TO STUDY THE INCIDENCE AND ETIOLOGY OF VENTILATOR ASSOCIATED EVENTS IN CASES ADMITTED IN ADULT ICU IN A TERTIARY CARE CENTRE IN WESTERN RAJASTHAN

THESIS

SUBMITTED TO

ALL INDIA INSTITUTE OF MEDICAL SCIENCES, JODHPUR

IN PARTIAL FULFILMENT OF THE REQUIREMENT FOR THE DEGREE

OF

DOCTOR OF MEDICINE (MD)

(MICROBIOLOGY)

JUNE, 2022 **DR. ZEESHAN NOORE AZIM**

AIIMS, JODHPUR

TO STUDY THE INCIDENCE AND ETIOLOGY OF VENTILATOR ASSOCIATED EVENTS IN CASES ADMITTED IN ADULT ICU IN A TERTIARY CARE CENTRE IN WESTERN RAJASTHAN

THESIS

SUBMITTED TO

ALL INDIA INSTITUTE OF MEDICAL SCIENCES, JODHPUR

IN PARTIAL FULFILMENT OF THE REQUIREMENT FOR THE DEGREE

OF

DOCTOR OF MEDICINE (MD)

(MICROBIOLOGY)

JUNE, 2022 **DR. ZEESHAN NOORE AZIM**

AIIMS, JODHPUR

CERTIFICATE

This is to certify that the thesis entitled "**To study the incidence and etiology of ventilator associated events in cases admitted in adult ICU in a tertiary care centre in western Rajasthan"** is the bonafide work of **Dr. Zeeshan Noore Azim** carried out under our guidance and supervision in the Department of Microbiology, All India Institute of Medical Sciences, Jodhpur

Guide:

Dr. Ashwini Agarwal
Additional Professor
Department of Microbiology
AIIMS, Jodhpur

Co-Guides:

Dr. Vijaya Lakshmi Nag
Professor and Head
Department of Microbiology
AIIMS, Jodhpur

Dr. Pradeep Kumar Bhatia
Professor and Head
Department of Anaesthesiology &
Critical care AIIMS, Jodhpur

Dr. Mahendra Kumar Garg
Professor and Head
Department of Medicine
AIIMS, Jodhpur

Dr. Vibhor Tak
Associate Professor
Department of Microbiology
AIIMS, Jodhpur

CERTIFICATE

This is to certify that the thesis entitled "**To study the incidence and etiology of ventilator associated events in cases admitted in adult ICU in a tertiary care centre in western Rajasthan"** is the bonafide work of **Dr. Zeeshan Noore Azim**, undertaken in the Department of Microbiology, All India Institute of Medical Sciences, Jodhpur.

It is further certified that the candidate has fulfilled the pre-requisites necessary for the submission of this thesis work.

Dr. Sneha Ambwani
Professor and Officiating Head
Department of Microbiology
AIIMS, Jodhpur

ACKNOWLEDGEMENT

I would like to express my deep and sincere gratitude to my Guide, Dr. Ashwini Agarwal, M.D, Microbiology, Additional Professor, Department of Microbiology, All India Institute of Medical Sciences, Jodhpur, for giving me the opportunity to do research and providing invaluable guidance throughout this research. His dynamism, vision, sincerity and motivation have deeply inspired me. He has taught me the methodology to carry out the research and to present the research works as clearly as possible. It was a great privilege and honor to work and study under his guidance. I am extremely grateful for what he has offered me. I would also like to thank him for his patience during the discussion I had with him on research work and thesis preparation.

Besides my Guide, I would like to thank the rest of my thesis committee and Dr. Vijaya Lakshmi Nag, MD Microbiology, Professor and Head of Department of Microbiology, and Dr. Pradeep Kumar Bhatia, MD Anaesthesiology, Professor and Head, Department of Anaesthesiology and Critical Care and Dr. Mahendra Kumar Garg, MD Medicine, Professor and Head, Department of Medicine for their insightful comments and encouragement, but also for the hard question which incented me to widen my research from various perspectives.

Also, I am extremely grateful to Dr. Prem Prakash Sharma, Associate Professor, Department of Community Medicine and Family Medicine, AIIMS, Jodhpur for his expert guidance in the statistical analysis of my thesis work.

I would like to extend my thanks to Dr. Vibhor Tak, Associate Professor in Department of Microbiology for providing his insightful comments in my thesis work. I am grateful to my teachers, Dr. Ravisekhar Gadepalli, Additional Professor, Dr. Sarika Kombade, Associate Professor, Dr. Vidhi Jain, Assistant Professor and Dr. S Abhishek Kumar Assistant Professor for their kind encouragement.

I would also like to extend my thanks to Senior Residents of Department of Microbiology, especially Dr. Jitu Moni Kalita, and Dr. Kavita Yedale Kalita for taking interest in my work and providing guidance for the same.

I am grateful to the staff of adult ICU and Department of Microbiology for their co-operation in sample collection and obtaining relevant clinical data of the patients enrolled in the thesis work.

I would like to say thanks to my Seniors, Dr. Parvathi Ravi, Dr. Alisha Agarwal, Dr. Twishi Shrimali, Dr. Salman Khan, Dr. Kirtika sharma, Dr. Malika, Dr. Nailah for their constant encouragement and support.

I am extending my thanks to my Juniors especially Dr. Tejashree, Dr. Kirti, Dr. Debaleena, Dr. Nischay and Dr. Sukanya for their support during my research work.

I also thank all the staff of Research section of AIIMS, Jodhpur for their kindness.

I am extremely grateful to my parents for their love, prayers, caring and sacrifices for educating and preparing me for my future. I am grateful to my wife for her encouragement and support.

Finally, I could not have completed this thesis without the support of my friend, Dr. Aditya Kundu who provided stimulating discussions as well as happy distractions to rest my mind outside of my research.

Dr. Zeeshan Noore Azim

SUMMARY

Aim: To study the incidence and etiology of ventilator associated events in cases admitted in adult ICU in tertiary care centre in western Rajasthan.

Objectives:

- To determine the rate of ventilator associated events i.e., Ventilator Associated Complications (VAC), Infection related Associated Complications (IVAC) and possible Ventilator Associated Pneumonia (VAP).
- To determine bacteriological profile of isolates obtained from relevant sample of patients having VAC.
- To determine antimicrobial susceptibility pattern of isolates obtained.

Methods: Male and female patient who were fit for inclusion criteria and those who qualified to have IVAC their relevant samples had been collected for Quantitative culture, bacteriological profiling and Antimicrobial susceptibility testing.

Results: A total of 386 cases who required mechanical ventilation were studied, in which 196 cases develop Ventilator Associated Events (VAE). Out of those 196 VAE cases, 12 develops VAC, 59 develops IVAC and 125 develops PVAP. The Rate of VAC is 3.4 VAE/1000 mechanical ventilation days and IVAC is 16.7 VAE/1000 mechanical ventilation days. Rate of PVAP is 35.39 VAE/1000 mechanical ventilation days. The most common organism isolated was *Acinetobacter baumannii* (66.66%), followed *Klebsiella pneumoniae* (22.48%), *Pseudomonas aeruginosa* (7.75%) and *Escherichia coli* (3.1%). Most of the above organism are MDR pathogen commonly resistant to higher order antibiotics like 3rd generation Cephalosporins, B-Lactam/B-lactamase inhibitors combination, Carbapenems etc. When we look at the susceptibility pattern of MDR isolates most of the isolated organism were sensitive to colistin.

Conclusion: This review will address concerns identified with parts of VAEs distinguished in chosen clinical circumstances. It can direct the Interventionist and clinicians to pick the suitable antimicrobials as per bacteriological profiling and AST

INDEX

LIST OF ABBREVIATIONS

- AKI: Acute Kidney Injury
- AMS: Antimicrobial Stewardship
- ARF: Acute Rheumatic Fever
- AST: Antimicrobial Susceptibility Testing
- BAL: Bronchoalveolor Lavage
- BSI: Blood Stream Infection
- CDC: Centers for Disease Control and Prevention
- CFU: Colony Forming Unit
- CKD: Chronic Kidney Disease
- COPD: Chronic Obstructive Pulmonary Disorder
- ETA: Endotracheal Aspirate
- FiO2: Fraction of inspired Oxygen
- GIT: Gastro Intestinal Tract
- GNB: Gram Negative Bacilli
- GPC: Gram Positive cocci
- HAP: Hospital Acquired Pneumonia
- IVAC: Infection related to Ventilator Associated Complications
- LF: Lactose Fermenter
- LRT: Lower Respiratory Tract
- LRTI: Lower Respiratory Tract Infections
- MDR: Multiple Drug Resistant
- MIC: Minimum Inhibitory Concentration
- MR: Methyl Red

- MTB: *Mycobacterium tuberculosis*
- MV: Mechanical Ventilation
- NLF: Non-Lactose Fermenter
- PBS: Protected Brush Specimen
- PE: Pulmonary Embolism
- PEEP: Positive End Expiratory Pressure
- PD: Pharmacodynamics
- PK: Pharmacokinetics
- PVAP: Possible or Probable Ventilator Associated Pneumonia
- URT: Upper Respiratory Tract
- URTI: Upper Respiratory Tract Infections
- VAE: Ventilator Associated Events
- VAP: Ventilator Associated Pneumonia
- VP: Voges Proskauer

LIST OF TABLES, GRAPHS AND DIAGRAMS

LIST OF FIGURES

LIST OF ANNEXURE'S

INTRODUCTION

Regardless of the various difficulties associated with it, the large percentage of sick patients who were admitted to ICUs requires mechanical ventilation (MV). One of the HAI in ICUs is Ventilator Associated Events (VAE), which seems to be a multi-dimensional design. VAE has already been tied to a prolonged duration of MV, longer ICU stays, a longer time period of insufficiency, higher death rates, and increasing healthcare centre expenses. Understanding VAE appears to be extremely important to conceptualising the study of transmission of infectious agents as well as the constant threat something which VAP stakeholders present [1].

Recently 2013, the Centers for Disease Control and Prevention (CDC) in the United States implemented its first Ventilator Associated Events (VAE) guidelines. The CDC created VAE classifications to augment their lengthy assessment concepts for Ventilator-Associated Pneumonia (VAP). The VAE concept was aimed at overcoming the numerous requirements of standard VAP definitions, including their relativism, uncertainty, and restricted correlation with mortality [2], Thus, the firm link of impression from pneumonia is clearly and unequivocally transferred to the establishment of hospital-associated respiratory issue in general. This transformation supplemented two crucial benefits over previous VAP knowledge. This widened the solid connection of assumption from pneumonia alone and include all important factors for respiratory impairment in ventilated patients (i.e., pneumonia nevertheless respiratory edema, ARDS, respiratory embolism, atelectasis, etc). The transformation furthermore consider the threat of generously unfolding and, in either scenario, robotising interpretation, provided that the surveillance concept also obligated acknowledging objective indicators of respiratory illness—it didn't have to perceive pneumonia explicitly. These two thoughts evolved into the rationale for VAE definitions[3].

The following are the elements of Ventilator Associated Events: 1) Ventilator Associated Condition (VAC) 2) Infection related to Ventricular Associated Complications (IVAC) 3) Possible Ventilator associated Pneumonia (PVAP) [4,1].

A VAC, according to the CDC, is a sustained increase in ventilator support following a period of consistent or decreasing ventilator support. The definition is practised by

using two ventilator settings, PEEP and FiO2. Eventually, an increase in daily minimum PEEP>3cm H_2O or an increase of the daily minimum FiO2>.20 sustained for $\geq$ 2 calendar days in a patient who had a base line period of stability or improvement. [4,1]. In the same way, the VAE description joins subcategories to try to distinguish between VAEs which were a direct result of infection and infection-related VAEs that had been a result of pneumonia. IVAC stands for infection-related subset and is defined by the presence of an unique temperature (<36°C or > 38°C) or white blood count (4,000 cells/mm3 or 12,000 cells/mm3), along with 4 days of antibacterial drugs initiating within 2 days of VAE started. Possible VAP accordingly is portrayed on either histological grounds or as the subset of IVACs with synchronous positive respiratory societies or positive microbiological examines for *Legionella* species or respiratory diseases. As a result, possible VAP was depicted histologically or as a subcategory of IVACs with simultaneous positive respiratory cultures or positive microbiological test results for Legionella species or respiratory disorders. Endotracheal aspirate with 105 colony-forming units/mL versus bronchoalveolar lavage with 104 colony-forming units/mL versus protected specimen brush test with 103 colony-forming units/mL) or any measure of comprises the development with Gram stain of purulence (25 neutrophils and 10 epithelial cells for each low-powered field). While the VAE principles for possible VAP are more objective than normal VAP guidelines, there was no evidence that they are any more (or less) accurate than standard measurements [4,1]. Accident, surgery, and neuroscience units had increased VAE rates than clinical and cardiovascular units. VAE rates was higher in prominent looking medical centers and lesser in non-significant training institutions, as per rationality. Although the risk of acquiring VAEs seems to be greater in the first fourteen days of mechanical ventilation (particularly days 3–7), individuals remain at high risk until they had been extubated. In terms of appearance, 33% of VAEs satisfy IVAC standards. In 2014, the overall site mortality probability for VAEs which showed all proper consideration to CDC was 31%. Patients who seem to had VAEs were about twice as likely to collapse severely than those that do not have VAEs [5].

According to an assessment of published literature, there is indeed a scarcity of information currently available in India as per result of the new standards, and the bulk of the reviews focus on one of the components, such as the rate of Ventilator Associated Pneumonia, or bacteriological profiling. Ventilator associated events have been used to

evaluate VAP, and typically comprise both clinical and research facility boundaries to monitor for diseases, along with complications connected with mechanical ventilation.

Concerns about sections of VAEs identified in specific clinical situations (ICUs, CCUs) will be addressed in this review. It can help physicians and interventionists to choose best antimicrobials based on microbiological characterization and AST.

AIM AND OBJECTIVES

AIM: To study the incidence and etiology of ventilator associated events in cases admitted in adult ICU in tertiary care centre in western Rajasthan.

OBJECTIVES:

- To determine the rate of ventilator associated events i.e., Ventilator Associated Complications (VAC), Infection related Associated Complications (IVAC) and possible Ventilator Associated Pneumonia (VAP).
- To determine bacteriological profile of isolates obtained from relevant sample of patients having VAC.
- To determine antimicrobial susceptibility pattern of isolates obtained.

MATERIALS AND METHODS

Study setting: - The study was carried out in patients on mechanical ventilation in adult ICU and trauma ICU (Dept of Anaesthesiology and Critical Care, Dept of General Medicine respectively) between January 2020 till June 2021.

Study design: Prospective Observational Study.

Study participants: - Adult Patients >18year both male and female who were on Mechanical ventilation in Adult ICU and Trauma ICU.

Inclusion criteria

- Adult Patients >18year both male and female on Mechanical ventilation in Adult ICU and Trauma ICU in AIIMS Jodhpur were included in the study.

Exclusion criteria

1. Patients <18 yrs. age

Sample/ specimen type: ETA/BAL were obtained from patients who have developed IVAC and sample**s** were processed through standard microbiological technique of bacteriology.

Sample size:

The sample size was calculated based on previously published study done by Surbhi Khurana *et al* 2017 [6], Ashu Sara Mathai *et al* 2016 [7], Harsha V Patil *et al* 2017 [8]. Assuming a Prevalence(p) of 40 percent of patients who acquire Ventilator Associated Pneumonia (VAP) of total patients admitted in Adult and Trauma ICU. VAP with Error (€)20% of p= .08, a sample size of 144 patients has been calculated.

Sample Size (N) = $[Z(1-\alpha/2)]^2 \times p(1-p)/(€P)^2 = (1.96)^2 \times 0.4(0.6)/(.08)^2 = 144$

α– Desired Confidence interval = 95%

p – Prevalence – 40%

€p-Error-20% of p-.08

Note: 386 samples were taken during the study period.

Study duration: From January 2020 to June 2021.

Data collection: General demographic details of patients like age, sex etc., history of present illness, diagnosis of patients, days of mechanical ventilation, value of PEEP and FiO2, temperature of patients, TLC counts, ongoing antibiotics which patient is on with change in antibiotics if any, and subsequent culture reports if patients fulfil IVAC criteria were collected and recorded in predesigned annexure 1.

Work flow

Patient on mechanical ventilation > 2 days

Baseline period of stability or improvement >2 days, followed by sustained period of worsening oxygenation

Ventilator-Associated Condition (VAC)

Patients having IVAC, their relevant sample had been collected and processed as standard microbiological technique for both Quantitative culture, Isolation and AST

General evidence of infection/inflammation
(To be noted on the basis of proforma)

Infection-Related Ventilator-Associated Complications (IVAC)

Positive results of microbiological testing

Possible or Probable VAP

Methodology:

VAEs were detected using a mix of reasonable criteria, such as decrease in respiratory function followed by a period of stabilisation or improvement on the ventilator, evidence of infection or inflammation, and laboratory evidence of respiratory infection [9].

