnosis of VAP and the median days of hospital stay.

AGE

Table 24. Mean age among the survivors and those who died.

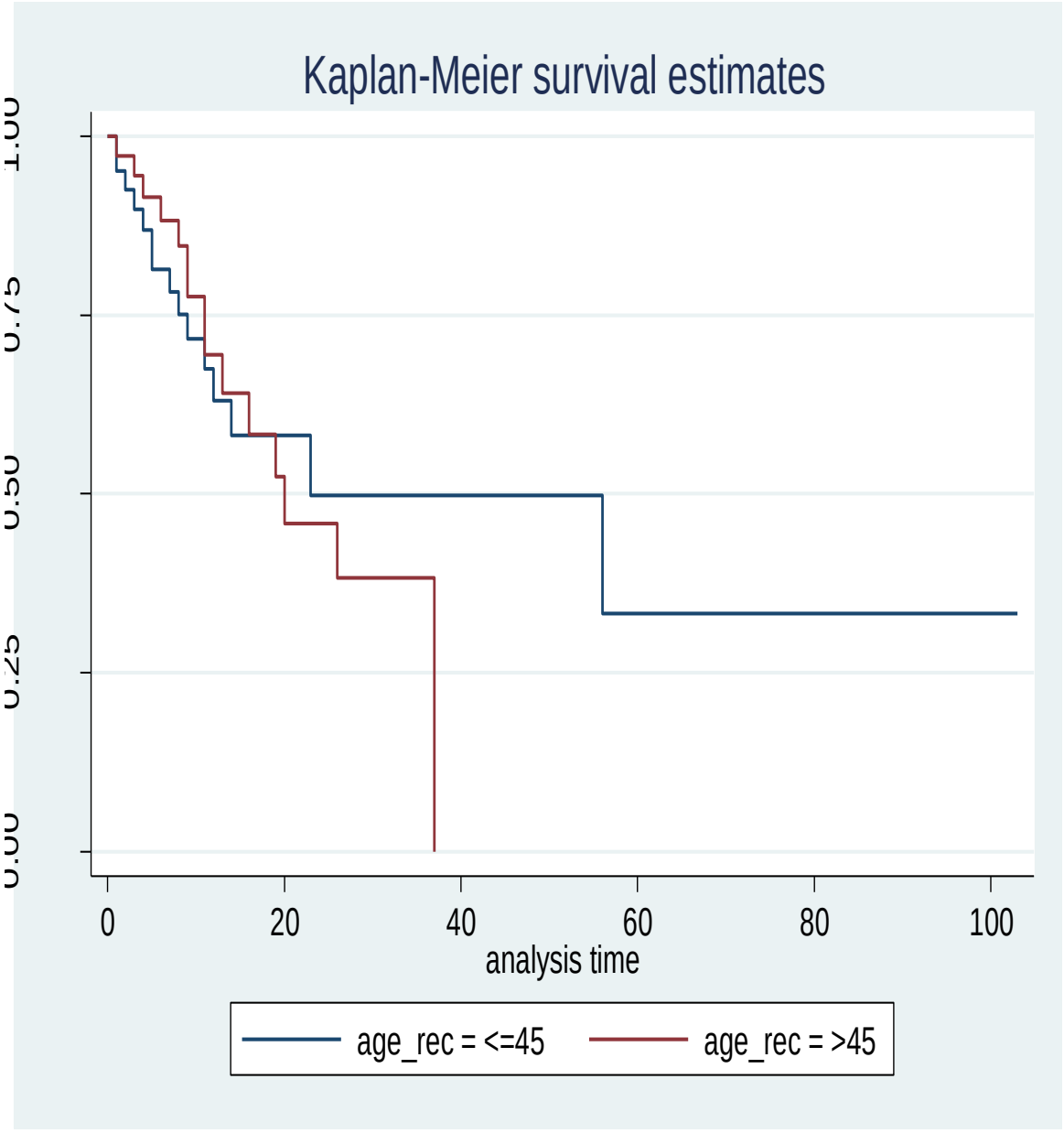
	MEAN	95% CI
MORTALITY (n=30)	46.9	39.77 - 54.03
ALIVE (n=47)	44.51	39.36 - 49.67

p= 0.5751

T-Test analysis was done to compare the mean age among the survivors and those who died.

There was significant association noticed between the 'age' and the outcome, in terms of 'mortality'.

Figure 13. Median survival analysis- Age



The median survival for patients with age less than or equal to 45 years was 23 ICU days, whereas those who had age more than 45 years, it was 20 ICU days (p=.75). The difference was not significant.

RESISTANT ORGANISMS

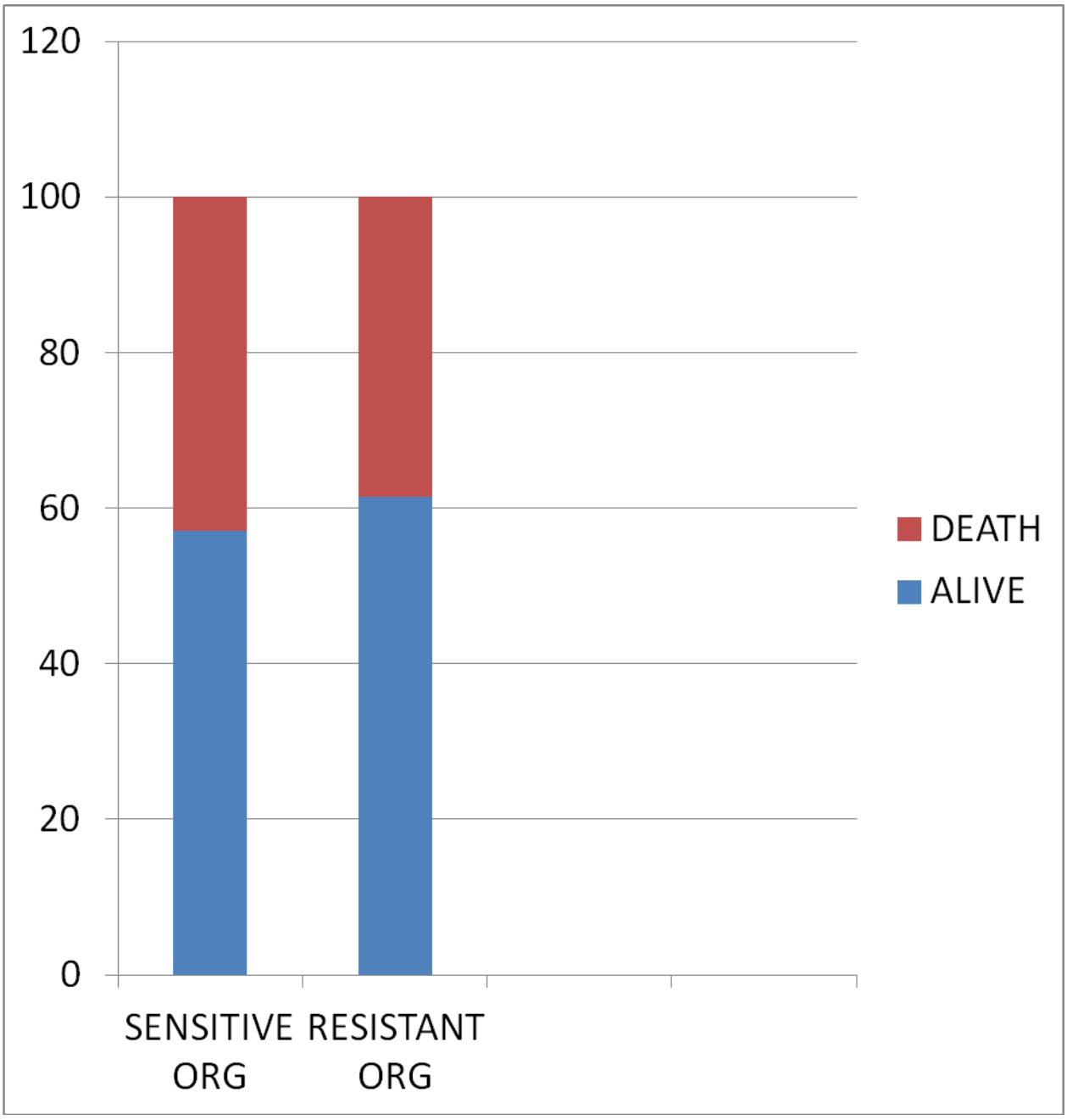
Table 25 Resistant organism and the mortality

	MORTALITY	ALIVE	TOTAL
SENSTIVE ORG % (n)	10 (3)	8.51 (4)	9.09 (7)
RESISTANT ORG % (n)	90 (27)	91.49 (43)	90.91 (70)

p=0.825

Of those who expired, 10% had sensitive organism grown in the ET aspirate culture and 90% had resistant organism. Mortality rate among those who had sensitive organism was 42.9%, whereas among those who had resistant organism was 38.6%. But these values were not statistically significant. The difference could be due to the fact that the commonest organism found in the study- Acinetobacter is a resistant organism, but responds well to the appropriate therapy.

Figure 14 Resistant organism and mortality



POLYMICROBIALS

Table 26. Poly-microbials and mortality

	MORTALITY	ALIVE	TOTAL
SINGLE ORGANISM (%)	17 (56.67%)	27 (57.45%)	44 (57.14%)
POLY MICROBIAL (%)	13 (43.33%)	20 (42.55%)	33 (42.86%)
TOTAL	30	47	77

p= 0.946

56.67% of the patients who succumbed to their illness had single organism grown in the ET aspirate culture, where as 43.33% had multiple organisms grown. The difference was not statistically significant. Mortality rate in the 'single organism' group and the 'polymicrobial' group were 38% and 39% respectively.

Table. 27 Poly-microbials and ICU Stay

	Median days of ICU stay	Min- Max
Single organism	10	1- 103
Multiple organism	10.5	1- 30

p= 0.5393

Irrespective of the fact that whether a single organism or multiple organisms were grown in the ET aspirate, the median number of ICU days was about 10.

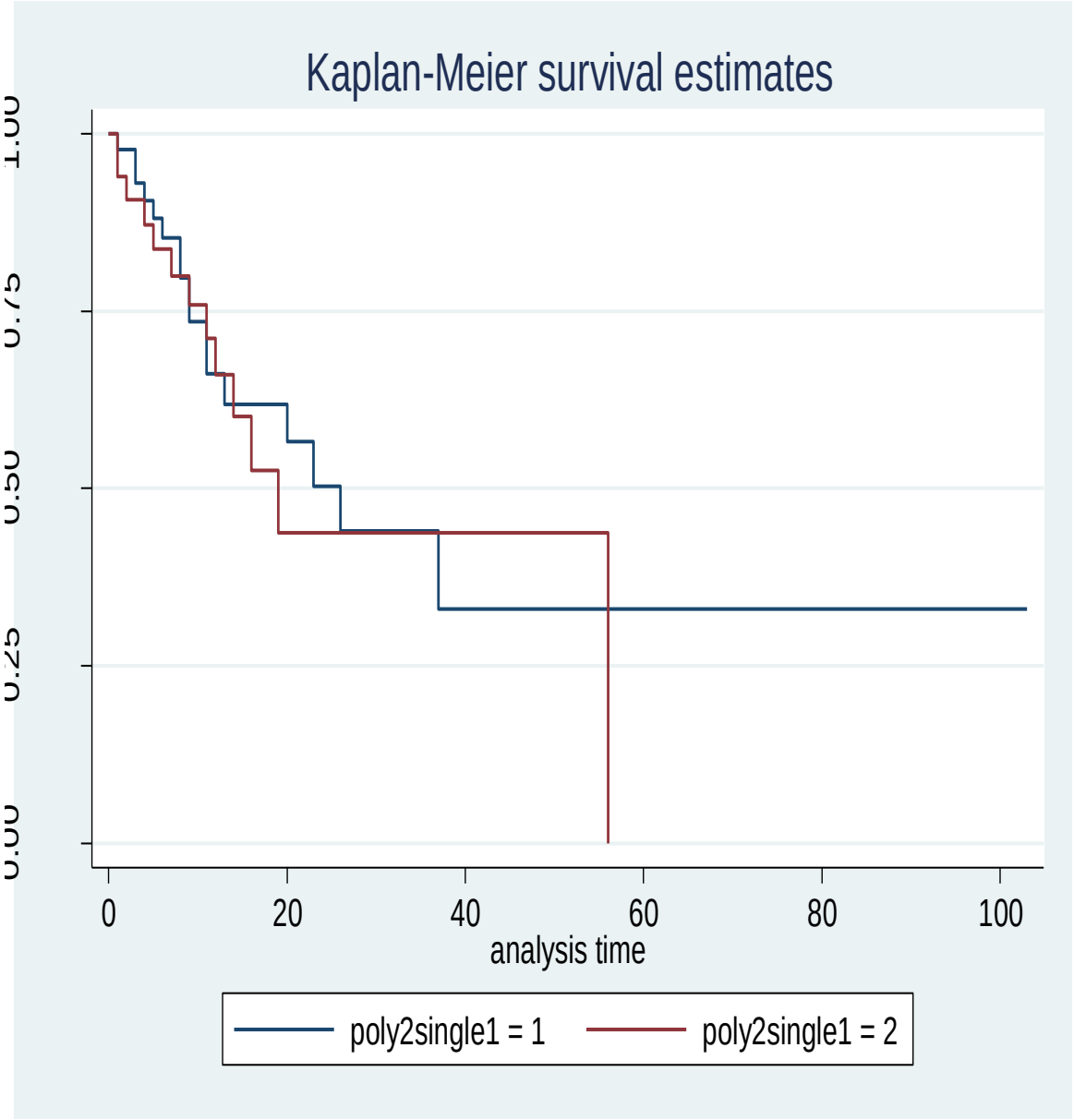
Table 28. Poly-microbials and hospital days

	MEDIAN HOSPITAL DAYS	MIN - MAX
SINGLE ORGANISM	18	4 - 103
MULTIPLE ORGANISMS	21	5 - 101

p=0.6983

The median number of hospital days in those who had a single organism grown in their ET aspirate was 18 days, whereas those who had multiple organisms grown in their ET aspirate had a median number of hospital days of 21, and the difference was not clinically or statistically significant.

Figure 15. Median survival- Polymicrobials



The patients whose ET aspirate grew only a single organism, had a median survival period of 26 ICU days, whereas the patients whose ET aspirate grew multiple organisms, the median survival period was 19 ICU days. The difference was clinically significant, but it was not statistically significant (p= 0.6812).

ACINETOBACTER sp

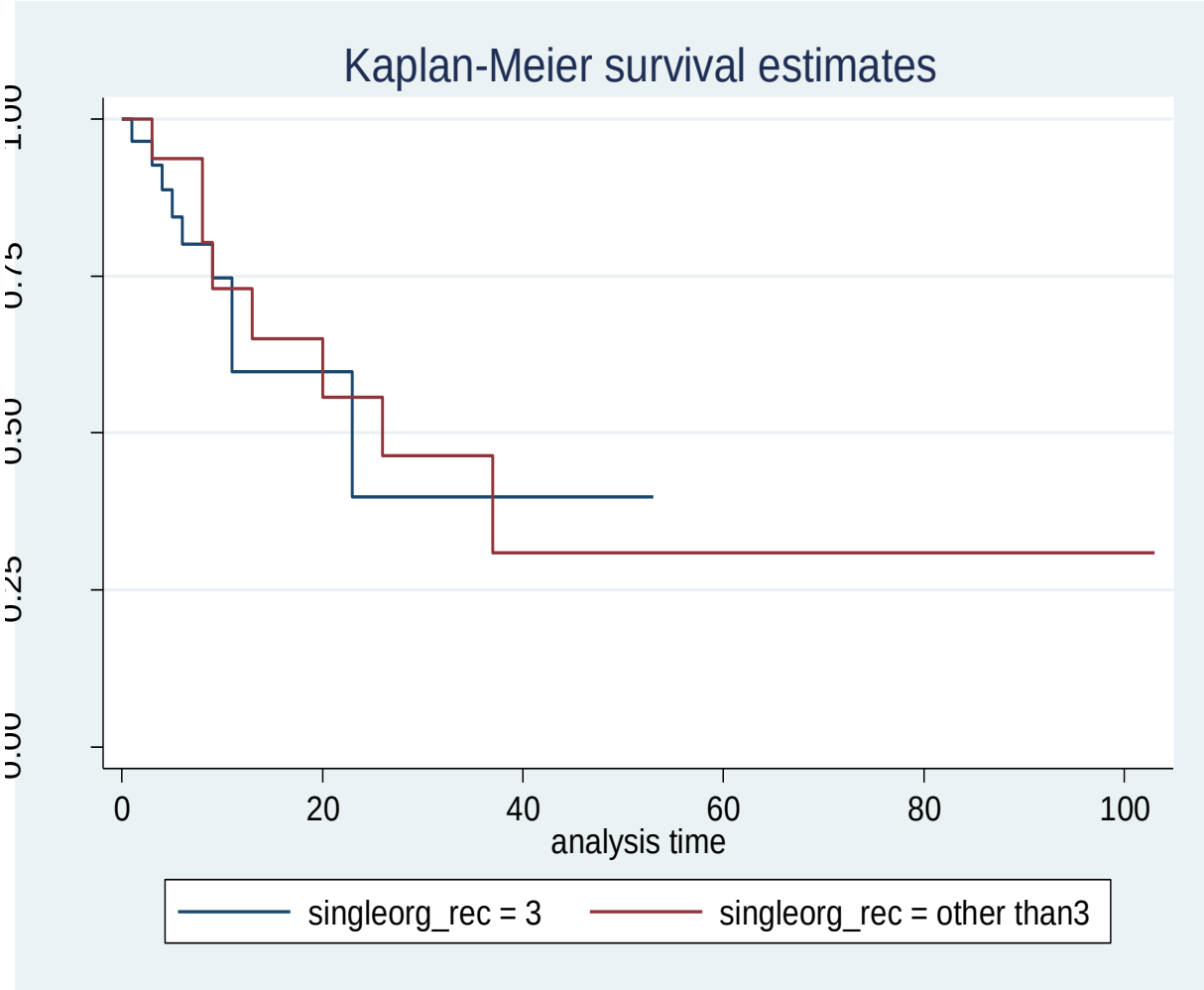
Table 29. Mortality in patients who had Acinetobacter infection