VAC: "Patient is on mechanical ventilation, patient has shown a baseline period of stability or improvement on the ventilator (≥ 2 calendar), The patient experienced at least one of the following signs of decreasing oxygenation after a period of stabilisation or improvement on the ventilator: 1) A rise in the daily minimum FiO2 level of ≥ 0.20 (20 points) over the daily minimum FiO2 of the first day in the baseline period, sustained for ≥ 2 calendar days. 2) An elevation of ≥ 3 cmH2O in daily minimum PEEP values above the daily minimum PEEP of the first day in the baseline period, sustained for ≥ 2 calendar days if patients fulfil the above criteria, they develop VAC" [9].

IVAC: "if on or after calendar day 3 of mechanical ventilation and within 2 calendar days before or after the onset the patient satisfies both of the following features of decreasing oxygenation: 1) Temperature greater than 38°C or less than 36°C, OR white blood cell count greater than 12,000 cells/mm3 or less than 4,000 cells/mm3. AND 2) A new antimicrobial agent(s) is started and is continued for ≥ 4 qualifying antimicrobial days (QAD), they fulfil the criteria of IVAC" [9].

Now, after completing IVAC their relevant samples (ETA/ BAL etc) had been collected and processed as standard microbiological technique for both Quantitative culture, Isolation and AST according to the criteria given by CDC [9].

PVAP: "To be qualified for PVAP, the patient should have a VAC and an IVAC, along with the following requirements on or after the calendar day 3 of MV and within 2 calendar days before or after the onset of worsening oxygenation" [9]:

Significant growth of one of the following samples, reaching quantitative or semi-quantitative criteria as specified in the procedure, without the need for purulent respiratory secretions [9]:

- ETA, $\geq 10^5$ CFU/ml

• BAL $\geq 10^4$ CFU/ml

• Lung tissue, $\geq 10^4$ CFU/g

• PBS $\geq 10^3$ CFU/ml

Ventilator-Associated Events (VAE) characterisation [9]:

1) **VAC:**

It is ordinarily inferable from pneumonia, respiratory edema, atelectasis, or acute respiratory distress syndrome. It has a solid relationship with increased mechanical ventilation, length of stay and mortality.

Definition: "An rise in daily minimum PEEP ≥ 3cm H2O or an elevation in daily minimum FiO2 ≥ .20 maintained for 2 calendar days in a patient who had a steady or improved baseline period. On the ventilation, described as having more than two calendar days of steady or declining daily minimum FiO2 or PEEP".

Note: "2 calendar days of steady or decreasing daily minimum FiO2 or PEEP levels characterise stability or improvement. The baseline period is the two calendar days leading up to the first day of increased daily minimum PEEP or FiO2".

"Daily minimum is defined as the minimum FiO2 or PEEP value maintained for more than 1 hour throughout a calendar day".

2) **IVAC:**

Element

a. Patient should had VAC to be qualified for IVAC.

b. The patient satisfies both of the following conditions on or after calendar day 3 of MV and

inside 2 calendar days before or after the start of decreasing oxygenation:

Patient has ***one*** of the following:

• Temperature >38°C (>100.4°F)

• Temperature <36°C <96.8°F)

• White blood cell count ≥ 12,000 cells/mm3

• White blood cell count ≤4,000 cells/mm3

AND Patient meets ***all*** of the following:

• A new antibacterial drug(s)* is introduced

• The new antibacterial agent(s)** is maintained for ≥ 4 qualifying antimicrobial days (QAD)

Note:

* Within the reasons of this definition, the agent was deemed new if it was not administered to the patient with either of the 2 days prior to the actual current start date..

**see following Table 1 showing list of Antimicrobials Agents Eligible for IVAC, PVAP [9] *(Revised January 1, 2019)*

Antimicrobial Agent	Antimicrobial Agent (cont.)	Antimicrobial Agent (cont.)
AMIKACIN	COLISTIMETHATE	OXACILLIN
AMPHOTERICIN B	DALBAVANCIN	PENICILLIN G
AMPHOTERICIN B LIPOSOMAL	DELAFLOXACIN	PERAMIVIR
AMPICILLIN	DORIPENEM	PIPERACILLIN
AMPICILLIN/SULBACTAM	DOXYCYCLINE	PIPERACILLIN/TAZOBACTAM
ANIDULAFUNGIN	ERTAPENEM	POLYMYXIN B
AZITHROMYCIN	FLUCONAZOLE	POSACONAZOLE
AZTREONAM	FOSFOMYCIN	QUINUPRISTIN/DALFOPRISTIN
CASPOFUNGIN	GEMIFLOXACIN	RIFAMPIN
CEFAZOLIN	GENTAMICIN	SULFAMETHOXAZOLE/TRIMETHOPRIM
CEFEPIME	IMIPENEM/CILASTATIN	SULFISOXAZOLE
CEFOTAXIME	ISAVUCONAZONIUM	TEDIZOLID
CEFOTETAN	ITRACONAZONE	TELAVANCIN
CEFOXITIN	LEVOFLOXACIN	TELITHROMYCIN
CEFTAROLINE	LINEZOLID	TETRACYCLINE
CEFTAZIDIME	MEROPENEM	TICARCILLIN/CLAVULANATE
CEFTAZIDIME/AVIBACTAM	MEROPENEM/VABORBACTAM	TIGECYCLINE
CEFTIZOXIME	METRONIDAZOLE	TOBRAMYCIN
CEFTOLOZANE/TAZOBACTAM	MICAFUNGIN	VANCOMYCIN (IV ONLY)
CEFTRIAXONE	MINOCYCLINE	VORICONAZOLE
CEFUROXIME	MOXIFLOXACIN	ZANAMIVIR
CIPROFLOXACIN	NAFCILLIN	
CLARITHROMYCIN	ORITAVANCIN	

Table 1: Showing list of Antimicrobials Agents Eligible for IVAC, PVAP

3) <u>Possible VAP (PVAP)</u>

Element

a. Patient should had VAC and an IVAC to be qualified for PVAP

b. **AND** Patient must meet ***one*** of following criteria on or after calendar day 3 of MV and within 2 calendar days before or after the onset of worsening oxygenation:

Criteria 1:

Positive culture of ***one*** of the following specimens, meeting quantitative or semi-quantitative thresholds as outlined in protocol, without requirement for purulent respiratory secretions:

- ETA $\geq 10^5$ CFU/ml
- BAL $\geq 10^4$ CFU/ml
- Lung tissue $\geq 10^4$ CFU/g
- PBS $\geq 10^3$ CFU/ml

VAE Rate:

"The VAE rate per 1000 ventilator days is calculated by dividing the number of VAEs by the number of ventilator days and multiplying the result by 1000 (ventilator days)".

$$\text{VAE Rate per 1000 ventilator days} = \frac{No.\ of\ VAEs}{No.\ of\ Ventilator\ Day} * 1000$$

The study was approved by the Institutional ethics committee.

Methods of Sample collection:

Endotracheal aspirate [10]**:**

1. Take the specimen through a tracheostomy.
2. Join a sterile catheter to a Lukens trap and cautiously go the catheter through the site into the windpipe.
3. Apply suction to collect the sample into the Lukens trap.
4. Put in sterile container (as per figure 2).

Bronchoalveolar lavage [11]**:**

1. The bronchoscope is progressed distally into the bronchopulmonary section of interest until it blocks the bronchus, in this manner "wedging" the scope.
2. Sequential aliquots of ordinary saline totalling something like 100 mL (and close to 300 mL) ought to be ingrained and essentially 30% returned for ideal examining.
3. A least 5 mL (and in a perfect world 10–20 mL) is required for cell investigation.
4. Strict wellbeing principles are instructed including the utilisation regarding narcotics and interventionist and determined observing of patients' important bodily functions, breaths, and oxygenation during the methodology.

5. BAL liquid ought to be gathered in a named sterile compartment and moved practically to the lab for investigation.

Procedure followed in the laboratory for identification of isolates and determining antimicrobial susceptibility pattern of isolates obtained.

The methods followed with ETA/BAL samples for identification of isolates and determining antimicrobial susceptibility pattern of isolates obtained were:

Gram's Stain:

"Found more than 100 years prior by Hans Christian Gram, is most usually utilized for microscopic depiction of specimens and subcultures. Crystal violet (gentian violet) fills in as the essential stain, restricting to the bacterial cell wall later treatment with a feeble arrangement of iodine, which fills in as the stringent to tie the color. Some bacteria, on account of the compound idea of their cell wall, can hold the crystal violet even later treatment with a natural decolourizer, like a combination of equivalent pieces of CH3)2CO (acetone) and 95% ethyl liquor. Color holding microorganisms seem blue-dark when seen under the magnifying lens and are called gram positive. Certain microbes lose the crystal violet essential stain when treated with the decolourizer, apparently as a result of the great lipid content of their cell divider and less plentiful peptidoglycan" [12].

Culture:

The ETA/BAL was inoculated on to Blood agar (BA) and MacConkey agar (MA) and incubated at 37°C overnight. Plates were then analysed for the growth and for isolated colony .

Identification of isolates:

Both lactose and non-lactose fermenting colonies as per figure 1 (after oxidase test) which have been isolated were inoculated to glucose broth, nitrate broth, Hugh Liefson's media, peptone broth, glucose phosphate broth, mannitol motility agar, Simmons citrate medium, Christensen's urea agar, Triple Sugar Iron (TSI) agar and phenylalanine agar.

The isolates identified by following characteristics:

1. Nitrate reduced to nitrite
2. Glucose fermented with or without gas formation
3. Cytochrome oxidase negative or positive
4. Catalase positive
5. Non fastidious

Further identification to species or genus level (of other organisms) were done by using the following tests:

1. Indole test
2. MR test
3. VP test
4. Citrate utilization test
5. Urease test
6. Triple Sugar Iron (TSI) test
7. Mannitol Motility agar test
8. Phenylalanine Deaminase test

Test method: Culture.

Materials required:

- Blood agar
- MacConkey agar
- 1-µL inoculation loops

Procedure:

1. For each isolate to be tested, 1µL loopful of specimen were inoculated making 4 quadrants [5] on blood agar and MacConkey agar for isolation of bacteria.
2. Plates were then incubated at 35°C ± 2°C.

Result:

"As per the following Criteria 1 of VAE CDC checklist" [9]:

"Positive culture of one of the accompanying specimens, meeting quantitative or semi-quantitative edges as laid out in convention, without prerequisite for purulent respiratory emissions":

- Endotracheal aspirate, $\geq 10^5$ CFU/ml or corresponding semi-quantitative result
- Bronchoalveolar lavage, $\geq 10^4$ CFU/ml or corresponding semi-quantitative result
- Lung tissue, $\geq 10^4$ CFU/g or corresponding semi-quantitative result
- Protected specimen brush, $\geq 10^3$ CFU/ml or corresponding semi-quantitative result

Semiquantitative culture interpretation:

"Nonferrous (Nichrome or platinum) or dispensable plastic circles, aligned to contain either 0.01 or 0.001 mL of liquid, are submerged into a respiratory sample. The circle is then painstakingly eliminated and the whole volume inside the circle is conveyed to the outer layer of an agar plate by making a solitary streak across the middle. The inoculum is spread equitably at right points to the essential streak; then, at that point, the plate is turned 90 degrees and the inoculum is spread cover the whole surface. Following 24 to 48 hours of incubation, the quantity of microbes in respiratory samples is assessed by counting the quantity of provinces on the outer layer of the agar. If a 0.001-mL loop had been used to inoculate the medium, the number of colonies would be multiplied by 1,000 and it gives colony count in CFU/ml" [13].

Test method: Kirby-Bauer disk diffusion susceptibility test.

Materials required:

- Mueller Hinton agar
- Antibiotic impregnated disks
- Cotton swabs
- MHA plates

Test procedure:

1. A 0.5 McFarland dilution of the test isolate were prepared.
2. Streaked as lawn on to a Mueller Hinton agar plate.
3. Suitable antibiotic impregnated disc had been selected from respective lactose and non-lactose fermenting antibiotic panel as per the CLSI [14].
4. The plate was then incubated overnight at 35±2°C in ambient air for 16–24 hours.
5. The zone of inhibition was determined next day (as per figure 3) and was interpreted using the 2020 and 2021 Clinical Laboratory Standards Institute (CLSI) guidelines for antimicrobial susceptibility testing according to the following table 2, for Colistin, Disc Elusion Test was performed shown in figure 4 [14].

Antibiotic impregnated disc used:

- Ampicillin-Sulbactam (10/10 µg)
- Piperacillin-tazobactam (100/10 µg)
- Ceftriaxone (30 µg)
- Ceftazidime (30 µg)
- Cefepime (30 µg)
- Ciprofloxacin (5 µg)
- Levofloxacin (5 µg)
- Gentamicin (10 µg)
- Amikacin (30 µg)
- Meropenem (10 µg)
- Imipenem (10 µg)
- Minocycline (30 µg)

Antibiotic **CLSI 2020**	**Disk diffusion test (in mm)**		
	S	**I**	**R**
Enterobacterales			
Ampicillin-sulbactam (10 / 10 µg)	**≥15**	**12 - 14**	**≤11**
Amikacin (30 µg)	**>17**	**15-16**	**<14**
Cefepime (30 µg)	**≥25**	**19-24**	**≤18**

Ceftriaxone (30 µg)	**≥23**	**20-22**	**≤19**
Ciprofloxacin (5 µg)	**≥26**	**22-25**	**≤21**
Ceftazidime-avibactam (30 / 10 µg)	**≥21**	**-**	**≤20**
Gentamicin (10 µg)	**≥15**	**13-14**	**≤12**
Imipenem (10 µg)	>23	20-22	<19
Levofloxacin (5 µg)	**≥21**	**17-20**	**≤16**
Minocycline (30 µg)	**≥16**	**13-15**	**≤12**
Meropenem (10 µg)	**≥23**	**20-22**	**≤19**
Piperacillin/tazobactam(100/10 µg)	**≥21**	**18-20**	**≤17**

Pseudomonas aeruginosa			
Amikacin (30 µg)	**>17**	**15-16**	**<14**
Cefepime (30 µg)	**≥18**	**15-17**	**≤14**
Ceftazidime (30 µg)	**≥18**	**15-17**	**≤14**
Ciprofloxacin (5 µg)	**≥25**	**19-24**	**≤18**
Ceftazidime-avibactam (30 / 10 µg)	**≥21**	**-**	**≤20**
Gentamicin (10 µg)	**≥15**	**13-14**	**≤12**
Imipenem (10 µg)	**≥19**	**16-18**	**≤15**
Levofloxacin (5 µg)	**≥22**	**15-21**	**≤14**
Meropenem (10 µg)	**≥19**	**16-18**	**≤15**
Piperacillin/tazobactam (100/10 µg)	**≥21**	**15-20**	**≤14**

***Acinetobacter* spp.**			
Ampicillin-sulbactam (10 / 10 µg)	**≥15**	**12 - 14**	**≤11**
Amikacin (30 µg)	**>17**	**15-16**	**<14**
Cefepime (30 µg)	**≥18**	**15-17**	**≤14**
Ceftazidime (30 µg)	**≥18**	**15-17**	**≤14**
Ceftriaxone (30 µg)	**≥21**	**14-20**	**≤13**
Ciprofloxacin (5 µg)	**≥21**	**16-20**	**≤15**
Cotrimoxazole (1.25/23.75 µg)	**≥16**	**11-15**	**≤10**
Gentamicin (10 µg)	**≥15**	**13-14**	**≤12**
Imipenem (10 µg)	**≥22**	**19-21**	**≤18**
Levofloxacin (5 µg)	**≥17**	**14-16**	**≤13**
Minocycline (30 µg)	**≥16**	**13-15**	**≤12**
Meropenem (10 µg)	**≥18**	**15-17**	**≤14**
Piperacillin (100 µg)	**≥21**	**18-20**	**≤17**
Piperacillin/tazobactam(100/10 µg)	**≥21**	**18-20**	**≤17**

Table 2: Clinical Laboratory Standards Institute (CLSI) guidelines for antimicrobial susceptibility testing.