	MORTALITY	ALIVE	TOTAL
ACINETOBACTER (%)	9 (52.94%)	19 (70.37%)	28 (63.64%)
OTHER ORG (%)	8 (47.06%)	8 (29.63%)	16 (36.36%)
TOTAL	17	27	44

p=0.242

There was no significant difference in the mortality between those who had grown acinetobacter sp in the ET aspirate and those who had grown some other organism (52.94% and 47.06% respectively).

Figure 16. Median survival time in patients infected with Acinetobacter when compared to others



p-0.81 (3- acinetobacter)

The median survival time of those who had acinetobacter infection was 23 ICU days, where as those who had other organism in their ET aspirate was 26 days. The difference was not statistically significant, but it was clinically significant.

ICU AND HOSPITAL DAYS

Table 30. Median ICU days in acinetobacter infection and others

	MEDIAN ICU DAYS	MIN- MAX
ACINETOBACTER	10	1 - 53
OTHER ORGANISMS	23.5	4 - 103

P= 0.0627

The median number of ICU days those who had grown acinetobacter sp in the ET aspirate was 10 days , where as in others it was 23.5 days. The difference was not statistically significant. But the difference was clinically significant.

Table 31. Median hospital days in acinetobacter infection and others

	MEDIAN HOSPITAL DAYS	MIN- MAX
ACINETOBACTER	14	4 - 67
OTHER ORGANISMS	39	10 - 103

P= 0.0629

The median number of hospital days those who had grown acinetobacter sp in the ET aspirate was 14 days , where as in others it was 39 days. The difference was not statistically significant. But the difference was clinically significant.

EARLY AND LATE VAP

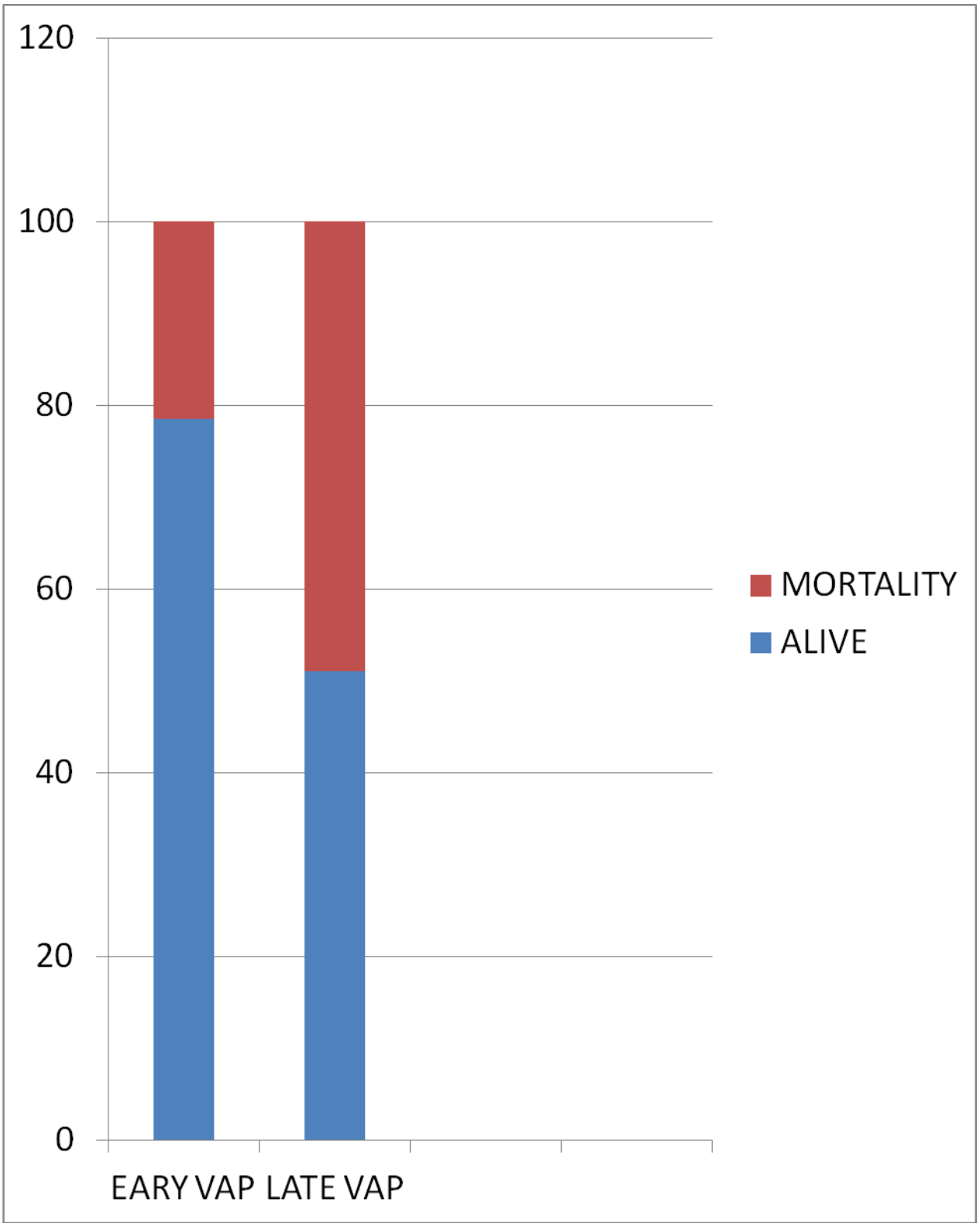
Table 32. Mortality in Early and Late VAPs

	DEATH	ALIVE	TOTAL
EARLY VAP % (n)	20 (6)	46.81 (22)	36.36 (28)
LATE VAP % (n)	80 (24)	53.19 (25)	63.64 (49)

p= 0.017

Among those who died 20% had early VAP and 80% had late VAP. Early VAP had a mortality rate of 21.4%, where as Late VAP had a mortality rate of 48.98%. Both were statistically significant. Mortality rate in the Early VAP and the Late VAP were 21.4% and 48.9% respectively and the significance was statistically significant.

Figure 17. Mortality in early and late VAP



ICU STAY

Table 33. Median ICU days in Early and Late VAPs

	MEDIAN ICU STAY (days)
EARLY VAP (n=28)	9.00
LATE VAP (n=49)	11.00

Median of number of ICU stay in the early VAP group was 9 days and that in Late VAP group was 11 days. A difference of 2 or more days was considered as a clinically significant difference.

Table 34. Median Hospital days in Early and Late VAPs

	MEDIAN HOSPITAL STAY(days)
EARLY VAP (n=28)	17.00
LATE VAP (n=49)	14.00

The median number of hospital days among those who had Early VAP was 17 days and that with Late VAP was 14 days. As a difference of 4 hospital days was considered as clinically significant value, early and late VAP did not show any clinically significant difference in this aspect.