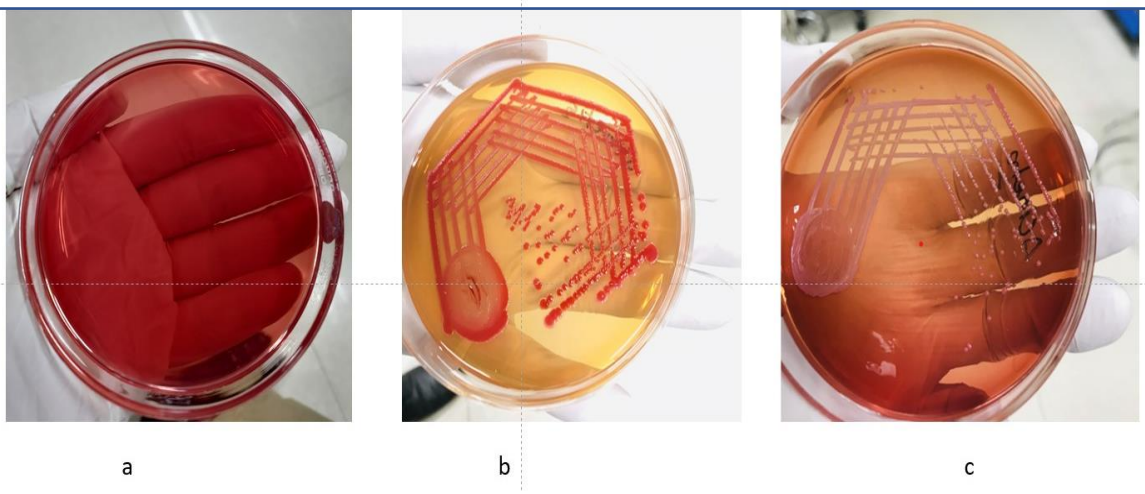
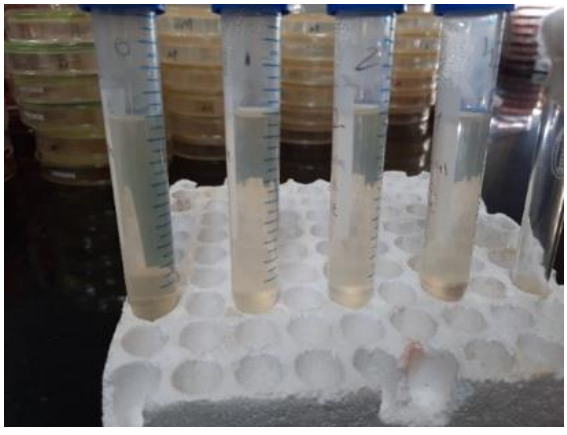


Figure1: Culture media and organism growth (a) Uninoculated MacConkey agar (b) Lactose fermenting on MacConkey agar (c) non-Lactose fermenting on MacConkey agar

Figure 2: Sterile container containing respiratory sample (ETA, BAL)

Figure 3: Antibiotic susceptibility test

Figure 4: Colistin Disc Elution Test



REVIEW OF LITERATURE

Contents

1. URT and LRT anatomy
2. Pathology and Pathogenesis of URT and LRT
3. Infections of URT and LRT
4. Nosocomial infections
5. Nosocomial respiratory tract infections (Pneumonia)
6. Hospital-acquired pneumonia (HAP) and Ventilator-associated pneumonia (VAP)
    - Epidemiology
    - Pathogenesis
    - Microbiology
    - Diagnosis
    - Risk factors
7. Ventilator Associated Events [VAE]
    - Definition of VAC, IVAC, PVAP
    - Diagnosis of VAC, IVAC, PVAP
    - Excluded organism
    - Secondary BSI
    - The NHSN VAE Definitions
    - VAE Epidemiology
    - VAE and Traditionally Defined VAP in agreement.
    - Shortcoming of Traditional VAP Surveillance
    - Surveillance Versus Clinical aspects
    - Vulnerability to ventilator-associated events
    - Prevention of VAP in the intensive care unit
    - Impact of VAE
    - Reviewing VAE research, things to keep in mind

URT and LRT anatomy:

The respiratory tract divided into following critical areas: the URT contains structure over the larynx, and the LRT under the windpipe to the bronchi and bronchioles, then, into the alveolar spaces [15], which has been shown by following figure 5 [16].

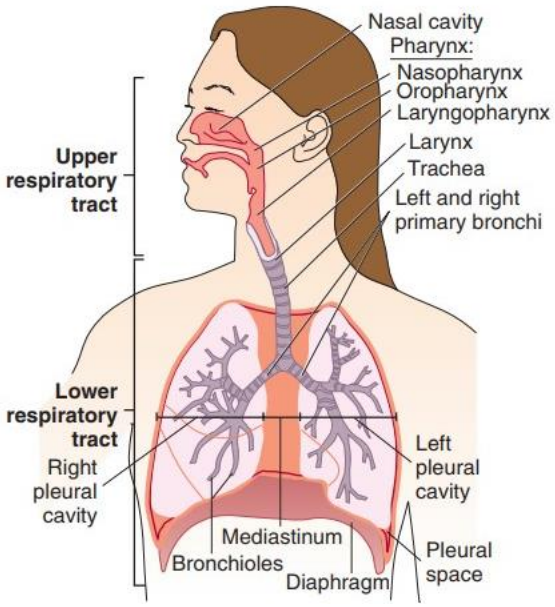


Figure 5: Anatomy of URT and LRT

The respiratory and gastrointestinal framework are the two significant associations. The respiratory tract starts with the nasal and oral sections, and reaches out to the nasopharynx and oropharynx to the windpipe and afterward into the lungs. The windpipe isolates into bronchi, which partition into bronchioles, the littlest branches that end in the alveoli. Somewhere in the range of 300 million alveoli are assessed to be available in the lungs; these are the essential tiny gas trade designs of the respiratory tract [17].

The thoracic depression, have the heart and lungs, and have three segments isolated from each other by pleura. First lungs possess the right and left pleural cavities, then, at that point, mediastinum (space between the lungs) is involved predominantly by the throat, windpipe, huge veins, and heart [18].

Pathology and Pathogenesis of URT and LRT: To establish the infections both pathogenicity of microorganism and also the host factors play important role [19].

Human association:

Factors are, the nasal hairs, tangled entries, and the mucous coating of the nasal turbinate's; secretory IgA and vague antibacterial substances (lysozyme) in respiratory discharges; the cilia and mucous covering of the windpipe; and reflexes like hacking, sniffling, and gulping. This multitude of components discourage unfamiliar items or creatures from entering the bronchi and further to the lungs [20].

Yearning of oropharyngeal emissions, during rest, has a significant influence in the pathogenesis of various sorts of pneumonia. At the point when particles escape the mucociliary cleaning movement and enter the alveoli, alveolar macrophages ingest particles and convey them to the lymphatics. Likewise, typical verdure of the nasopharynx and oropharynx forestall colonization by pathogenic creature. Ordinary bacterial greenery forestalls the colonization by microorganisms by going after similar space and supplements just as creation of bacteriocins and metabolic items that are poisonous to attacking organic entities. Conditions which change colonization into pathogenic circumstance are past harm by a viral disease, loss of some host insusceptibility, or actual harm to the respiratory epithelium (e.g., from smoking). Nature of respiratory example (presence of pus cells) can undoubtedly separate colonization versus pathogenic strains. (Organic entities segregated from regularly sterile destinations in the respiratory tract by sterile strategies that stay away from pollution with ordinary vegetation ought to be absolutely recognized and answered to the clinician) [21].

Organism association:

Microorganism deliveries items that advance colonization and disease in the host. The variables answerable for harmfulness of microorganism incorporate adherence factor, poison creation, amount of development or multiplication, tissue harm, staying away from the host insusceptible reaction, and capacity to disperse [22].

Cohesion: Microorganism initially hold fast to respiratory tract and multiply to increment in numbers. The ordinary greenery and host factor influence the capacity of

microorganisms to follow. Prior to causing harmfulness and showing its pathogenicity all microorganism needs to colonize otherwise called colonization. Overall Streptococcus pyogenes contains fimbriae comprise atoms, for example, lipoteichoic acids and M proteins known to cause adherence. These particles encompass the microorganisms. *Staphylococcus aureus* and certain viridans streptococci are different microorganisms that have lipoteichoic corrosive adherence edifices. Most gram-negative microorganisms (which don't have lipoteichoic acids), including Enterobacteriaceae, *Legionella* spp., *Pseudomonas* spp., *Bordetella pertussis*, and *Haemophilus* spp., get follow by substances known as proteinaceous finger-like surface fimbriae. Infections have either a hemagglutinin (flu and parainfluenza infections) or different proteins that cause epithelial connection [22].

Substances released by microorganisms: Following microorganisms are typically consistently viewed as etiologic specialists of sickness either present in modest quantity or in any numbers in the respiratory tract since they have harmfulness factors that are communicated in each host. The having of extracellular poison was one of the primary destructiveness factor found among microorganisms. *Corynebacterium diphtheriae* is an exemplary model. On the off chance that the organic entity colonizes the upper respiratory epithelium, they produce a poison which can scatter methodicallly, can relate CNS just as cardiovascular tissue. Fundamental affiliation are myocarditis, fringe neuritis, and neighborhood affiliation that can cause respiratory misery. Development of C. diphtheriae causes rot and sloughing of the epithelial mucosa, creating a "diphtheritic (pseudo) film," can continue to include foremost nasal mucosa then bronchi or it could be restricted to region between the tonsillar and peritonsillar regions. The pseudomembrane can cause sore throat and may meddle with aviation route (breath and gulping). Those nontoxic strain of *C.diptheriae* are milder in nature and ordinarily connected with nearby illness. Scarcely any strains of *Pseudomonas aeruginosa* produce a toxin identified with diphtheria poison however its relationship with respiratory tract has not been build up. *Bordetella pertussis*, can likewise shape toxins yet the job of this poison isn't clear they can hinder the movement of phagocytic cells or can harm cells of the respiratory tract. Staphylococcus aureus and beta-haemolytic streptococci additionally structure extracellular proteins can harm have tissue and cells. These chemicals can make tissue putrefaction and leads ulcer development. In any case,

S. aureus is less known to cause upper RTI. Different proteins are hyaluronidases, by streptococci known to cause quick scattering of microscopic organisms [23].

Organism Multiplication: Microorganism fills in numbers attracts granulocytes like neutrophils and prompts microbe have cell connection which prompts further tissue harm. Respiratory microbes typically show as such are *Streptococcus* spp, *Haemophilus* spp, *Neisseria* spp, *Moraxella* spp, *Mycoplasma* spp, MTB, and most gram-negative bacilli [24].

Circumvent the Host reaction: The accompanying microorganism can get away from have protection systems are *Streptococcus* spp, *Neisseria* spp, *Haemophilus spp, Klebsiella pneumoniae, Pseudomonas spp,* and some different microbes which incorporate polysaccharide cases which assist them with sidestepping the engulfment by phagocytic host cells and keep them from being presented to immunoglobulins. This capsular material is delivered by explicit microbes in plenitude, like pneumococci. Immunization having capsular antigens forestalls diseases, demonstrating that the capsular polysaccharide is a significant harmfulness instrument of *H. influenzae, S. pneumoniae,* and *N. meningitidis*. Hardly any microbes tend to multiply intracellularly and increase inside have cells this is an exceptional method of getting away from have insusceptible framework models incorporate *Chlamydia spp*, and all viruses. When inside the cells these microorganisms are protected until the host cells get harmed up to that level where they perceived as an unfamiliar cell by have safe frameworks. One more instrument of sidestepping host invulnerable reaction is to multiply inside the host phagocytic cells like macrophages regular microorganisms are, *Pneumocystis jiroveci*, and *Histoplasma* spp and MTB of an intracellular microbe. In primary tuberculosis, organism includes alveolar macrophages, which further include closest lymph hub and the beginning increasing gradually inside macrophage. At last, MTB annihilates the macrophage and is in this manner taken up by other phagocytic cells. Tubercle bacilli multiply in secured climate (no lysosome interactions). In the wake of arriving at the basic level these bacilli burst out, some are phagocytosed by other phagocytic cells and other spread into circulation system, conveying tubercle bacilli to many parts of the body. Much of the time, insusceptibility of host frameworks handles these bacilli

however some tubercle bacilli stay lethargic in spaces of typically high oxygen fixation, for example, the apical (top) part of the lung. These bacilli in not so distant future, when the patient go immunosuppressive they can present as dynamic disease known as secondary tuberculosis. In immunocompromised patients the bacteraemia examine prompted scattered or miliary tuberculosis. Developing microbes inside the macrophages and histiocytes of lung can bring about granuloma, which could additionally shape cavitation [25].

The following figure 6 shows the viral and bacterial pathogenesis for respiratory tract infections [26].

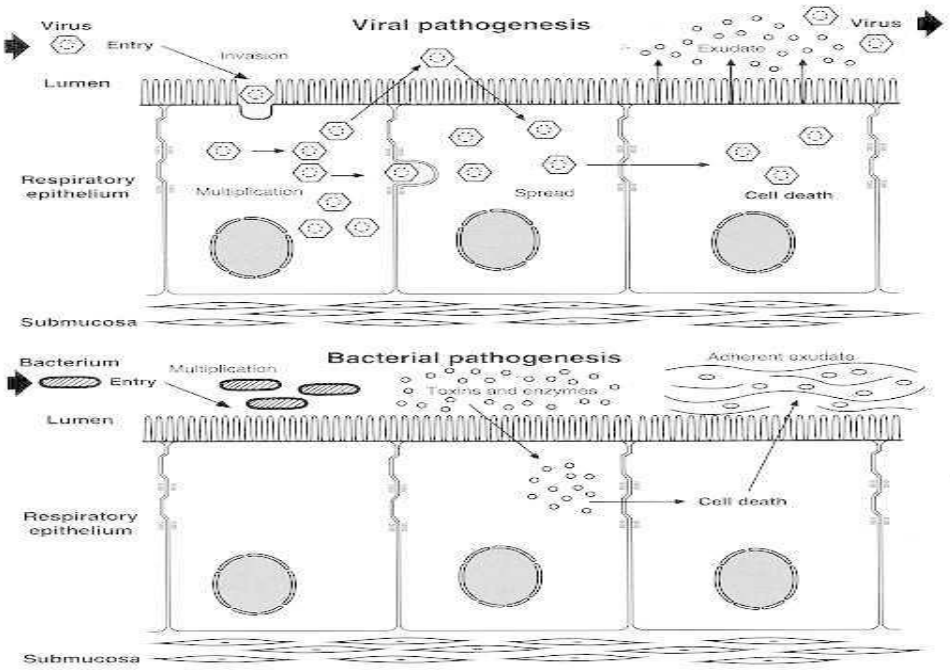


Figure 6: Pathogenesis of viral and bacterial mucosal respiratory infections

Infections of URT and LRT:

Infections are connected to their effects and anatomic inclusion. Intense URTI are the cold, pharyngitis, epiglottitis, and laryngotracheitis. These infections are harmless in nature, self-restricted, however epiglottitis and laryngotracheitis show as a genuine

sickness in kids and infants. Etiologic specialists causing URTI are viruses, microbes, mycoplasma etc. These infections are inclined to winter [27].

LRTI incorporate bronchitis, bronchiolitis and pneumonia. Pneumonia, can be become extreme or deadly. Most infections are brought about by viruses, mycoplasma etc, yet bacteria are the prevailing microbes; representing a higher heap of lower than of URTI [28].

URTI

Anatomy:

The URT incorporates structures down to the larynx: the sinuses, throat, nasal cavity, epiglottis, and larynx; the throat is otherwise known as pharynx.

The pharynx is additionally partitioned into three sections as per the following figure 7 [29]:

- Nasopharynx (over the soft palate).
- Oropharynx (between soft palate and epiglottis).
- Laryngopharynx (underneath the epiglottis that opens into the larynx).

The oropharynx and nasopharynx related with delineated squamous epithelial cells. The tonsils are held inside the oropharynx; the larynx is situated between the base of the tongue and the upper finish of the windpipe [29].

Infection of larynx:

Acute laryngitis is generally connected with the cold or flu . For the most part, patients gripe of roughness and turning down the volume. They are normally a harmless ailment. They are only connected with viral etiology. The most well-known etiologic specialists causing laryngitis are flu and parainfluenza viruses, rhinoviruses, adenoviruses, Covid-19, and human metapneumovirus. If on assessment, larynx uncovers an exudate or film on the pharyngeal or laryngeal mucosa, *streptococcal* infection, mononucleosis, or *C.diphtheria* ought to be suspected. Chronic laryngitis, albeit less regularly connected with infections, might be brought about by bacteria or fungus. [30].

Croup:

Acute laryngotracheobronchitis, or croup is a somewhat normal ailment in child, <3 years old. Ailment causes fever, inspiratory stridor (trouble in moving sufficient air through the larynx), dryness, and a cruel, yelping, non-productive cough, indications normally keep going for 3-5 days. In infants, extreme respiratory distress and fever are normal presentation. Viruses are an essential driver of croup; parainfluenza viruses are most important causes. Different etiologies are flu viruses, respiratory syncytial infection, and adenoviruses [30].

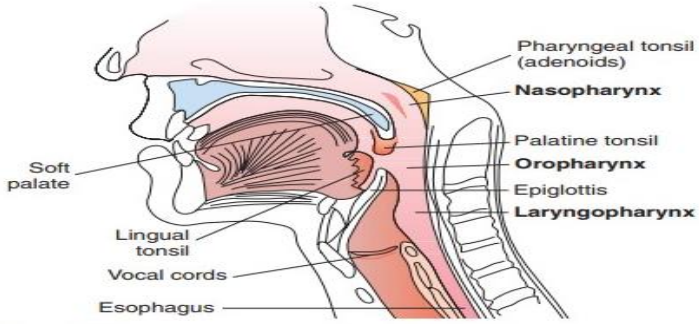


Figure 7: Anatomy of Pharynx

Infection of Epiglottis:

Epiglottitis is a disease of the epiglottis and other delicate tissues over the vocal strings lead to huge edema (enlarging) and irritation. Most normal age bunch are 2 and 6 years of child. These youngsters ordinarily present with fever, trouble in gulping on account of agony, slobbering, and respiratory hindrance with inspiratory stridor. It is a possibly dangerous infection on the grounds that the patient's respiratory route can turn out to be totally discouraged (impeded) if not treated. Generally connected with bacterial diseases. Before, *Haemophilus influenzae* type b was the essential driver of epiglottitis however because of the utilisation of vaccines the episode diminishes slowly, the important patient is a grown-up with an irritated throat. Other periodic causes are streptococci and staphylococci. Conclusion is set up on clinical grounds, including the representation of the epiglottis, which seems enlarged and dazzling red in shading. Bacteriologic culture of the epiglottis is contraindicated on the grounds that cleaning of the epiglottis might prompt respiratory chock. Of significance, *H. influenzae*

bacteraemia normally happens in kids with epiglottitis brought about by this microorganism [32].

Infection of Pharynx and Tonsils:

Pharyngitis (sore throat) and tonsillitis are normal URTI influencing both kids and grown-ups [33].

Sign and symptoms: Disease of the pharynx is related with pharyngeal torment. Representation of the pharynx uncovers erythematous (red) and enlarged tissue. Contingent upon the causative microorganism, either exudate (Inflammatory cells, vesicles and mucosal ulceration, or nasopharyngeal lymphoid hyperplasia (enlarged lymph hubs) might be noticed [34].

Pathophysiology: Pathogenic systems vary and rely upon the organic entity causing the pharyngitis. For instance, a few living beings straightforwardly attack the pharyngeal mucosa (e.g., *Arcanobacterium haemolyticum*), Some secrets toxins and other harmfulness factors at the site (e.g., *Corynebacterium diphtheriae*), and some attack the pharyngeal mucosa and secretes toxins and other destructiveness factors (e.g., group A *streptococci* [*Streptococcus pyogenes*] [35].

Causative agent: Most instances of pharyngitis happen during the colder months and regularly go with different diseases, fundamentally those brought about by viruses. Cases with RTI brought about by Influenza, parainfluenza, coxsackie viruses, rhinoviruses, or Coronavirus every now and again complain of an irritated throat. Pharyngitis, regularly with ulceration, is additionally usually found in patients with IM brought about by one or the other Epstein Barr virus or Cytomegalovirus [35].

Uncommon, causes are adenovirus or herpes simplex virus is clinically serious. Human immunodeficiency infection 1 (HIV-1) can likewise connected with intense pharyngitis. The essential driver of bacterial pharyngitis is *Streptococcus pyogenes* (or group A beta-hemolytic streptococci). Viral pharyngitis should be separated from S. pyogenes pharyngitis, in light of the fact that bacterial pharyngitis can be treatable with penicillin and an assortment of different antimicrobials, while viral causes are not. Moreover, treatment is significant for *S. pyogenes* on the grounds that it can prompt inconveniences like intense rheumatic fever and glomerulonephritis. These

inconveniences are alluded to as poststreptococcal sequelae (illnesses that follow a *streptococcal* contamination) and are basically immunologically intervened. *S. pyogenes* may likewise cause pyogenic infection (incidents of decay) of the tonsils, sinuses, and center ear, or cellulitis later an episode of pharyngitis. C and G streptococci (delegated as *Streptococcus dysgalactiae* subsp. *equisimilis*) are pyogenic streptococci with comparative harmfulness qualities as *S. pyogenes*; manifestations of pharyngitis brought about by these specialists are likewise like *S. pyogenes*. As opposed to S. pyogenes, these specialists are seldom connected with poststreptococcal sequelae, to be specific glomerulonephritis and potentially rheumatic fever. Ongoing investigations have shown that these streptococci can trade hereditary data with S. pyogenes and along these lines possibly get destructiveness factors ordinarily connected with S. pyogenes like M proteins, streptolysin O, and superantigen qualities. *Arcanobacterium haemolyticum* is likewise a reason for pharyngitis among young people. Societies of examples got from the front nares regularly yield *S. aureus*. The carriage rate for this living being is particularly high among medical care workers, and 10%-30% of everybody can be colonized with this microorganism [35].

Following table 3 gives the major causes of pharyngitis and Tonsillitis [36].

Microorganism	**Infection**	**Association**
S. pyogenes	Pharyngitis/tonsillitis/ ARF/ scarlet fever	15% to 35%
Group C and G *streptococci*	Pharyngitis/tonsillitis	<3% to 11%
C. diphtheriae	Pharyngitis/tonsillitis/ rash	<1% to 10%
Neisseria spp	Pharyngitis/ Systemic Manifestation	Uncommon
C. ulcerans	Pharyngitis	Uncommon
M. pneumoniae	Pneumonia/ bronchitis/ pharyngitis	Uncommon
HIV-1	Pharyngitis/acute retroviral disease	Uncommon

Table 3: Etiologies of bacteria that can cause infections of Pharynx and Tonsils

Examination:

An assortment of clinical choice standards have been created to work on the conclusion of Group A beta-hemolytic *streptococcal* pharyngitis and to direct diagnosis and management. The Centor Score is most utilized, especially for grown-up patients as shown in following table 4 [37].

Factors	Number characterisation
Temperature >38°C	1
Absence of cough	1
Swollen, tender anterior cervical nodes	1
Tonsillar swelling or exudate	1

Score	Incidence of s*treptococcal* infections	Treatment
<=0	1%–2.5%	No test or antibiotics
1	5%–10%	No test or antibiotics
2	11%–17%	Culture all: antibiotics just for positive culture report
3	28%–35%	Culture all: antibiotics just for positive culture report
4	51%–53%	Manage empirically with antibiotics and/or culture

Table 4: Modified Centor Score

DISEASES OF THE LRT

Bronchitis:

Acute

Acute bronchitis is showed by intense irritation of the tracheobronchial tree. Most infections happen in the colder time of year. The pathogenesis has no particular etiology except for is by all accounts a combination of viral cytopathic occasions and a reaction by the host safe framework. Ultimately enormous measure of liquid/discharge collects

in the bronchi. Obliteration of the bronchial epithelium is broad for flu virus or insignificant for rhinovirus colds. Side effects incorporate cough, fever, and sputum creation. Sputum (discharge from the lungs) in starting stage is clear however may change over to purulent as the ailment endures. Bronchitis might show as croup. The microbiologic boundaries to set up the reason for intense bronchitis in any case for immunocompetent has not been set up [38].

The etiology of acute bronchitis is enlisted in table 5 below [39].

Chronic versus Acute

Chronic bronchitis is a standard reason influencing around 10% to 25% of grown-ups. It is described by extreme bodily fluid creation prompts hacking up sputum generally speaking during something like 3 months back to back time for 2 progressive years. Cigarette smoking, disease, and inward breath of residue or vapor are significant contributing elements.

Probable etiology are *Haemophilus influenzae, Streptococcus pneumoniae,* and *Moraxella catarrhalis,* are habitually causes this infection. Albeit the job of microbes in intense infections in these patients is problematic, viruses are successive causes [39].

Bacteria	**Viruses**
Bordetella spp *M. pneumoniae,* *C. pneumoniae*	Influenza , adenovirus, rhinovirus, coronavirus (uncommon viruses: RSV, human metapneumovirus, coxsackie A21 virus)

Table 5: Major Causes of Acute Bronchitis.

BRONCHIOLITIS

Bronchiolitis, the aggravation of the more modest distance across bronchiolar epithelial surfaces, it is an intense viral lower RTI that normally happens during the initial 2 years of life. Most clinical indications are intense beginning of wheezing and excessive inflation just as cough, rhinorrhoea (runny nose), tachypnoea (fast breathing), and respiratory trouble. The sickness is essentially brought about by viruses including an as of late found virus, human metapneumovirus. RSV represents 40% to 80% of instances of bronchiolitis and shows a stamped irregularity [40]. Occasional affiliation are available during winter to late-winter. In beginning stage, the virus imitates in the epithelium of the upper respiratory lot, yet in the newborn child, it quickly spreads to

the lower lot aviation routes. Early irritation of the bronchial epithelium advances to corruption. Manifestations, for example, wheezing are identified with the sort of provocative reaction by host to virus. For the most part conclusion of patients depends on clinical boundaries, research facility boundaries are ruined the individuals who require hospitalisation [40].

PNEUMONIA

Pneumonia (irritation of the lower respiratory tract including the lung's airways and supporting tissue) is a most significant reason for disease and demise. Pneumonias are of 2 kinds: Community acquired pneumonia (patients are accepted to have gained their infection outside the medical clinic setting) and those including emergency clinic or ventilator-related (patients are accepted to have obtained their disease inside the emergency clinic setting, as a rule no less than 2 days keeping affirmation) or medical services related pneumonia (influences just patients hospitalized in an intense consideration medical clinic for 2 or more days inside 90 days of disease from a drawn out care, or patients who have gotten ongoing intravenous anti-microbial treatment, chemotherapy, or twisted consideration inside 30 days of the momentum contamination, or who have gone to a clinic or hemolysis facility) [41].

Pathophysiology:

Life forms can cause infection of the lung by four potential courses: by upper respiratory route colonization or infection that in this manner stretches out into the lung, by yearning of organism (consequently staying away from the upper respiratory route guards), by inward breath of airborne drops containing the organism, or by cultivating of the lung by means of the blood from a far off site of infection. Viruses cause essential infections of the respiratory tract, just as restrain have safeguards that, thusly, can prompt an optional bacterial infection. For instance, viruses may annihilate respiratory epithelium and disturb typical ciliary movement. Apparently, the development of viruses in have cells disturbs the capacity of the last option and empowers the deluge of vague resistant effector cells worsening the harm. Harm to have epithelial tissue by virus infection is known to incline patients to optional bacterial infection.

Desire of oropharyngeal substance is significant in the pathogenesis of many sorts of pneumonia. Goal might happen during a deficiency of awareness, for example, during

sedation or a seizure, or later liquor or chronic drug use, yet others, especially geriatric patients, may likewise foster desire pneumonia. Neurologic illness or oesophageal pathology and periodontal infection or gum disease are other significant danger factors.

Helped by gravity and regularly by loss of some host vague defensive systems, organic entities arrive at lung tissue, where they increase and attract have provocative cells.

Different components incorporate inward breath of sprayed material and hematogenous cultivating. The development of cell flotsam and jetsam and liquid adds to the deficiency of lung capacity and in this way to the pathology [41].

The accompanying figure 8 portrays the pathophysiology of *S.pneumoniae* pneumonia [42].

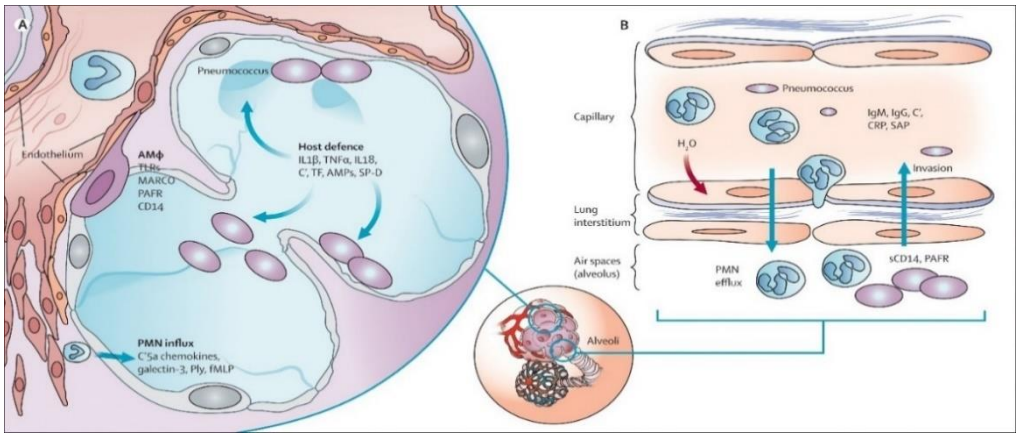


Figure 8: Pathophysiology of *S.pneumonia causing* pneumonia

Sign and Symptoms:

The side effects incorporate fever, chills, chest agony, and cough. Pneumonias were divided into two gatherings: (1) Typical pneumonias (e.g., *Streptococcus pneumoniae*) and (2) Atypical pneumonias, described on whether the cough was productive or non-productive. Notwithstanding respiratory side effects, 10% to 30% of patients with pneumonia shows issue of migraine, sickness, retching, stomach torment, loose bowels, and body pain [43].

Causative Agents:

CAP:

2 million to 3 million instances of CAP happen yearly, and approx. one fifth of them needs hospitalization. The etiology of intense pneumonias is firmly subject to age. Over 80% of pneumonias in babies and kids are brought about by viruses, contrasted with under 10% to 20% of pneumonias in grown-ups [43].

Kids: Among patients from 2 months to 5 years of age, RSV, human metapneumovirus, parainfluenza, flu, and adenoviruses are the most well-known etiologic causes. Youngsters experience less ordinarily with bacterial pneumonia, normally brought about by *Haemophilus. influenzae*, *Streptococcus. pneumoniae,* or *Staphylococcus. aureus*. Youngsters are related with *C. trachomatis* or *P. jiroveci* (HIV) [44].

Mycoplasma. pneumoniae and *Chlamydia. pneumoniae* are the most well-known reasons for bacterial pneumonia in young youngsters (5-14 years old). The four most normal reasons for CAP viral pneumonia in kids incorporate flu, RSV, parainfluenza, and adenovirus. Blended viral and bacterial infection have been introduced in 35% of patients. [45].

Young Adults: The most widely recognized etiologic specialist among those younger than 30 years old is *Mycoplasma pneumoniae*. Contact with fluid and airborne transmission are the reason for infections. *Chlamydia pneumoniae* is the third important etiology of LRTI in younger adults, following *Mycoplasma* and flu infections; it additionally influences more geriatric people. [46].

Adults (Viral causes). CAP viral pneumonia are achieved by influenza, adenovirus, enteroviruses, Covids, particularly during epidemics. Influenza is associated with extended risk for pregnant women of around 4-9 times. Particularly in the third trimester. RSV is the third most typical justification for neighbourhood pneumoniae with 78% of the passings in patients over 65 years of age. Human metapneumovirus are connected with episodes in long stretch consideration workplaces. Later well known pneumonia, helper bacterial ailment achieved by beta-hemolytic *streptococci, S. aureus, M. catarrhalis, H. influenzae,* and Chlamydia pneumoniae can occur. Various experts may be Hantavirus bundle, the most broadly perceived of which is sin nombre

disease similarly as outrageous exceptional respiratory problem (SARS). Out of these subject matter experts, influenza infection, RSV and adenovirus have been associated with nosocomial episodes. [47].

Adults (Fungal pneumonia):

The fungal etiologies are *Histoplasma capsulatum*, *Blastomyces dermatitidis, Paracoccidioides brasiliensis*, *Coccidioides immitis*, *Cryptococcus neoformans*, and, less commonly, *Aspergillus fumigatus* [48].