DISCUSSION

Patients who were admitted and intubated in various ICUs during the study period were evaluated once they developed signs and symptoms of Ventilator Associated Pneumonia. Modified CDC criteria was applied to make a diagnosis of VAP. Patients who had lung opacities at the time of admission or intubation were excluded, to ensure that only those who with definite VAP were included in this study. This may have resulted in the under-estimation of the VAP cases. APACHE-III score, MODS score, Modified CPIS score were calculated and the Procalcitonin level was noted at the time of diagnosis of VAP. The study population was followed up till the day of discharge or death. Clinical profile and bacteriological profile of the study population was studied and analyzed in detail. Analysis was done to find out whether various previously validated scores and the procalcitonin levels can be used as predictors of the clinical outcome- Mortality and in patients who survived, the days of ICU stay and the days of hospital stay. A difference of 2 ICU days and 4 hospital days was arbitrarily considered as clinically significant difference.

The mean age of the patients included in the study was 45years. Mean day of development of Ventilator associated pneumonia (VAP) was 7 days post intubation. They had an average of 14 days of hospital stay and 23 days of total number of days in the hospital. Only 59 patients had Procalcitonin levels analyzed. One patient was discharged against the medical advice from the ICU itself, before completion of the treatment. So he was not included in the analysis for the primary objective of 'prognostic factors towards the outcome'.

Patients from the Surgical ICU had a mean age of 45 years. Mean day of development of VAP was 7 days. Average number of ICU stay was 15 days and that of total hospital days was 22 days. Patients from Medical ICU had an average age of 46 years , mean day of development of VAP was 6 days, ICU stay for 15 days and hospital stay for 25 days. AICU patients had an average age of 47 years, mean day of development of VAP was 12 days, ICU stay of 9 days and Hospital stay of 15 days.

Variables including Hospital days, ICU days, Day of developing VAP, APCHE-III, MODS, Modified CPIS and Procalcitonin levels were taken as the median, as there was a wide range of values. ANOVA test was used to compare the mean age between the three ICUs and Kruskal Wallis test was used to compare the median of the rest of the variables from the three ICUs. APACHE-III score was significantly high in the AICU arm, when compared to the rest of the cohort. The median score was 108 in

AICU arm, where as average of all the median values were 76. (p=0.009). The Procalcitonin level was significantly low in the Medical ICU arm- 3.11ng/dl , in comparison to 13.86 ng/dl and 14.87 ng/dl in AICU and Surgical ICU respectively (p=0.012). There was no significant difference among the 3 different arms with regard to the other variables.

A total of 37.18% had early VAPs. Incidence of early VAP (within 4 days of intubation) was much lesser than the incidence of late VAP (after 4 days of intubation) in all the ICUs. ANOVA test was used to compare the values from the various ICUs. There was no significant statistical difference noticed between the three ICU on the incidence of the Early and the Late VAP. ANOVA test was used to compare the sex distribution among the three arms and there was no significant difference noticed. There were 31 females (39.74%) and 47 males (60.26%) in the cohort.

25.64% of all VAP patients had primarily infectious diseases as a reason for the ICU admission. It includes necrotizing fascitis, meningitis, scrub typhus, sepsis, splenic abscess rupture, septic shock, disseminated tuberculosis etc. Majority of the patients under this study were immunocompetent. A total of 11.54% of the study population were immunocompromised. Haematological malignancies, disseminated malignancies on chemotherapy, liver and renal cell failure were the causes of immunosuppression.

A total of 37.18% of the patients developed VAP in the first 4 days. 32.05% developed VAP between the 5th and the 7th day of post intubation. 11.54%

developed VAP between 8th and 10th day, 10.26% between 11th and 13th day, 5.13% between 14th and 16th day, 3.85% developed VAP after 16th day of post intubation. 37.18% of the cohort developed VAP by day 4 of intubation. It increased to 69.23% by day 7 and 80.77% by Day 10. 96.15% developed VAP by day 16 of intubation.

ANOVA test was used to compare the mortality among the patients who had developed VAP in various ICUs. In AICU the mortality was 100% (case fatality of VAP) which was significant in comparison with the mortality rates in medical and surgical ICU. All the 6 patients from AICU was critically ill with multiple organ dysfunction and many of them were having disseminated or hematological malignancies and on chemotherapy. The high APACHE III score for these patients in AICU compared to other ICUs throws light to this high mortality rate. There was an overall mortality of 38.96%.

45 of 78 patients (57.69%) had multiple organisms grown in the ET aspirate culture in significant amount. The bacteriological profile was almost the same in all the ICU , irrespective of the cases being surgical or medical. Ainetobacter sp was the most commom organism, followed by pseudomonas and the klebsiella. There was no difference noticed in the bacteriological profile , between the early and late VAP.

Other organisms which were detected in this cohort were-

- Serratia
- Staphylococcus aureus
- E.coli

- Proteus sp
- Sterotrophomonas
- NFGNB
- Enterobacter
- Providencia
- Citrobacter
- Chrysobacterium indolgeis

5/6 (83.33%) patients from AICU, 37/41 (90.24%) patients from MICU and 29/31 (93.55%) patients from SICU had significant growth of a resistant organism in there ET aspirate culture. A total of 91.03% of the study population had resistant organisms in the ET aspirate culture. 'Resistant organisms' were defined as per the recommendations by the Centers for Disease Control and Prevention (CDC) and the European Centre for Disease Prevention and Control (ECDC) , which was published in Clinical Microbiology and Infectious disease in 2011 (48). According to this recommendation, an organism which is resistant to drugs from 3 or more different group of drugs, to which that particular species is naturally susceptible to, is defined as a resistant organism. Proportion of resistant organisms grown in the ET Aspirate from the cohort was 91.03%. ANOVA test was used to compare the proportion of resistant organisms in various ICUs and there was no statistically significant difference noticed.

Mean age and median of various score including APCHE-III, MODS and Modified

CPIS and Procalcitonin levels were calculate and analysis was done to find out whether they can be used as predictors of the clinical outcome- Mortality and in patients who survived, the days of ICU stay and the days of hospital stay. Median value of the scores and the procalcitonin levels were used as there was a wide range of values. Ranksum Test was used to compare the median values of different scores and procalcitonin levels, and T-test was used to compare the mean 'age' among those who succumbed to their illness and those who survived. Median APACHE-III score among those who died was 96, where as the score among those who survived was 66. Median MOD score among those who died was 10 and the score among the survivors was 7. The difference in both APACHE-III score and the MOD score between the two groups were statistically significant. There was no significant difference noticed in relation to modified CPIS score and the Procalcitonin levels.

Mean Procalcitonin level among those who survived was 17.47 and those who succumbed to their illness was 35.36. But there was no statistical significance noticed. A procalcitonin level of 4 ng/dl was taken to see whether a high level like that can be considered as a predictor of mortality. But there was no significance noticed. Procalcitonin failed as an independent predictor of mortality. As a definite ROC curve was not able to be obtained, an arbitrary cutoff of 4ng/dl , which was much higher than the cutoff of 1.5ng/dl in the previous studies (9) was used to look for any significance in the median survival analysis , as well as the days of ICU and Hospital stay. The median survival for patients with Procalcitonin <4 ng/dl was 37 ICU days, whereas those who had Procalcitonin level more than or equal to 4 ng/dl had only 16

ICU days (p=.06). But the difference was clinically significant.

Patients with a procalcitonin level of less than 4ng/dl at the time of diagnosis had a median of 13 ICU days and those with a procalcitonin level equal to or more than 4ng/dl had 9.5 days, the difference was not statistically significant. Patients with a procalcitonin level of less than 4ng/dl at the time of diagnosis had a median of 26 hospital days and those with a procalcitonin level equal to or more than 4ng/dl had 17 days, the difference was not statistically significant. Apart from the median survival in terms of ICU days, our study failed to establish Procalcitonin as a predictor of the outcome in VAP patients. May be a continuous monitoring of Procalcitonin and the trend of rise or fall in the values, would have been a actual predictor of the outcome.

Mean APACHE III score of those who survived was 69.40 and those who succumbed to illness was 94.07 and it was statistically significant. In a previous study comparing APACHE III score to King's college hospital criteria, MELD score and APACHE II score , as a better predictor of poor outcome or mortality in patients who undergo liver transplantation for acute hepatic failure, a APACHE III score of 80 was taken as a cutoff (49). This study had shown that APACHE score of 80 or more has a specificity of 90% and positive predictive value of 50% in predicting poor outcome. In our study, APACHE-III score of 80 or more has a 63.33% sensitivity and 70.21% specificity in predicting mortality in patients with ventilator associated pneumonia.