Chronic Lower Respiratory Tract Infections: *Mycobacterium tuberculosis* is the most reason different Mycobacteria, related are MAC and *Mycobacterium. kansasii*. *Actinomyces* and *Nocardia* can likewise cause constant state. Cystic fibrosis (CF) is a hereditary issue causing aviation route divider harm and persistent obstructive lung infection. *Staphylococcus aureus* is the most well-known bacterial microorganism tainting 55% of kids 0–9 years old with CF, with *P. aeruginosa* the most well-known (81%) in more establish adolescents. Different causes related with CF are *H. influenzae, S. pneumoniae,* S*tenotrophomonas maltophilia, Achromobacter xylosoxidans, Ralsotnia spp. Cupriavidus spp., Pandoraea spp., Escherichia coli,* strains *of Burkholderia cepacia complex,* quickly developing *mycobacteria, RSV, flu and* growths *Aspergillus, Scedosporium spp., and Exophiala dermatidis* [49].

PLEURAL INFECTIONS:

Organism gaining access to the pleural space via an abnormal passage (fistula), the patient can get empyema (pus in a body cavity such as the pleural cavity). Symptoms are lethal because disease are related to primary infection in the lung [52].

NOSOCOMIAL INFECTIONS

Other name of “hospital acquired infection” also known as: An infection acquired in hospital by a patient who was admitted for a reason other than that infection (53). An infection occurring in a patient in a hospital or other health care facility in whom the infection was not present or incubating at the time of admission. This includes infections acquired in the hospital but appearing after discharge, and also occupational infections among staff of the facility (54).

Different types and sites of nosocomial infections:

Following Table 6 shows the different types of nosocomial infections occurs in hospital settings [55].

Following Figures 9 shows impact of nosocomial infections [56].

Type of nosocomial infection	**Simplified criteria**
Surgical site infection	Any purulent release, ulcer, or spreading cellulitis at the careful site during the month later the operation.
Urinary infection	Positive urine culture (1 or 2 species) with somewhere around 105 microorganisms/ml, with or without clinical manifestations.
Respiratory infection	Respiratory effects with something like two of the accompanying signs showing up during hospitalization: cough, purulent sputum, new infiltrate on chest radiograph steady with infection.
Vascular catheter infection	Aggravation, lymphangitis or infectious purulent release at the inclusion site of the catheter.
Septicaemia	Fever or afflictions and something like one certain blood culture.

Table 6: Different types of nosocomial infections occurs in hospital settings

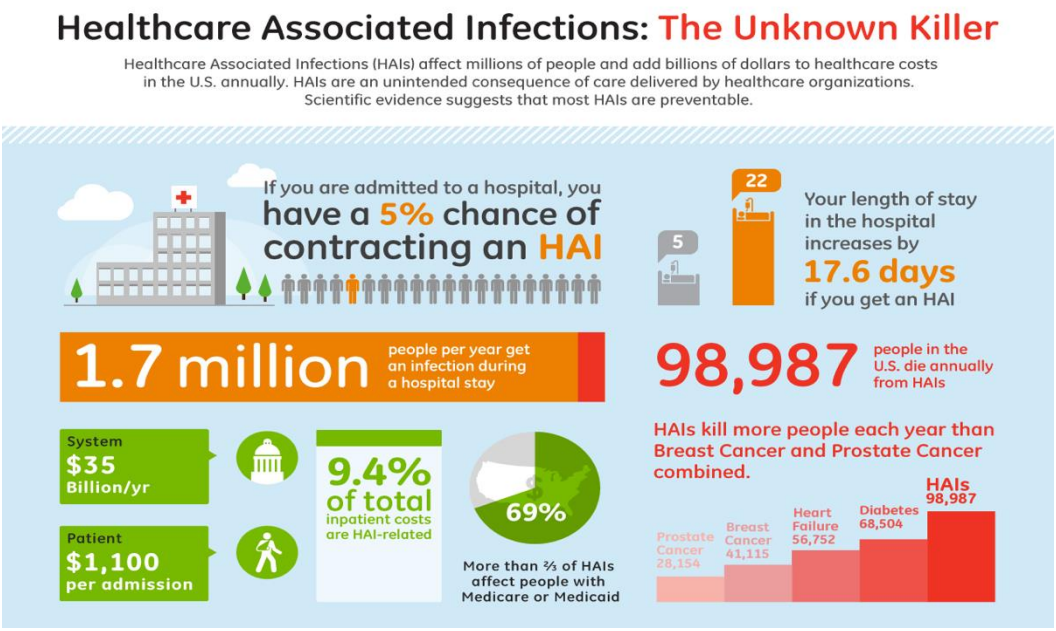


Figure 9: The Impact of HAI.

Nosocomial RTI (Pneumonia)

Nosocomial pneumonia is pneumonia that develops in a hospital setting. It is separated into two categories: HAP and VAP. VAP is indeed the basis of the majority of nosocomial pneumonia literature [57].

Definitions:

Pneumonia acquired during 48 hours after admission to the hospital is known as hospital-acquired pneumonia (HAP).

Ventilator-associated pneumonia (VAP): A pneumonia in which the patient has been on mechanical ventilation for more than 2 calendar days on the day of the event, with Day 1 being the day of ventilator placement, and the ventilator had been in operation on the event date or the day before. The ventilator day count starts with the admission date to the first inpatient site, if the ventilator had been in place at the time to inpatient admission [58].

Hospital-acquired pneumonia (HAP) and Ventilator-associated pneumonia (VAP):

Epidemiology:

HAP is one of the most well-known and severe hospital-acquired diseases. The majority of HAP cases occur in individuals who are not ventilated. Despite this, the most serious risk of HAP is in patients who are on ventilation (i.e., VAP) [59].

Every year, 300,000 HAP episodes occur in emergency departments across the United States. More than 90% of HAPs occur in people who are on intubation, with 10% to 20% of explicitly intubated patients likely develop VAP. In U.S. ICUs, VAP is the 2nd most frequent nosocomial illness, with median incidence ranging from 2.3 cases per 1000 ventilator days in paediatric facilities to 11.4 cases per 1000 ventilator days in trauma units. When compared to controls who had not established VAP, VAP lengthens hospital stay by 6.1 days and increases medical care expenses by $10,019. VAP promotes greater nosocomial deaths than any other illness in a U.S. health environment, with roughly 50,000 deaths per year, and increases medical centre mortality by double in impacted patients [60].

In India, the prevalence of HAP is 17.44% [60].

Pathogenesis:

The pathophysiology is determined by the amount and severity of organisms that enter the LRT as well as the host's reactivity (e.g., mechanical, humoral, and host immune system). Microaspiration of organisms that have colonised the oropharyngeal tract (or, less importantly, the gastrointestinal tract) is the key course of illness [61]. Approximately 45 percent of immunocompetent individuals drew in organism when sleeping, while a far greater percentage of very ill people drew in organism on a regular basis [62]. Oropharyngeal secretions and microorganisms are pulled into the lungs when an endotracheal tube is present [63].

Colonization of hospitalised patients with microbes obtained from the health clinic environment, with 75 percent of very sick patients infected within two days [62, 63]. Immediate contact between a respiratory device and contaminated water reservoirs is

another route of aspiration in precisely ventilated patients [64]. Disposable tubes in respiratory instruments, tracheostomy tubes, and endotracheal tubes can be contaminated during regular nursing care or by the (unclean) hands of medical clinic staff.

Additionally, variations in gastric pH caused by illness, treatment, or gastrointestinal feedings might disrupt gastric and upper digestive tract sterility [65].

The aetiology and variables related with HAP and VAP are shown in Figure 10 [64, 65].

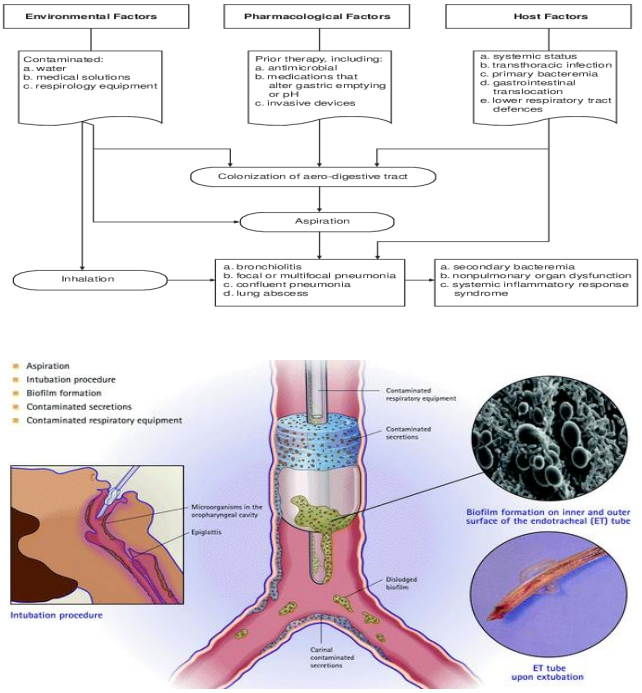


Figure 10**:** Pathogenesis of HAP and VAP.

Microbiology:

HAP (also known as nosocomial pneumonia) and VAP are multimicrobial infections. GNB (*E. coli, K. pneumoniae, Acinetobacter baumannii, Enterobacter spp, P. aeruginosa*) and GPC (e.g., *S. aureus*, including MRSA, *Streptococcus* spp) are the most prevalent pathogens, as illustrated in Figure 11 [66, 67]

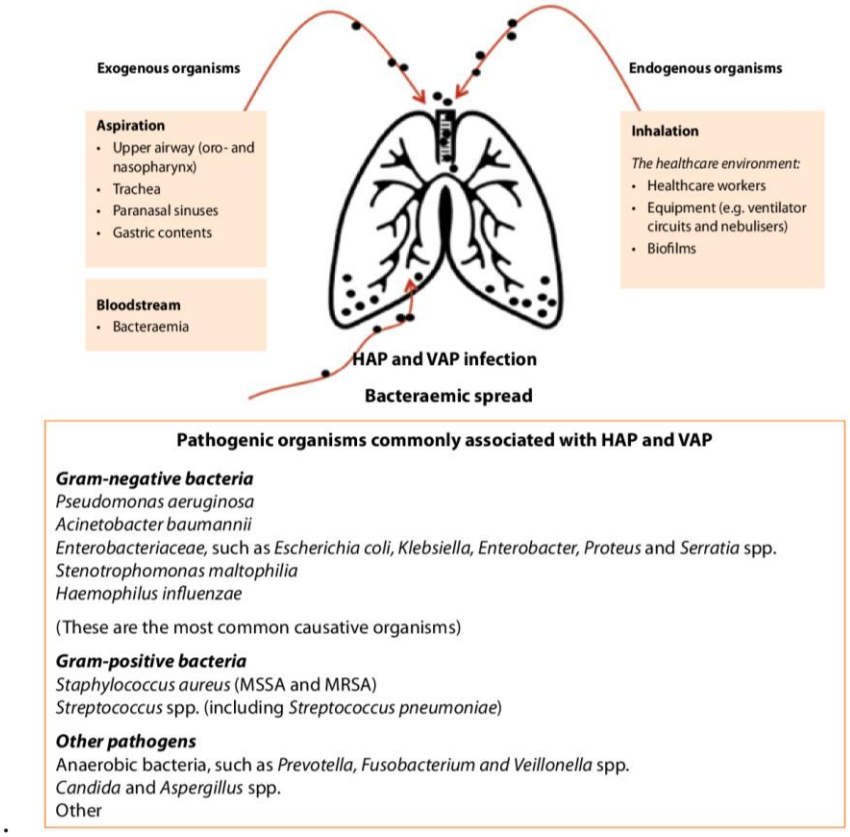


Figure 11**:** Pathogenic organism of HAP and VAP.

Diagnosis of HAP and VAP:

Following table gives that diagnosing HAP and VAP requires imaging study with respective signs and symptoms [68].

Table 7: Diagnosis of HAP and VAP [68]:

Radiological Parameters	Clinical Manifestation
At least two sequential chest imaging test results with no less than one of the accompanying: New and persistent **or** Progressive and persistent • Infiltrate • Consolidation	For every case, something like one of the accompanying: • Fever (>38.0°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

• Cavitation • Pneumatoceles, in infants ≤1 year old **Note:** In patients without basic pneumonic or heart sickness (for instance: respiratory issue, bronchopulmonary dysplasia, PE, or COPD), one conclusive imaging test result is satisfactory**.**	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 (for example: O2 desaturations (for example: PaO2/FiO2 <240)7, increased oxygen requirements, or increased ventilator demand).

Vulnerability of host for MDR pathogens and/or increase death rate in patients with HAP [69]:

Vulnerability for increased mortality:
▪ Ventilatory support for HAP. ▪ Septic shock
Vulnerability for MDR *Psuedomonas spp,* GNB and MRSA:
▪ IV antibiotics within the past 90 days.
Vulnerability for MDR *Psuedomonas spp* and GNB:
▪ Anatomical respiratory disorder (bronchiectasis or CF). ▪ Sputum/ETA/BAL on microscopy shows predominant GNB. ▪ Establishment with and OR earlier isolation of MDR *Pseudomonas* or other GNB.
Vulnerability for MRSA:
▪ Treatment in a unit in which >20 percent of MRSA. ▪ Treatment in a unit in which the predominance of MRSA isn't known ▪ Establishment with and OR earlier isolation of MRSA..

Vulnerability for MDR ventilator-associated pneumonia [69]:

Vulnerability for Multidrug resistant pathogens
▪ IV antimicrobials use inside the past 90 days. ▪ Sepsis with shock and VAP. ▪ ARDS with VAP. ▪ ≥5 days of hospital admission preceding the event of VAP. ▪ Intense renal substitution treatment preceding VAP beginning.
Vulnerability for Multidrug resistant *Psuedomonas spp and other GNB*:
▪ Management in critical care unit where >10 percent of GNB organism are resistant to a higher order antimicrobials. ▪ Management in critical care unit where organism AST patterns are not known. ▪ Establishment with and OR earlier isolation of MDR *Pseudomonas* or other gram-negative bacilli.
Vulnerability for MRSA:
▪ Treatment in a unit in which >20 percent of *Staphylococcus aureus* isolates are methicillin resistant. ▪ Treatment in a unit in which the prevalence of MRSA is not known ▪ Establishment with and OR earlier isolation of MRSA.

Ventilator Associated Events [VAE] [70]:

The VAE is used for surveillance purposes, this is not a clinical algorithm and is not made for use in the clinical management of patients.

Definition: "VAEs are distinguished by utilizing a blend of true measures: disintegration in lung parameters after a period of stability or improvement on the ventilator, documentation of infection or inflammation, and lab confirmation of lung disorder".

The definitions within the VAE method are: 1) Ventilator-Associated Condition (VAC); 2) Infection-related Ventilator-Associated Complication (IVAC); and 3) Possible VAP (PVAP).

1) **Ventilator-associated condition (VAC)**

It is regularly owing to pneumonia, PE, atelectasis, or ARDS. It has a solid relationship with

extended mechanical ventilation, duration of residence in hospitals and fatality.

Definition: "An increment in every day least PEEP>3cm H2O or an increment of the day by day least FiO2>.20 supported for > 2 schedule days in a base patient line time of dependability or improvement. On the ventilator, characterized by >2 schedule long stretches of steady or diminishing every day least FiO2 or PEEP".

Calculation of Daily minimum PEEP or FiO2:

Calculating Daily minimum PEEP or FiO2 is shown by following examples.

Method 1: The patient is ventilated at 6 pm. PEEP is set at the accompanying qualities through the rest of the schedule day:

Time	6 pm	7 pm	8 pm	9 pm	10 pm	11 pm
PEEP (cmH_2O)	10	8	5	5	8	8

"In this Method, the daily minimum PEEP value is 5 cmH2O. PEEP are tracked and take down entire hour. There are two successive hours where the PEEP is distinguished to be 5 cmH2O (8 pm and 9 pm), and hence minimum duration of > 1 hour is fulfilled".

Method 2: The patient is ventilated at 6 pm. PEEP is set at the accompanying qualities through the rest of the schedule day:

Time	6 pm	7 pm	8 pm	9 pm	10 pm	11 pm
FiO_2	1.0	0.8	0.5	0.5	0.8	0.8

"In this Method, the daily minimum FiO2 is 0.5. FiO2 are tracked and take down entire hour. There are two successive hours where the FiO2 is distinguished to be 0.5 (8 pm and 9 pm), and hence minimum duration of > 1 hour is fulfilled".

Method 3: “In following method, the baseline period is defined by MV days 1 through 4 (coloured in light gray), and the period of worsening oxygenation by MV days 5 and 6 (coloured in darker gray), where the daily minimum PEEP is ≥ 3 cmH2O greater than the daily minimum PEEP of the first day in the baseline period. Note that there is no VAC

on MV day 3, because PEEP values 0-5 cmH2O are considered equivalent for the purposes of this surveillance”.