The median survival for patients with APACHE-III score <80 was 37 ICU days,

whereas those who had APACHE-III score more than or equal to 80 had only 12 ICU days (p=.0038). The difference was both clinically and statistically significant. Patients with a APACHE III score of less than 80 at the time of diagnosis had a median of 9 hospital days and those with a APACHE III score equal to or more than 80 had 14.5 days, the difference was not statistically, but clinically significant. Patients with a APACHE III score of less than 80 at the time of diagnosis had a median of 19 hospital days and those with a APACHE III score equal to or more than 80 had 28.5 days, the difference was not statistically, but clinically significant. In this study, APACHE III score, especially a score of more than or equal to 80 was proven to be a good outcome predictor in Ventilator Associated Pneumonia.

The mean mod CPIS score was 5.5 in the patients who succumbed to their illness and 5.26 among those who survived. There was no significant difference among the both groups. Analysis was done to see whether a modified CPIS score of 6 or more can be used as a predictor of mortality. Previous studies has shown CPIS score less than 6 as an indication to stop antibiotics in patients with ventilator associated pneumonia. But there was no significant correlation noticed. The median survival for patients with modified CPIS score <6 was 37 ICU days, whereas those who had modified CPIS score more than or equal to 6 had only 23 ICU days (p=.4182). The difference was clinically significant. Patients with a mod.CPIS score of less than 6 at the time of diagnosis had a median of 10 ICU days and those with a mod.CPIS score equal to or more than 6 had 10.5 days, the difference was not statistically or clinically

significant.

Patients with a mod. CPIS score of less than 6 at the time of diagnosis had a median of 19 hospital days and those with a mod.CPIS score equal to or more than 6 had 22 days, the difference was not statistically significant, but it was clinically significant. Modified CPIS score of 6 or more was proven to be a good predictor of outcome in VAP, in terms of median survival expressed as ICU days and total days of hospital stay, once shifted out from ICU.

The mean MOD Score among those who survived was 7.0 and among those who succumbed to illness was 9.6, and it was statistically significant. 33.33% of the patients who died had a MOD score between 9 and 12. Specificity of a MOD score between 9 and 12 in predicting mortality was 74.47%. This finding was statistically significant as well. The median survival for patients with MOD score <9 was 37 ICU days, whereas those who had MOD score more than or equal to 9 had only 14 ICU days (p=.019). The difference was both clinically and statistically significant. There was no significant correlation noticed between the MODS score at the time of diagnosis of VAP and the median days of ICU stay. There was no significant correlation noticed between the MODS score at the time of diagnosis of VAP and the median days of hospital stay.

APACHE III score and MOD Score were proven to be good predictors of outcome in VAP patients in terms of mortality, median ICU days of survival and

median days of hospital or ICU stay, whereas modified CPIS score and procalcitonin levels failed to be so. It might be because of the fact that APACHE III scoring and MOD scoring were introduced as predictors of mortality, where as modified CPIS score was introduced as a diagnostic criteria.

Other factors like age above 45 years, drug resistant organism grown in the ET aspirate culture , significant growth of multiple organisms in the ET aspirate culture and late VAP were analyzed to find whether they could be predictors of poor outcome. T-Test analysis was done to compare the mean age among the survivors and those who died. There was significant association noticed between the 'age' and the outcome, in terms of 'mortality'. The median survival for patients with age less than or equal to 45 years was 23 ICU days, whereas those who had age more than 45 years, it was 20 ICU days (p=.75). The difference was not significant.

Of all the mortality, 10% had sensitive organism grown in the ET aspirate culture and 90% had resistant organism. Mortality rate among those who had sensitive organism was 42.9%, whereas among those who had resistant organism was 38.6%. But these values were not statistically significant. 56.67% of the patients who succumbed to their illness had single organism grown in the ET aspirate culture, where as 43.33% had multiple organisms grown. The difference was not statistically significant. Irrespective of the fact that whether a single organism or multiple organisms were grown in the ET aspirate, the median number of ICU days was about 10.

The median number of hospital days in those who had a single organism grown in their ET aspirate was 18 days, whereas those who had multiple organisms grown in their ET aspirate had a median number of hospital days of 21, and the difference was not clinically or statistically significant. The patients whose ET aspirate grew only a single organism, had a median survival period of 26 ICU days, whereas the patients whose ET aspirate grew multiple organisms, the median survival period was 19 ICU days. The difference was clinically significant, but it was not statistically significant (p= 0.6812).

Acinetobacter was the most common organism grown in the ET aspirate culture from the patients with VAP, in our study . Most of them were resistant to all the drugs tested for susceptibility , except Colistin. There was no significant difference in the mortality between those who had grown acinetobacter sp in the ET aspirate and those who had grown some other organism (52.94% and 47.06% respectively). The median survival time of those who had acinetobacter infection was 23 ICU days, where as those who had other organism in their ET aspirate was 26 days. The difference was not statistically significant. But the difference was clinically significant.

The median number of ICU days those who had grown acinetobacter sp in the ET aspirate was 10 days , where as in others it was 23.5 days. The difference was not statistically significant. But this difference was also clinically significant. The median number of hospital days those who had grown acinetobacter sp in the ET aspirate was 14 days , where as in others it was 39 days. The difference was not statistically

significant. But the difference was clinically significant. Even if most of the Acinetobacter sp grown in the ET aspirate culture was resistant to most of the drugs tested for susceptibility, except Colistin, the outcome was good for those who had acinetobacter infection when compared to those who had VAP due to any other organism. This might be due to the difference in the in-vivo and in-vitro susceptibility of this organism to the drugs tested.

Among those who died 20% had early VAP and 80% had late VAP. Early VAP had a mortality rate of 21.4%, where as Late VAP had a mortality rate of 48.98%. Both were statistically significant. Median of number of ICU stay in the early VAP group was 9 days and that in Late VAP group was 11 days. A difference of 2 or more days was considered as a clinically significant difference. The median number of hospital days among those who had Early VAP was 17 days and that with Late VAP was 14 days. As a difference of 4 hospital days was considered as clinically significant value, early and late VAP did not show any clinically significant difference in this aspect.

Compared to previous studies, this study showed no significant difference among the infections caused by the sensitive organism and the resistant organisms, in terms of the outcome. APACHE III and MOD score were proved to be good prognostic factors, where as modified CPIS score which was developed as a diagnostic scoring system failed as a prognostic scoring system, even if the previous studies had showed its significance as a prognostic factor. Commonest organism was acinetobacter, not pseudomonas. Other factors like age, polymicrobial infection, immunosuppression etc

were considered in this study.

CONCLUSION

In Ventilated patients who had a normal chest xray at the time of intubation, and who developed VAP later

- Late VAP is more common than Early VAP.
- Most common organism is Acinetobacter , followed by Pseudomonas and Klebsiella
- Resistant organisms are more common than sensitive organisms, but this had no bearing on their outcomes.
- APACHE III score at the time of the diagnosis of VAP is a good predictor of mortality, number of days of ICU and hospital stay
- Modified CPIS score at the time of diagnosis of VAP is a predictor of the median survival in terms of ICU days
- MODS score at the time of diagnosis of VAP is a predictor of mortality and the median survival in terms of ICU days
- Age > 45 is a risk factor for mortality
- Whether the ET aspirate culture grew a resistant organism or multiple organisms, did not have any significant effect on the outcome in terms of mortality, but polymicrobial infection will increase the ICU and the hospital stay.
- Mortality is higher in those who develop late VAP.

- Acinetobacter infection had a better outcome in terms of total number of ICU days and hospital days , even if most of them were resistant to more than 3 groups of first line anti-microbial agents.

LIMITATION

- As only the patients those who had normal chest x ray at the time of intubation was included in the study, the findings cannot be extrapolated to the entire VAP infection.
- For the same reason incidence of VAP and per day risk of developing VAP could not be calculated based on this study
- Not all patient had procalcitonin levels and there was no serial monitoring of procalcitonin done. The rate of decrease in Procalcitonin would have been a better predictor of outcome as seen in previous studies.

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APPENDIX 1

PATIENT INFORMATION SHEET

STUDY TITLE:- THE INCIDENCE, RISK FACTORS, CLINICAL AND MICROBIOLOGIC PROFILE AND PROGNOSTIC FACTORS OF VENTILATOR ASSOCIATED PNEUMONIA IN AN INDIAN TEACHING HOSPITAL SETTING.

A clinical study is being conducted to evaluate the prevalence, risk factors, clinical and microbiological profile and prognostic factors of Ventilator Associated Pneumonia. This study involves collecting historical data regarding the patient's illness, detailed clinical examination of the patient, collecting blood and ET aspirate/ bronchial lavage samples for laboratory tests, and following up the patient till discharge.

Only those patients who develop features suggestive of pneumonia, 48 hours after the intubation are included in the study. The study requires no additional blood or any other tests, other than those which are done routinely for the evaluation and treatment of new onset pneumonia in intubated patients. The study incurs no additional cost to the participants in any manner. The study does not involve any invasive procedure on the patient, other than the collection of patient's blood sample and the ET aspirate/ bronchial lavage samples. The patient will be followed up till the discharge.

The data collected from history, examination and investigations of the patient will be kept confidential, analyzed separately and results published in standard medical journals, without revealing the identity of the patient.

The results anticipated from the study are expected to improve the understanding about the various aspects of Ventilator Associated Pneumonia, thereby guiding the treating physician in his/her approach towards the management of such cases.

DATE:

APPENDIX 2

INFORMED CONSENT FORM TO PARTICIPATE IN RESEARCH STUDY

STUDY TITLE: THE INCIDENCE, RISK FACTORS, CLINICAL AND MICROBIOLOGIC PROFILE AND PROGNOSTIC FACTORS OF VENTILATOR ASSOCIATED PNEUMONIA IN AN INDIAN TEACHING HOSPITAL SETTING.

NAME OF THE SUBJECT: **AGE:**

HOSPITAL NUMBER:

(i) I confirm that I have read and understood the information sheet dated _____ for the above study and have had the opportunity to ask questions. [ ]

(ii) I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. [ ]

(iii) I understand that the investigators of this research study, the Ethics Committee and the regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the trial. I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published. [ ]

(iv) I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s) [ ]

(v) I agree to take part in the above study. [ ]

Signature (or Thumb impression) of the Subject/Legally Acceptable Representative:_____

Date: _____/_____/_____

Signatory's Name: _____

Signature of the Investigator: _____

Date: _____/_____/_____

Study Investigator's Name: _____

Signature of the Witness: _____

Date: ____/_____/_____

Name of the Witness: _____

APPENDIX 3

PROTOCOLS AND CRITERIAS USED

The APACHE II Severity of Disease Classification System

Physiologic Variable	+4	+3	+2	+1	0	+1	+2	+3	+4
Temperature - rectal (°C)	≥41	39-40.9		38.5-38.9	36-38.4	34-35.9	32-33.9	30-31.9	≤29.9
Mean Arterial Pressure (mm Hg)	≥160	130-159	110-129		70-109		50-69		≤49
Heart Rate	≥180	140-179	110-139		70-109		55-69	40-54	≤39
Respiratory Rate (nonventilated or ventilated)	≥50	35-49		25-34	12-24	10-11	6-9		≤5
Oxygenation (mmHg) a. $FiO_2 > 0,5$ use A-aDO_2 b. $FiO_2 < 0,5$ use PaO_2	a ≥500	350-499	200-349		<200				
	b				> 70	61-70		55-60	<55
Arterial pH	≥7.7	7.6-7.69		7.5-7.59	7.33-7.49		7.25-7.32	7.15-7.24	<7.15
Serum Sodium (mmol/l)	≥180	160-179	155-159	150-154	130-149		120-129	111-119	≤110
Serum Potassium (mmol/l)	≥7	6-6.9		5.5-5.9	3.5-5.4	3-3.4	2.5-2.9		<2.5
Serum Creatinine (mg/dl, Double point score for acute renal failure)	≥3.5	2-3.4	1.5-1.9		0.6-1.4		<0.6		
Hematocrit (%)	≥60		50-59.9	46-49.9	30-45.9		20-29.9		<20
White Blood Count (in 1000/mm³)	≥40		20-39.9	15-19.9	3-14.9		1-2.9		<1
Glasgow-Coma-Scale (GCS)	Score = 15 minus actual GCS								
Serum HCO_3 (venous, mmol/l, use if no ABGs)	≥52	41-51.9		32-40.9	22-31.9		18-21.9	15-17.9	<15
A = Total Acute Physiology Score APS	Sum of the 12 individual variable points								
B = Age Points	**C = Chronic Health Points**								
≤44 years 0 points 45-54 years 2 points 55-64 years 3 points 65-74 years 5 points ≥75 years 6 points	If the patient has a history of severe organ system insufficiency or is immunocompromised assign points as follows: a. For nonoperative or emergency postoperative patients – 5 points b. For elective postoperative patients – 2 points								
APACHE II Score = Sum of A (APS points) + B (Age points) + C (Chronic Health points)									

(From: Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II: a severity of disease classification system. Crit Care Med 1985;13(10):818-29)

Modified CPIS Score-

CPIS Points	0	1	2
Tracheal secretions	Rare	Abundant	Abundant＋purulent
Chest X-ray infiltrates	No infiltrate	Diffused	Localized
Temperature, ℃	≧36.5 and≦38.4	≧38.5. and≦38.9	≧39 or≦36
Leukocytes count, per mm^3	≧4,000 and≦11,000	＜4,000 or＞11,000	＜4,000 or＞11,000＋band forms≧500
P_{AO2}/F_{IO2}, mmHg	＞240 or ARDS		≦240 and no evidence of ARDS

Pugin J, Auckenthaler R, Milli N, Janssens JP, Lew PD, Suter PM. Diagnosis of ventilator-associated pneumonia by bacteriologic analysis of bronchoscopic and nonbronchoscopic "blind" bronchoalveolar lavage fluid. Am Rev Respir Dis 1991;143:1121-9

Multi Organ Dysfunction Score-

Organ System	0	1	2	3	4
Respiratory PO_2/FiO_2 (mmHg)	>300	226–300	151–225	76–150	≤ 75
Renal serum creatinine (µmol/liter)	≤ 100	101-200	201–350	351–500	>500
Hepatic serum bilirubin (µmol/l)	≤ 20	21–60	61–120	121–240	>240
Cardiovascular PAR[1)]	≤ 10,0	10,1–15,0	15,1–20,0	20,1–30,0	>30,0
Hematologic platelets/nl	>120	81–120	51–80	21-50	≤ 20
Neurologic Glasgow Coma Score	15	13–14	10–12	7–9	≤ 6

Marshall JC, Cook DJ, Christou NV, et. al. Multiple organ dysfunction score: a reliable descriptor of a complex clinical outcome. *Crit Care Med*. 1995 Oct;23(10):1638-52. Review

APPENDIX 4

VENTILATOR ASSOCIATED PNEUMONIA

Serial No: (MICU/MHDU/SICU/SHDU/AICU/KHDU)

NAME: **HOSP NO:**

PLACE: **AGE:** **SEX: (M=1, F=2)**

DIAGNOSIS: **DOA: Hospital-** **ICU-**

HISTORY: **Medical/ surgical/ trauma**

Intubation- Date: **Time:** **place:**

Hours post-intubation , when clinical diagnosis of VAP is made-

Tracheal Secretion- None/ Non-Purulent/ Purulent - (0 / 1 / 2)

ORGAN FAILURE- (No=0, Yes=1)

Dyspnoea of NYHA grade-IV? 0 / 1

On dialysis? 0 / 1

Known case of hepatic failure/ liver cirrhosis/ Portal hypertension? 0 / 1

On home Oxygen/ chronic hypoxia or hypercapnia / severe PAH/ polycythemia ? 0 / 1

Any Immunosuppressive state? 0 / 1 (AIDS / Lymphoma/ Leukemia/ metastatic cancer)

Others-

Non-operated / post emergency operation/ post elective operation- 0 / 1 / 2

CLINICAL: **MAP:** **CVP:** **HR:** **TEMP:** **RR:**

GCS: E V M = /15 **Urine Output:**

ABG: **pH:** **A-a Gradient:** **FIO2:** **PAO2:** **PF Ratio:**

LAB: **Hematocrit:** **Platelets:** **WBC:** **Na:** **K:**

Creatinine: **Bilirubin:** **Urea:** **Glucose:** **Albumin:**

CHEST X-RAY- No infiltrate/ Diffused or patchy/ Localized infiltrate- (0 / 1 / 2)

MICROBIOLOGY: ET Aspirate/ BAL Culture Report:

PROGNOSTIC FACTORS: Mod.CPIS Score= MOD Score=

APACHE-II Score= Procalcitonin=

OUTCOME: Days of ICU stay= Days of Hospital stay=

FINAL OUTCOME- Dead/ Alive - 0 / 1 DOD:

APPENDIX 5

SLNO	AGE	SEX	SYSTEM	DIAGNOSIS	MONTH	DOAHOSP	DOAICU	TYPE	INTUBATION	ICU	VAPDAY	SECRETIONS	DIALYSIS	DYSPNOEA	LIVER	LUNG	IMMUNO	OPERATED	MAP	CVP
1	39	M	1	EARLY DEMENTIA UNDER EVALUATION	2	28/02/2014	28/02/2014	MEDICAL	28/02/2014	M	4	2	0	0	0	0	0	0	118	10
2	51	F	2	CKD-III, DM, HTN, OSA, HYPOTHYROIDISM	2	17/02/2014	22/02/2014	MEDICAL	22/02/2014	M	9	2	1	0	0	1	0	0	80	12
3	21	F	3	EMERGENCY LSCS, HTN, AKI	3	10/03/2014	10/03/2014	SURGICAL	10/03/2014	S	15	2	0	0	1	0	0	1	101	12
4	36	F	4	BOWEL PERFORATION	3	09/03/2014	13/03/2014	SURGICAL	13/03/2014	S	6	2	0	0	0	0	0	1	80	9
5	64	M	5	CAROTID ARTERY LACERATION	3	12/03/2014	13/03/2014	SURGICAL	15/03/2014	S	4	1	0	0	0	0	0	1	859	10
6	52	M	6	POLYTRAUMA	3	13/03/2014	13/03/2014	TRAUMA	13/03/2014	S	11	2	0	0	0	0	0	1	93.329	8
7	22	M	7	OP POISONING	3	23/03/2014	23/03/2014	MEDICAL	23/03/2014	M	35	2	0	0	0	0	0	0	96.65	10
8	26	M	6	RTA	4	27/0	28/0	TRA	28/0	S	5	1	0	0	0	0	0	1	11	1

	2					3/20/2014	3/20/2014	UMA	3/20/2014												25	0
9	45	M	11	MENINGITIS	4	26/03/2014	29/03/2014	MEDICAL	29/03/2014	M	12	2	0	0	0	0	0	0	85	8
10	55	M	6	RTA	4	02/04/2014	02/04/2014	TRAUMA	02/04/2014	S	6	1	0	0	0	0	0	1	93	11
11	21	M	6	RTA	4	07/04/2014	07/04/2014	TRAUMA	07/04/2014	S	14	2	0	0	0	0	0	1	54	10
12	36	F	4	TAH, BSO, ILEAL RESECTION ANASTOMOSIS	4	16/04/2014	16/04/2014	SURGICAL	16/04/2014	S	5	2	0	0	0	0	0	1	73	11
13	52	F	9	MDS AUTOIMMUNE MYOCLONIC JERKS, SEIZURE PARTIAL	5	08/05/2014	10/05/2014	MEDICAL	10/05/2014	A	4	2	0	0	0	0	1	0	78	10
14	66	M	1	HANGING	4	15/04/2014	19/04/2014	MEDICAL	19/04/2014	A	26	2	0	0	0	0	0	0	72	11
15	65	M	1	CARCINOAMA THYROID WTH METS	5	05/05/2014	05/05/2014	MEDICAL	05/05/2014	M	3	2	0	0	0	0	0	0	81	12
16	65	F	10		5	23/04/2014	24/04/2014	SURGICAL	24/04/2014	S	15	2	0	0	0	0	1	2	90	9
17	27	M	6	RTA	5	02/05/2014	03/05/2014	TRAUMA	03/05/2014	S	3	2	1	1	1	1	0	1	103	12
18	28	M	7	OP POISON	5	22/05/2014	22/05/2014	MEDICAL	22/05/2014	M	3	2	0	0	0	0	0	0	96	10

				ING		14	14	AL	14													
19	62	M	12	LBBB, MI, PULMONARY EDEMA	5	15/05/2014	15/05/2014	MEDICAL	15/05/2014	M	6	2	0	0	0	1	0	0	65	8
20	65	M	2	DM, HTN, OSA, TYPE-II RF	7	10/07/2014	11/07/2014	MEDICAL	10/07/2014	M	4	2	0	0	0	0	0	0	100	0
21	47	F	11	NECROTIZING FASCITIS	7	12/07/2014	13/07/2014	SURGICAL	13/07/2014	S	3	1	0	0	0	0	0	2	122	1
22	41	M	11	NECROTIZING FASCITIS	7	13/07/2014	13/07/2014	SURGICAL	14/07/2014	S	3	1	1	0	1	0	0	1	64	0
23	24	M	9	LARGE B CELL LYMPHOMA	7	06/06/2014	01/07/2014	MEDICAL	01/07/2014	A	8	2	0	0	0	0	1	0	100	1
24	25	F	11	SPLENIC ABSCESS RUPTURE, SEPSIS ABDOMEN	6	03/06/2014	13/06/2014	MEDICAL	13/06/2014	M	13	2	1	0	1	1	0	0	92	0
25	26	F	6	BKUNT TRAUMA	7	02/07/2014	02/07/2014	TRAUMA	02/07/2014	S	8	2	0	0	0	0	0	0	80	0
26	68	M	1	INTRACEREBRAL HEMORRHAGE	9	07/09/2014	10/09/2014	MEDICAL	10/09/2014	M	5	2	0	0	0	0	0	0	85	2
27	18	F	1	CVT	9	30/08/2014	30/08/2014	MEDICAL	30/08/2014	M	15	2	0	0	0	0	0	0	95	0
28	58	M	7	OP POISON	9	07/09/2014	07/09/2014	MEDICAL	07/09/2014	M	4	2	0	0	0	0	0	0	100	1

				ING		14	14	AL	14											0			
				OP		05/0	05/0	ME	05/0														
2	3			POISON		9/20	9/20	DIC	9/20											9	1		
9	0	M	7	ING	9	14	14	AL	14	M	6	2	0	0	0	0	0	0		9	1		
				OP		29/0	29/0	ME	29/0														
3	3			POISON		8/20	8/20	DIC	8/20											7	1		
0	1	M	7	ING	9	14	14	AL	14	M	9	2	0	0	0	0	0	0		9	0		
				NECRO																			
				TIZING		12/0	13/0	ME	13/0														
3	4			FASCITI		9/20	9/20	DIC	9/20											7	1		
1	8	M	11	S	9	14	14	AL	14	M	3	2	0	0	0	0	0	0		0	0		
				SEPSIS,																			
				OSA,																			
				COPD,		10/0	11/0	ME	11/0														
3	3			DM		7/20	7/20	DIC	7/20											9	1		
2	3	M	11	HTN	7	14	14	AL	14	M	3	2	0	0	0	0	0	0		0	0		
				MCTD,		06/0	11/0	ME	11/0														
3	6			DM,		7/20	7/20	DIC	7/20											9	1		
3	6	F	13	HTN	7	14	14	AL	14	M	6	2	0	0	0	0	0	0		0	1		
				CARCIN		06/0	07/0	SU	07/0											1			
3	7			OMA		7/20	7/20	RGI	7/20		1									0	1		
4	7	F	10	COLON	7	14	14	CAL	14	S	2	2	0	0	0	0	1	2		0	0		
				LAPROS																			
				COPIC																			
				CHOLEC		13/0	17/0	SU	17/0														
3	5			YSTECT		7/20	7/20	RGI	7/20											8	1		
5	5	F	4	OMY	7	14	14	CAL	14	S	5	2	0	0	0	0	0	2		1	0		
				ACUTE																			
				FLACID		09/0	15/0	ME	15/0														
3	4			PARALY		9/20	9/20	DIC	9/20		2									9	1		
6	5	F	1	SIS	10	14	14	AL	14	M	8	2	0	0	0	0	0	0		5	0		
				SEPTIC																			
				SHOCK,																			
				RIGHT																			
				ATRIAL		10/1	11/1	ME	10/1														
3	7			THROM		0/20	0/20	DIC	0/20											8	1		
7	2	M	11	BUS	10	14	14	AL	14	M	3	2	0	0	0	0	0	0		9	1		
				SCRUB		09/1	09/1	ME	09/1														
3	4			TYPHUS		0/20	0/20	DIC	0/20											7	1		
8	5	F	11	, ARDS	10	14	14	AL	14	M	3	1	0	0	0	0	0	0		5	0		
						06/0	06/0	ME	06/0														
3	2			HANGI		8/20	8/20	DIC	8/20											8	1		
9	4	F	1	NG	8	14	14	AL	14	M	7	2	0	0	0	0	0	0		0	0		
4	3			ACUTE		28/0	29/0	SU	29/0											1	1		
0	3	M	4	PANCR	8	7/20	7/20	RGI	7/20	S	4	2	1	0	0	0	0	1		1	2		