MV Day	Daily minimum PEEP (cmH_2O)	Daily minimum FiO_2 (oxygen concentration, %)	VAE
1	0 (5)	1.00 (100%)	-
2	0 (5)	0.50 (50%)	-
3	**5**	0.50 (50%)	-
4	**5**	0.50 (50%)	-
5	**8**	0.50 (50%)	**VAC**
6	**8**	0.50 (50%)	-

Method 3: Onset of VAC through change in Daily minimum PEEP (cmH_2O)

Method 4: “In following method, the baseline period is defined by MV days 3 and 4 (coloured in light gray), and the period of worsening oxygenation by MV days 5 and 6 (coloured in darker gray), where the daily minimum FiO2 is ≥ 0.20 (20 points) over the daily minimum FiO2 of the first day in the baseline period”.

MV Day	Daily minimum PEEP (cmH_2O)	Daily minimum FiO_2 (oxygen concentration, %)	VAE
1	8	1.00 (100%)	
2	6	0.50 (50%)	
3	5	**0.40 (40%)**	
4	5	**0.40 (40%)**	
5	6	**0.70 (70%)**	**VAC**
6	6	**0.70 (70%)**	

Method 4: Onset of VAC through change in Daily minimum PEEP (cmH_2O).

2) **<u>Infection-related Ventilator-Associated Complication (IVAC)</u>**

Element

Patient should meet VAC to be qualified for IVAC.

b. “On or later schedule day 3 of mechanical ventilation (MV) and inside 2 schedule days prior or later the beginning of deteriorating oxygenation, the patient meets both of the accompanying” :

Patient has one of the accompanying:

• Temperature >38°C (>100.4°F)

• Temperature <36°C <96.8°F)

• White cell count ≥ 12,000 cells/mm3

• White cell count ≤4,000 cells/mm3

Furthermore Patient meets the entirety of the accompanying:

• Another antimicrobial agent(s)* is begun

• The new antimicrobial agent(s) * * is proceeded for ≥ 4 qualifying antimicrobial days (QAD)

Note:

*The specialist is viewed as new for the motivations behind this definition on the off chance that it was NOT given to the patient on both of the 2 days going before the current beginning date.

* * **List of Antimicrobials Agents Eligible for IVAC, PVAP (refer Table 1)** ***(Revised January 1, 2019)***

New Antibiotic Agent:

"Characterized as any parameters recorded in the Table 1 that is started on or later the third schedule day of mechanical ventilation AND in the VAE Window Period (explicitly, the period normally characterized by the 2 schedule days prior, the day of, and the 2 schedule days later the beginning date of the VAE). The parameters is viewed as new for the motivations behind this definition assuming it was NOT given to the patient on both of the 2 days going before the current beginning date and further rearranged through following method".

Method 5: "A patient is intubated and precisely ventilated on medical clinic day 1 in the ICUs. Ceftriaxone and azithromycin are begun on day 1 and managed every day. Following 3 days of working on respiratory status, the patient's oxygenation falls apart on days 4 and 5, with an every day least PEEP that is 4 cmH2O higher than it was on days 2 and 3. Models for the VAC definition are met; the date of the occasion is emergency clinic day 4. Ceftriaxone is suspended and meropenem is started on day 5. Azithromycin is proceeded. For this situation, meropenem is another antimicrobial specialist: 1) it was started on day 5 of mechanical ventilation, and 2) inside the VAE Window Period (on the day later VAE beginning), and 3) it was not given to the patient

on both of the 2 days going before the current beginning date. Paradoxically, ceftriaxone and azithromycin would not be viewed as new antimicrobial specialists, since they were started on day 1 of mechanical ventilation and proceeded with day by day into the VAE Window Period".

Qualifying Antimicrobial Day (QAD):

"A day on which the patient was controlled an antimicrobial drugs still up in the air to be "new" inside the VAE Window Period. Four sequential QADs are expected to meet the IVAC antimicrobial measure—beginning inside the VAE Window Period. Days on which another antimicrobial drugs is controlled consider QADs. Days between organizations of another antimicrobial drugs additionally consider QADs as long as there is a hole of something like 1 schedule day between drugs. For instance, assuming levofloxacin is given on VAE Day 1, has not been given in the 2 going before schedule days, and is given again on VAE Days 3, 5, and 7, there are 7 QADs—in light of the fact that the days between levofloxacin dosages likewise consider QADs. Conversely, days between organizations of various antimicrobial drugs don't consider QADs; for instance, in the event that levofloxacin is given to the patient on VAE Days - 2 and - 1 in particular, no antimicrobials are given on VAE Day 1, and meropenem is given distinctly on VAE Day 2 (recall there is no VAE Day 0), then, at that point, there are not 4 successive QADs. VAE Days - 2 and - 1 consider 2 sequential QADs, however VAE Day 1 can't be considered a QAD on the grounds that it is a day between various antimicrobial specialists. For additional direction on distinguishing proof of new antimicrobial specialists and on the best way to decide if the prerequisite for 4 QADs is met".

3) <u>Possible VAP (PVAP)</u>

Element

a. Component

a. Patient should meet VAC and an IVAC to be qualified for PVAP

b. Furthermore Patient should meet one of following rules on or later schedule day 3 of MV and inside 2 schedule days prior or later the beginning of deteriorating oxygenation:

Criterion 1:

Positive culture of one of the accompanying examples, meeting quantitative or

semi-quantitative limits as illustrated in convention, without prerequisite for purulent respiratory discharges:

- Endotracheal aspirate, $\geq 10^5$ CFU/ml or corresponding semi-quantitative result
- Bronchoalveolar lavage, $\geq 10^4$ CFU/ml or corresponding semi-quantitative result
- Lung tissue, $\geq 10^4$ CFU/g or corresponding semi-quantitative result
- Protected specimen brush, $\geq 10^3$ CFU/ml or corresponding semi-quantitative result

Criterion 2:

Purulent respiratory discharges (characterized as emissions from the lungs, bronchi, or windpipe that contain ≥25 neutrophils and ≤10 squamous epithelial cells per low power field [lpf, x 100]) PLUS organic entity distinguished from one of the accompanying examples (to incorporate subjective culture, or quantitative/semi-quantitative culture without adequate development to meet criteria as above::

- Sputum, $\geq 10^5$ CFU/ml or corresponding semi-quantitative result
- Endotracheal aspirate, $\geq 10^4$ CFU/ml or corresponding semi-quantitative result
- Bronchoalveolar lavage, $\geq 10^4$ CFU/ml or corresponding semi-quantitative result
- Lung tissue, $\geq 10^4$ CFU/g or corresponding semi-quantitative result
- Protected specimen brush, $\geq 10^3$ CFU/ml or corresponding semi-quantitative result

Note:

Microorganism detailed for PVAP events, when they are obtained or cultured from fitted specimen types as per the protocol and are never listed on the list of excluded microorganisms and culture or non-culture based laboratory parameters method results.

Criterion 3:

One of the accompanying positive tests:

1. Microorganism recognized from pleural fluid (where sample was acquired during thoracentesis or earliest positioning of chest tube and NOT from an indwelling chest tube).
2. Lung histopathology, characterized as:

A) Ulcer development or foci of combination with extraordinary neutrophil collection in bronchioles and alveoli.

B) proof of lung parenchyma attack by organisms (hyphae, pseudohyphae or yeast structures); 3) Proof of infection with the viral microbes.

3. Demonstrative test for Legionella species.

4. Demonstrative test on respiratory discharges for flu infection, respiratory syncytial infection,

adenovirus, parainfluenza infection, rhinovirus, human metapneumovirus, Covid.

Note:

There is an order of definitions inside VAE:

- In the event that a patient meets standards for VAC and IVAC, report as IVAC.
- In the event that a patient meets standards for VAC, IVAC, and PVAP, report PVAP..

VAE Rate:

The VAE rate per 1000 ventilator days is calculated by dividing the number of VAEs by the number of ventilator days and multiplying the result by 1000 (ventilator days).

$$\text{VAE Rate per 1000 ventilator days} = \frac{No.\ of\ VAEs}{No.\ of\ Ventilator\ Day} * 1000$$

Excluded organisms:

a. Commensals of the oral cavity or upper respiratory tract; Candida species or yeast not in any case indicated; coagulase-negative Staphylococcus species; and Enterococcus species, when distinguished from sputum, endotracheal aspiration, bronchoalveolar lavage, or protected brushings. These creatures can be accounted for as PVAP microorganisms whenever recognized from lung tissue or pleural liquid examples.

b. Following are sometimes or are not known to be purposes behind clinical benefits related sicknesses, they are in like manner kept away from, and can't be used to meet the PVAP definition when restricted from any certified model sort (to join lung and pleural fluid): Blastomyces, Histoplasma, Coccidioides, Paracoccidioides, Cryptococcus, and Pneumocystis.

Secondary BSI:

Optional BSIs are not announced for VAC or IVAC occasions. Secondary BSIs might be accounted for PVAP occasions, provided that at least one organism identified from the blood matches an organism isolated from an appropriate respiratory tract specimen (including respiratory secretions, pleural fluid, and lung tissue). The respiratory tract specimen must have been collected on or later the third day of mechanical ventilation and inside 2 schedule days prior or later the day of beginning of demolishing oxygenation to be considered as a basis for meeting the PVAP definition. Likewise, the organic entities distinguished from blood probably been gathered during the 14-day occasion period, where day 1 is the day of beginning of demolishing oxygenation. In situations where PVAP is met with just the histopathology model and no culture or non-culture-put together testing is performed with respect to a qualified respiratory example, and there is likewise a positive blood example an auxiliary BSI isn't accounted for.

- In situations where a culture or non-culture-based testing of respiratory secretions, pleural fluid, or lung tissue is performed and doesn't recognize a organism that matches a microorganism distinguished from blood, a secondary BSI isn't accounted for.
- A matching microorganism is characterized as one of the accompanying:

1. Assuming that genus and species are recognized in the two examples, they should be something very similar.
    a) Example: A blood sample came about with *Enterobacter cloacae* and a BAL sample came about with *Enterobacter cloacae* are matching microorganism.
    b) Example: A blood sample came about with *Enterobacter cloacae* and a BAL sample came about with *Enterobacter agglomerans* are NOT matching organisms as the species are different.
2. Assuming the microorganism is less authoritatively recognized in one example than the other, the lesser distinguished microorganism should be distinguished to at minimum the genus level and at that level the microorganism should be something similar.

a) Example: In a BAL *Escherichia* spp is obtained and a blood specimen resulted with *Escherichia coli* are considered a match at the genus level and therefore the BSI can be reported as secondary BSI to VAE.

The NHSN VAE Definitions [71]:

As per the new definitions the following attributes have been included:

- It is more Objective
- Maximally efficient
- Likely mechanised
- Characterises a wide scope of conditions and complexities happening in precisely ventilated patients.

VAE Epidemiology:

VAE rates are higher in injury, medical procedure, and neuroscience units and lower in clinical and heart units. Probable, VAE rates will more often than not be higher in significant showing clinics and lower in non-significant teaching emergency clinics. Hazard for creating VAEs is by all accounts most elevated in the initial fourteen days of mechanical ventilation (especially days 3–7), however patients stay in danger until extubation [71]. Roughly 33% of VAEs satisfy IVAC models. The general clinic death rate for VAEs answered to CDC in 2014 was 31%. Patients having VAEs are about twice powerless in contrast with the people who didn't foster VAEs [72].

VAE and Traditionally Defined VAP in agreement:

A meta-investigation from 18 examinations led in 8 nations that have 61,489 subjects. The pooled affectability of VAE for generally characterized VAP across 11 investigations and 1,633 subjects was 42% (95% CI 18–66%). The pooled positive prescient worth of VAE for generally characterized VAP across 9 investigations and 3,572 subjects was 23% (95% CI 13–34%). Subjects with VAEs were bound to have more complications contrasted with subjects with customarily characterized VAPs (pooled chances proportion for death in subjects with VAE versus VAP 1.49, 95% CI 1.11–2.01, and with IVAC versus VAP 1.76, 95% CI 1.23–2.52) [73].

The following figure 12 shows VAE and Traditionally Defined VAP in agreement [73].

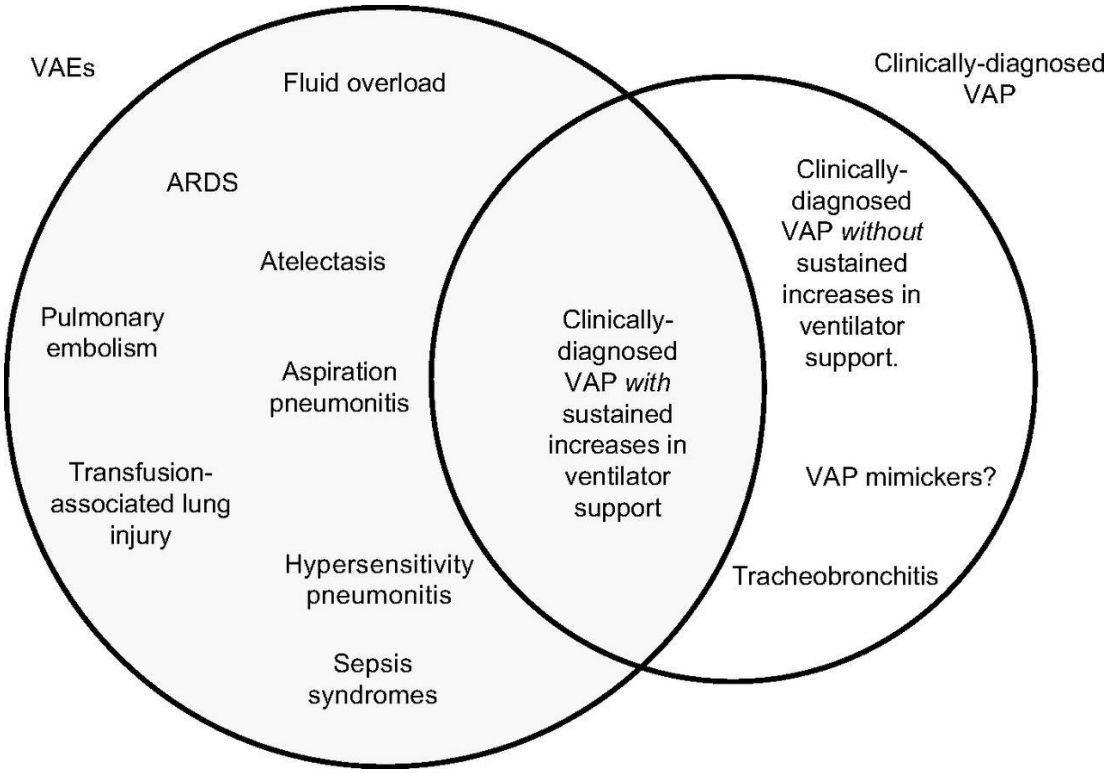


Figure 12: The VAE and Traditionally Defined VAP in agreement .

Shortcoming of Traditional VAP Surveillance:

It is exceptionally abstract. The customary surveillance definition for VAP included models, for example, "a new or moderate invade," "deteriorating oxygenation," and a "adjustment of the quality or amount of sputum." They are exceptionally abstract and along these lines permit various examiners to arrive at various decisions concerning whether a given patient meets CDC measures for VAP. Significant degrees of eyewitness inconstancy subvert the adequacy of utilizing VAP rates to contrast clinics since it is outlandish with know whether noticed contrasts are because of varieties in nature of care or contrasts in surveillance conclusions [74].

Surveillance Versus Clinical aspects:

VAE is an observation idea, not a clinical idea. The primary component of clinical consideration is on early determination and quick treatment, that is the reason they favor affectability and speed over explicitness. While the surveillance centers around, objectivity, reproducibility, and the recognition of occasions identified with the most

dismalness to focused on for counteraction. Surveillance results are utilized to illuminate and follow the effect of avoidance methodologies at the populace level. VAE definitions offer accentuation on true clinical hints rather than abstract measures [75].

Vulnerability to ventilator-associated events: The accompanying elements were viewed as significant in patients like sex, age, presence of comorbidities, seriousness of-disease, purposes behind intubation incorporated the accompanying: respiratory disappointment, medical procedure, cardiogenic shock, adjusted degree of cognisance, sepsis/septic shock, aspiratory embolism, liquid over-burden, ARDS, span of intubation. Different factors could be unconstrained breath preliminaries, pharmacological loss of motion, early portability, tracheostomy, vasopressors, red blood units bonded, daze, kind of sedation (constant or irregular), drugs for sedation just as medications for absense of pain [76].

Prevention of VAP in the intensive care unit [77].

Recommendations include:

- Proper sanitisation and being used consideration of tubing, respirators, and humidifiers to restrict pollution.
- No standard changes of respirator tubing.
- Keep away from acid neutralizers and H2 blockers.
- Clean tracheal suctioning.
- Nurture in head-up position.

Impact of VAE [77, 78] :

- Drawn out necessity of mechanical ventilation [MV] and expanded span of emergency clinic stays: Ventilator-related pneumonia (VAP), sepsis, Acute Respiratory Distress Syndrome (ARDS), aspiratory embolism, barotrauma, and pneumonic edema are among the intricacies that can happen in patients getting mechanical ventilation; such inconveniences can prompt longer length of mechanical ventilation, longer stays.
- Cost burden: those patients who are on MV their relatives had to pay more amount of cost because putting patients on MV is more costly at the same time, the effects of VAE increases the days of MV and duration of hospital stay.

- Infections with MDR pathogens: most of the pathogen associated with VAEs are *Acinetobacter baumannii,* followed by *Klebsiella pneumoniae, Pseudomonas aeruginosa and Escherichia coli*. All of these pathogens are MDR organism.
- Increases chances of catheter associated infections (BSI, CAUTI).
- Expanded pace of mortality: Prolonged necessity of mechanical ventilation [MV] and expanded length of clinic stays, expanded possibilities of disease with MDR microorganisms this multitude of elements builds the pace of horribleness and mortality of VAE patients.

Reviewing VAE research, things to keep in mind:

Current knowledge:

2020 National and State Healthcare-Associated Infections Progress Report

Result:

According to the review directed universally, roughly 2,000 U.S. medical clinics revealed their VAE rates to CDC in 2016. The generally speaking VAE rate for CCUs in entire nation was 6.8 events per 1,000 ventilator-days [78].

Prevalence, Clinical Characteristics, and Outcomes Related to Ventilator-Associated Events in Neurocritically Ill Patients

Result:

By and large VAE rate was viewed as 13 for each 1000 ventilator days and a VAC in 58% of events, IVAC in 22% of events, and PVAP in 20% of events . At the point when we associate with the microorganism secluded it was tracked down that *Enterobacter* spp (7.9%), *Escherichia. coli* (6.6%), *Klebsiella* spp (6.6%), *Acinetobacter* species (7.9%), *Moraxella catarrhalis* (2.6%), and *Proteus* spp (2.6%) were confined [79].

Ventilator-associated events versus ventilator-associated respiratory infections-moving into a new paradigm or merging both concepts, instead?

Result:

The VAE surveillance improves the spectra of MV difficulties however prohibits less serious VARIs. Noninfective events disclose up to 30% of VAEs, the primary driver being atelectasis, ARDS, respiratory edema and PE. The bundles surveying VAE are related with less occurrence of VAP and further developed results however they neglect to decrease the paces of VAE [80].

Updated Approach for the Assessment of Ventilator Associated Pneumonia

Result:

As indicated by the creator new definitions are dynamic and dependent upon progress by an iterative interaction. Further, these rules are customised stringently for surveillance, and are not intended to direct clinical navigation. Future work will be important to decide the relationship between this new surveillance definition and significant clinical results [81].

The epidemiology and clinical outcomes of ventilator-associated events among 20,769 mechanically ventilated patients at intensive care units: an observational study

Result:

The rate of VAC (16.7 per 1000 ventilator-days), IVAC (6.4 per 1000 ventilator-days), and rate of PVAP (1.64 per 1000 ventilator-days) [82].

Accuracy of ventilator-associated events for the diagnosis of ventilator-associated lower respiratory tract infections

Result: A sum of 1059 patients (15,029 ventilator-days) were incorporated. 268 VAP (17.8 per 1000 ventilator-days), 127 VAT (8.5 per 1000 ventilator-days) and 262 VAE (17.4 per 1000 ventilator-days) were analysed [83].

An automated retrospective VAE-surveillance tool for future quality improvement studies

Result: The yearly VAE incidence rate per 1000 device days went from 22.1/1000 ventilator days (95% CI 17.4–26.3) in 2008 to 10.1/1000 (CI 7.0–15.8) 2016. Over the

whole perception time frame there was an incidence rate of 15.9/1000 ventilator days (95% CI 14.7–17.2) [84].

Ventilator-associated events: Incidence and mortality in intensive care unit of a superspecialty hospital of North India

Result: The by and large VAE rate was 23.7/1000 ventilator days. VAC (6.7/1000 ventilator days), IVAC (11.57/1000 ventilator days), and PVAP (5.7/1000 ventilator days). All VAC cases (100%) lived, and 83.3% of IVAC cases terminated. In any case, 77.7% of PVAP cases lapsed [85].

What this present study contributes to our knowledge:

At the point when we attempt to go through the writings there were numerous regions which are immaculate and requires definite review. Present review is managing those regions which requires further review like definite AST profiling, factors related with VAEs, characterisation in regards to mortality of VAEs and it will likewise bargain the future viewpoints (relationship with BSI) identified with VAE.

Results

A total of **386** individuals requiring mechanical ventilation were examined, with **196** of them experiencing Ventilator Associated Events (VAE). Twelve of the 196 VAE patients progress to VAC, 59 to IVAC, and 125 to PVAP.

The VAC rate is **3.4** VAE per 1000 mechanical ventilation days, while the IVAC rate is **16.7** VAE per 1000 mechanical ventilation days. PVAP is **35.39** VAE/1000 days of mechanical ventilation.

Ventilator Associated condition (VAC) characteristics:

VAC Incidence:

Out of 196 VAE patients, 12 (6.12 percent) developed VAC, according to the research. The following figure 13 illustrates this.

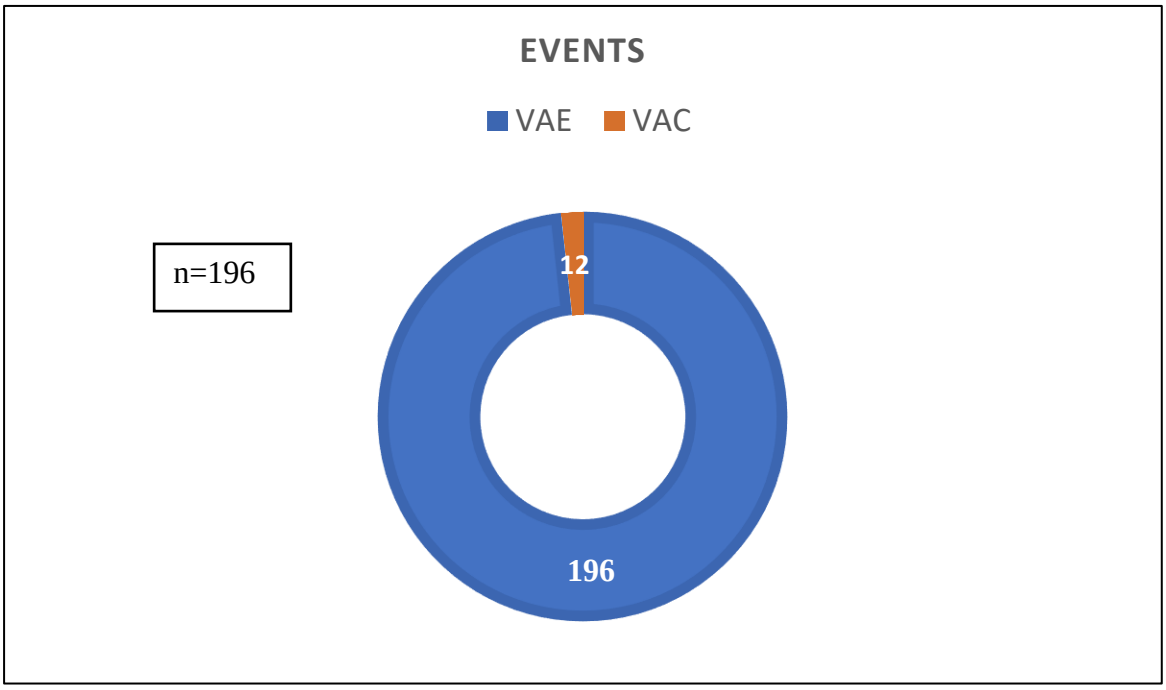


Figure 13: The incidence of VAC

VAC Rate:

The rate of VAC in this research was 3.4 VAE/1000 mechanical ventilation days, compared to 16.7 VAE/1000 mechanical ventilation days for IVAC and 35.39

VAE/1000 mechanical ventilation days for PVAP, as shown in figure 14.

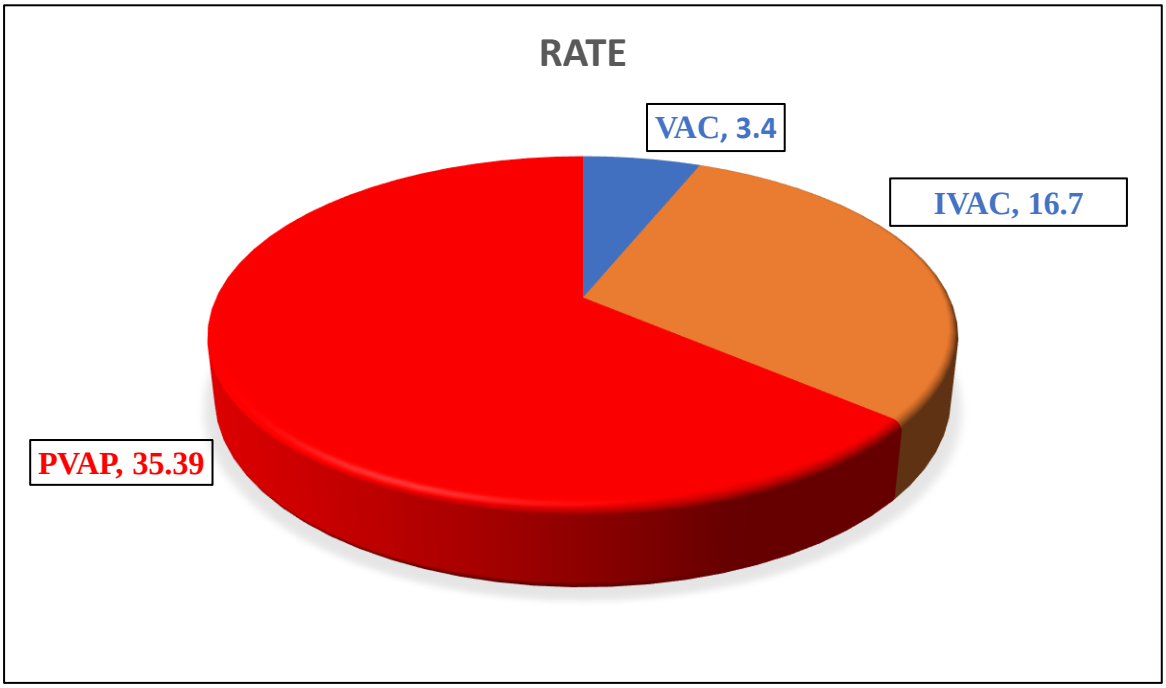


Figure 14: The Rate of VAC in correlation with IVAC and PVAP

VAC onset Correlation with Time from Intubation/Mechanical Ventilation:

Out of 12 (n=12) instances with VAC, 2 (16.66%) occur on Day 3, 1 (8.33%) on Day 4, 1 (8.33%) on Day 5, 4 (33.33%) on Day 6, and 2 (16.66%) on Day 7. As per the following table 8 and figure 15, the majority of the events occur between Days 3 and 7.

	Percentage of Days	Number (No.) of VAC Events
Day <3	0	0
Day 3	16.66	2
Day 4	8.33	1
Day 5	8.33	1
Day 6	33.33	4
Day 7	16.66	2
Day 8	0	0
Day 9	0	0
Day 10+	0	0

Table 8: Correlation between Percentage of Days and Number (No.) of VAC Events

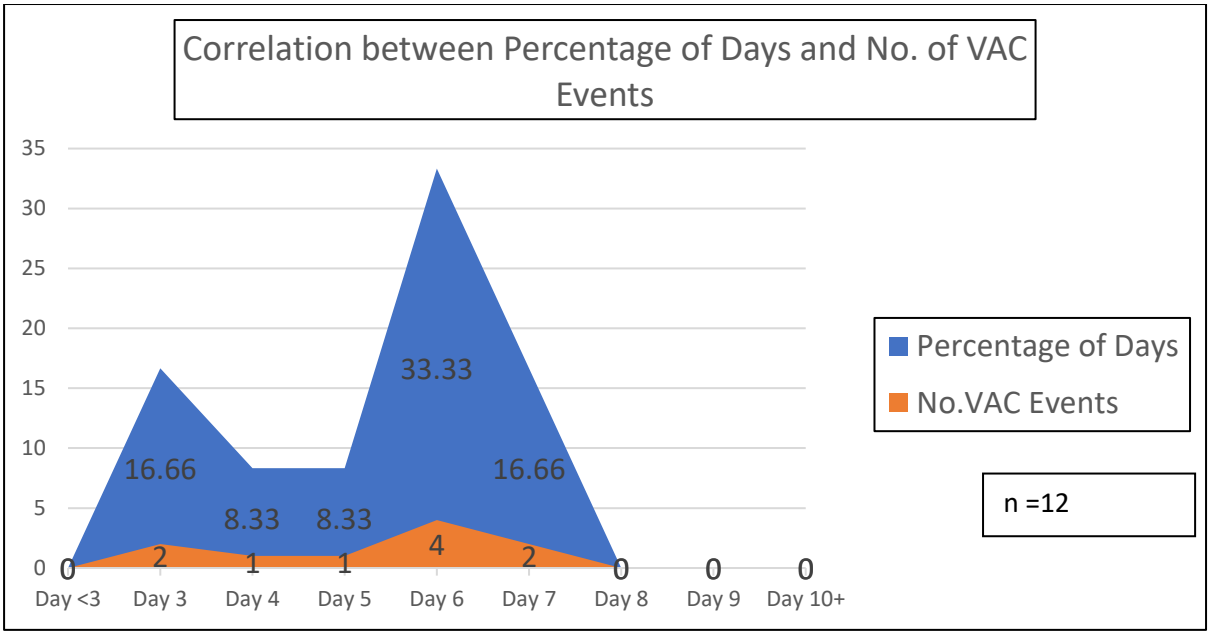


Figure 15: Correlation between Percentage of Days and Number (No.) of VAC Events

Criteria Used to Report VACs:

According to the study, of the 12 instances that develop VAC, four (33.33 percent) exhibit an increase in FiO2 (>20 points) and six (50 percent) cases show an increase in PEEP (3 mm H2O in contrast to its normal value), and two (16.33 percent) cases show an increase in both Fio2 and PEEP. This is depicted in Figure 16, which demonstrates that the majority of instances have an increase in PEEP followed by an increase in FiO2.

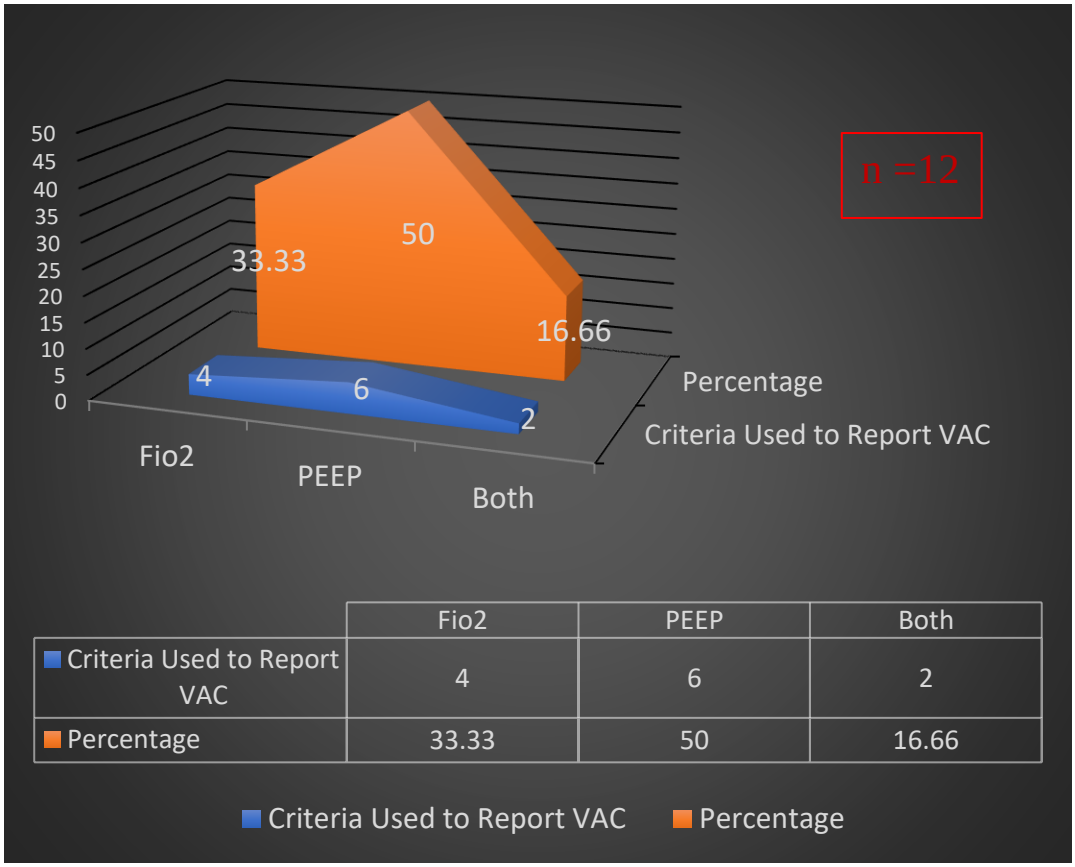


Figure 16: Percentage association of Criteria used to Report VAC

Age Association of VAC Events (n=12):

The following figure 17 depicts the age group and its relationship with VAC Events in this analysis. According to the figure, 2 (16.66%) patients were between the ages of 20 and 40, 7 (58.33%) patients were between the ages of 40 and 60, and 3 (25%) patients were beyond the age of 60. As per figure below, the most common age range for VAC Events was 40-60 years old, followed by patients >60 years old and 20-40 years old.