				EATITIS		14	14	CAL	14													0		
41	35	M	9	AML - POST BMT SUPERIOR SAGITTAL SINUS THROMBOSIS SCRUB TYPHUS, ARDS CARCINOMA CERVIX SEPTIC ABORTION POST NATAL-VAGINAL WOUND DEBRIDEMENT NSTEMI, CARDIOGENIC SHOCK ACUTE FEBRILE ILLNESS, AKI SCRUB TYPHUS, ARDS MUSCULAR DYSTROPHY SEPTIC	8	18/06/2014	18/06/2014	MEDICAL	24/07/2014	A	1 8	1	0	0	0	0	1	0	74	10
42	20	F	1		8	06/08/2014	06/08/2014	SURGICAL	06/08/2014	M	1 0	2	0	0	0	0	0	1	80	11
43	60	F	11		1	27/12/2014	29/12/2014	MEDICAL	29/12/2014	M	4	2	0	0	0	0	0	0	60	10
44	60	F	10		1	31/12/2014	01/01/2015	SURGICAL	01/01/2015	S	5	1	0	0	0	0	1	1	71	10
45	24	F	3		1	27/12/2014	30/12/2014	SURGICAL	30/12/2014	S	6	2	1	0	0	0	0	1	74	11
46	22	F	3		1	25/12/2014	26/12/2014	SURGICAL	29/12/2014	S	3	1	0	0	0	0	0	1	70	10
47	65	F	12		12	20/12/2014	23/12/2014	MEDICAL	23/12/2014	M	6	2	0	0	0	0	0	0	81	10
48	64	M	11		12	21/12/2014	21/12/2014	MEDICAL	21/12/2014	M	5	2	0	0	0	0	0	0	81	10
49	45	F	11		11	16/12/2014	17/12/2014	MEDICAL	17/12/2014	M	7	2	1	0	0	0	0	0	67	10
50	20	M	1		11	11/12/2014	11/12/2014	MEDICAL	13/12/2014	M	3	2	0	0	0	0	0	0	80	10
51	52	F	3		10	13/02	16/02	SURGICAL	14/02	S	1	1	0	0	0	0	0	1	91	10

1	6			SHOCK, RETAINED MOP		8/20/2014	8/20/2014	RGICAL	8/20/2014		3									1	0
52	52	M	6	POLYTRAUMA	10	18/10/2014	18/10/2014	TRAUMA	18/10/2014	S	8	1	0	0	0	0	0	1	80	10
53	50	M	1	MYASTHENIA GRAVIS, THYMOMA	10	07/10/2014	09/10/2014	MEDICAL	09/10/2014	M	1 1	2	0	0	0	0	1	0	80	10
54	34	M	11	DISSEMINATED TB	10	14/10/2014	22/10/2014	MEDICAL	22/10/2014	M	6	2	0	0	0	0	0	0	70	12
55	66	M	11	SCRUB TYPHUS, ARDS	10	29/09/2014	29/09/2014	MEDICAL	29/09/2014	M	7	2	0	0	0	0	0	0	10 0	10
56	79	M	9	CML	9	08/09/2014	20/09/2014	MEDICAL	24/09/2014	A	6	2	1	0	0	0	1	0	68	10
57	74	F	4	UMBILICAL HERNIA - MESH REPAIR	9	01/09/2014	05/09/2014	SURGICAL	05/09/2014	S	1 1	2	0	0	1	0	0	2	70	10
58	50	M	4	DUODENAL PERFORATION	9	21/09/2014	21/09/2014	SURGICAL	21/09/2014	S	3	2	0	0	0	0	0	1	10 3	11
59	62	M	11	NECROTIZING FASCITIS	9	18/09/2014	19/09/2014	SURGICAL	19/09/2014	S	4	2	0	0	0	0	0	1	70	10
60	87	M	11	ACUTE PYELONEPHRITIS, DM, HTN	9	13/09/2014	15/09/2014	MEDICAL	15/09/2014	M	9	2	0	0	0	0	0	0	92	10
61	68	F	11	SCRUB TYPHUS, ARDS	9	21/09/2014	21/09/2014	MEDICAL	21/09/2014	M	5	2	0	0	0	0	0	0	96	10
62	33	M	6	POLYTRAUMA	10	01/10/2014	02/10/2014	TRAUMA	02/10/2014	S	4	1	0	0	0	0	0	1	98	10

						02/1	02/1	TRA	02/1													
6	3			POLYTR		0/20	0/20	UM	0/20												8	1
3	2	F	6	AUMA	10	14	14	A	14	S	4	2	0	0	0	0	0	1	0	0
						29/0	30/0	ME	03/1													
6	4			SNAKE		9/20	9/20	DIC	0/20												9	1
4	0	M	14	BITE	10	14	14	AL	14	M	3	2	1	0	0	0	0	0	0	0
				ACUTE		21/1	23/1	ME	23/1													
6	2			FEBRILE		1/20	1/20	DIC	1/20												7	1
5	0	F	11	ILLNESS	12	14	14	AL	14	M	8	2	0	0	0	0	0	0	0	0
				HIATUS																		
				HERNIA		30/1	03/1	SU	03/1													
6	6			RUPTU		1/20	2/20	RGI	2/20												7	1
6	5	M	4	RED	12	14	14	CAL	14	S	7	2	0	0	0	0	0	1	5	0
						28/1	30/1	ME	30/1													
6	2					1/20	1/20	DIC	1/20												7	1
7	8	M	8	CKD	12	14	14	AL	14	M	4	2	1	0	0	0	0	0	0	0
						09/1	09/1	ME	09/1													
6	3			SCRUB		2/20	2/20	DIC	2/20												8	1
8	9	M	11	TYPHUS	12	14	14	AL	14	M	4	2	0	0	0	0	0	0	5	0
						24/1	24/1	ME	24/1													
6	4					1/20	1/20	DIC	1/20												7	1
9	5	M	11	H1N1	12	14	14	AL	14	M	7	1	0	0	0	0	0	0	0	0
				COPD		22/0	24/0	ME	29/0													
7	7			EXACER		5/20	5/20	DIC	5/20												7	1
0	6	M	15	BATION	6	14	14	AL	14	M	4	2	0	0	0	1	0	0	0	1
						25/0	25/0	TRA	25/0													
7	2			POLYTR		5/20	5/20	UM	5/20												9	1
1	9	M	6	AUMA	5	14	14	A	14	S	4	2	0	0	0	0	0	1	9	0
				ECLAM																		
				PSIA,		30/0	31/0	SU	31/0													
7	2			POST		5/20	5/20	RGI	5/20												8	1
2	4	F	3	LSCS	6	14	14	CAL	14	M	3	2	0	0	0	0	0	1	8	2
				AAA		04/0	04/0	SU	04/0												1	
7	5			RUPTU		6/20	6/20	RGI	6/20												2	1
3	5	M	5	RE	6	14	14	CAL	14	S	6	2	0	0	0	0	0	1	1	2
						30/0	30/0	TRA	30/0													
7	3			POLYTR		5/20	5/20	UM	5/20		1										6	1
4	1	F	6	AUMA	6	14	14	A	14	S	1	1	0	0	0	0	0	1	5	0
				ACUTE		10/0	11/0	ME	11/0													
7	5			PANCR		6/20	6/20	DIC	6/20												7	1
5	7	M	4	EATITIS	6	14	14	AL	14	M	5	2	0	0	0	0	0	0	0	0
				NECRO																		
				TIZING		14/0	15/0	SU	15/0													
7	5			FASCITI		6/20	6/20	RGI	6/20												5	1
6	4	F	11	S	6	14	14	CAL	14	S	5	1	0	0	0	0	0	1	7	0

7	2			PORPH		13/06/2014	14/06/2014	MEDICAL	14/06/2014											1	1	1
7	4	M	13	YRIA	6					M	6	2	0	0	0	0	0	0	0	0	1	
7	2					09/01/2015	29/01/2015	MEDICAL	29/01/2015											7	1	
8	7	M	9	AML	2					A	8	2	0	0	0	0	1	0	0	0		