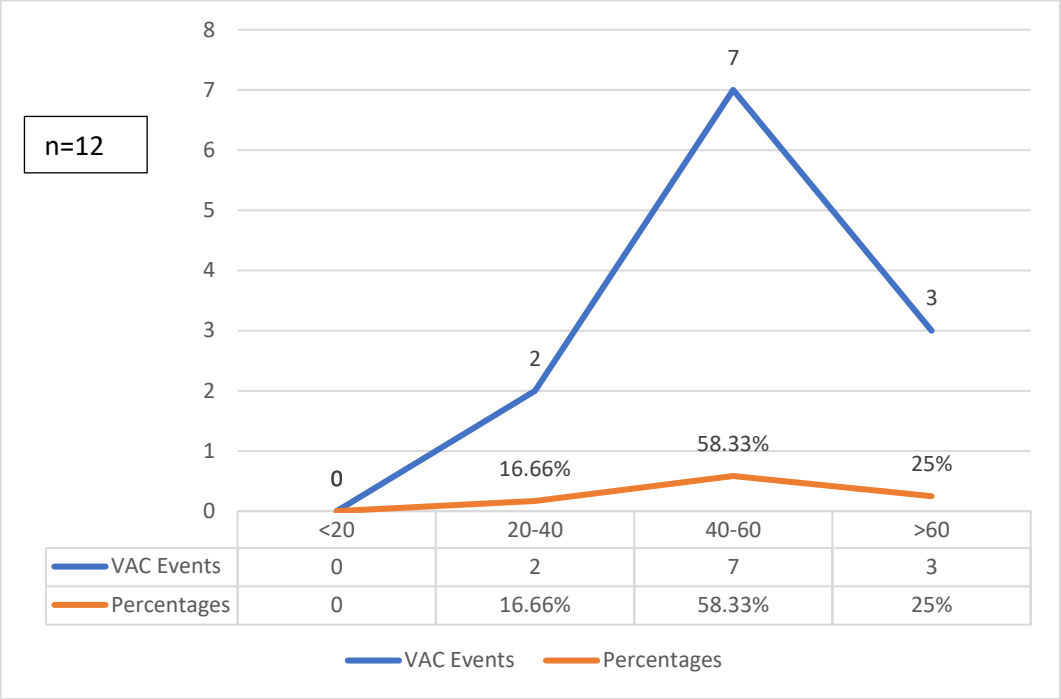


Figure 17: Age Association of VAC Events

Disease relation of VAC Cases (n=12):

According to table 9 and figure 18, 2 (16.66%) cases were related to basal ganglia bleed, 1 (8.33%) case was related to subdural hematoma, 2 (16.66%) cases were post-operative cases of abdominal laparotomy, 1 case was related to acute pancreatitis, 2 cases were CKD patients, and 1 case was related to AKI. The majority of instances are linked to symptoms of the central nervous system, followed by a equal predisposition to both gastrointestinal and renal problems.

Disorders	No. of VAC cases
Basal ganglia bleed	2
Meningitis	1
Subdural hematoma	3
P/o/c/o abdominal laparotomy	2
Acute pancreatitis	1
CKD	2
AKI	1
Total	12

Table 9: Disease relation and No. of VAC Event.

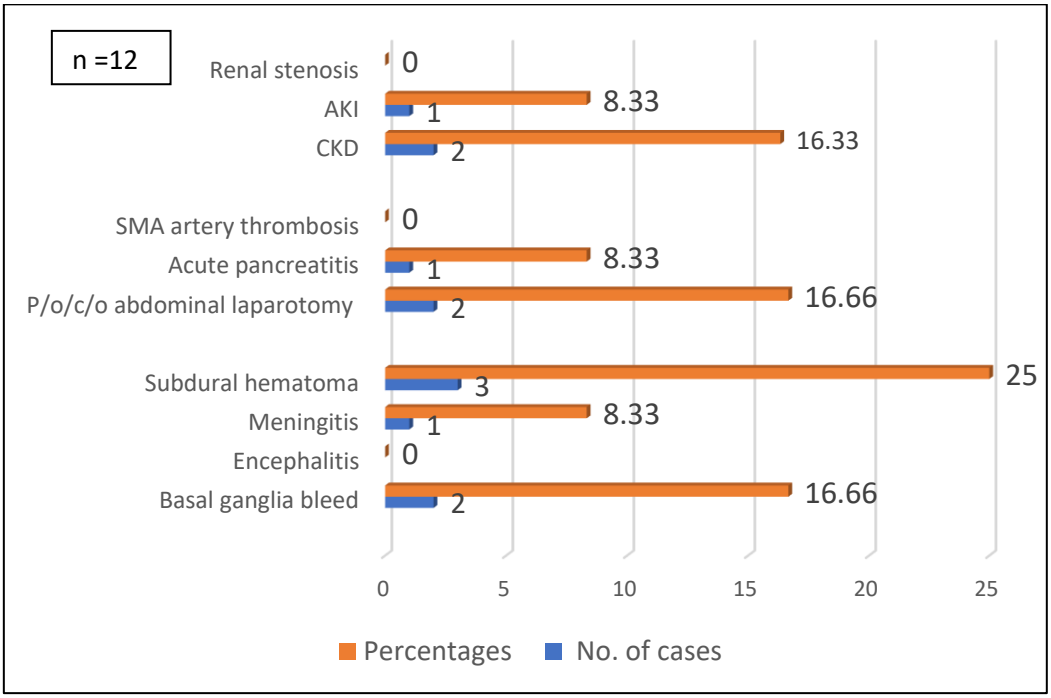


Figure 18: Percentage wise Disease association of VAC cases

Characterisation of Disease association, VAC Events and Survival outcome:

According to table 10 and figure 19, two cases (16.66%) of basal ganglia bleed that developed VAC survived, as did 3 (25 %) case of subdural hematoma, two (16.66 percent) cases of post-operative abdominal laparotomy, two (16.66%) cases of CKD, one (8.33%) case of meningitis one (8.33%) case of acute pancreatitis, and one (8.33%) case of AKI, all of whom developed VAC and survived. This suggests that those cases who developed only VAC have a good survival outcome.

Disorders	No. of cases	Percentages	Survived
Basal ganglia bleed	2	16.66	2
Encephalitis		0	
Meningitis	1	8.33	1
Subdural hematoma	3	25	3
P/o/c/o abdominal laparotomy	2	16.66	2
Acute pancreatitis	1	8.33	1
SMA artery thrombosis		0	
CKD	2	16.33	2
AKI	1	8.33	1
Renal stenosis		0	
Total	12	100	12

Table 10: Shows the Disease association, VAC rate and Survival outcome

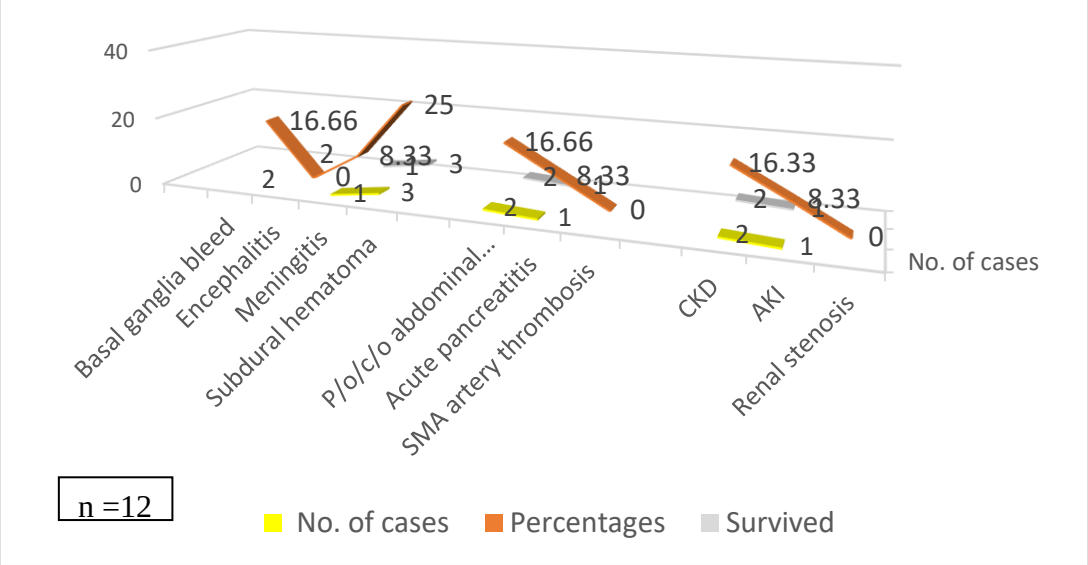


Figure 19: Combined percentage wise correlation between Disease association, VAC rate and patient survived

Infection related to Ventilator Associated complication (IVAC) characteristics:

IVAC Incidence:

According to the study, 59 (30.10 %) of 196 VAE Events patients acquire IVAC, as shown in Figure 20.

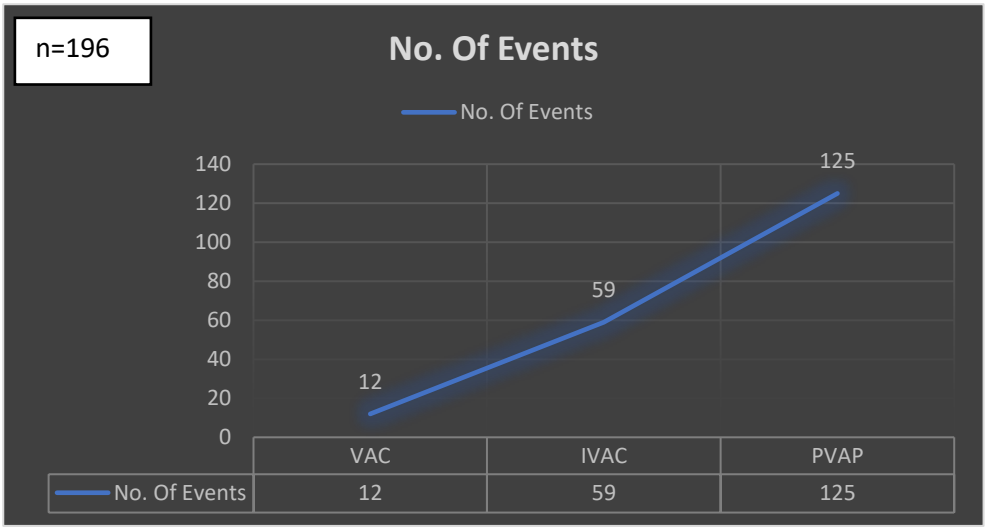


Figure 20: Showing number of IVAC Events

IVAC Rate:

The rate of IVAC in this research was 16.7 VAE/1000 mechanical ventilation days, compared to 3.4 VAE/1000 mechanical ventilation days for VAC and 35.39 VAE/1000 mechanical ventilation days for PVAP (Following figure 21 shows the correlation between the rate of VAC, IVAC and PVAP).

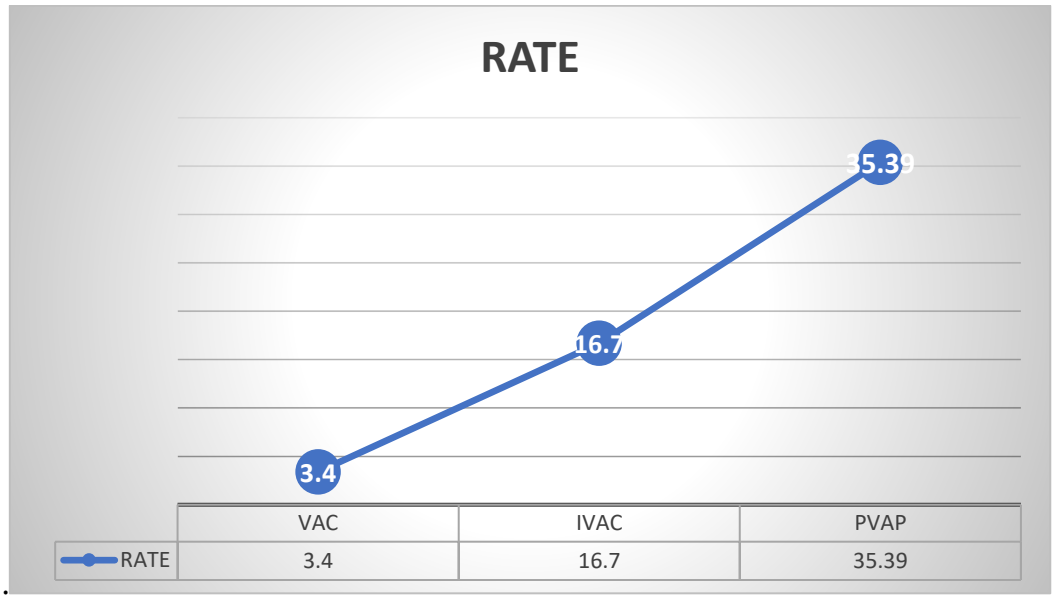


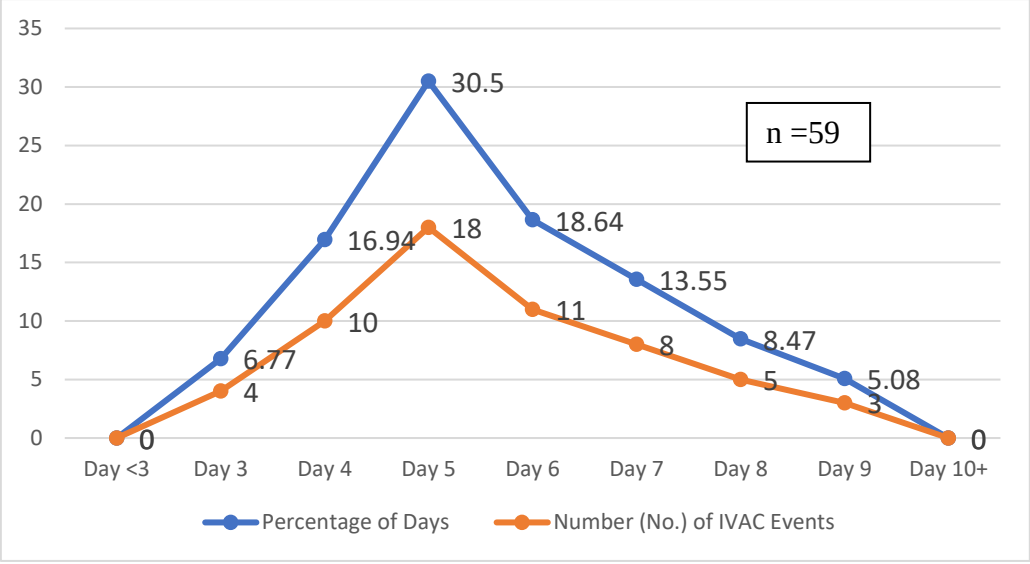
Figure 21: The Rate of IVAC in correlation with VAC and PVAP

IVAC Event onset Correlation with Time from Intubation/Mechanical Ventilation:

According to table 11 and graph 1, there are 59 (n=59) instances that develop IVAC, and the period from intubation/mechanical ventilation to the onset of IVAC event is as follows: 4 (6.77%) events happen on Day 3, 10 (16.94%) events happen on Day 4, 18 (30.50%) events happen on Day 5, 11 (18.64%) events happen on Day 6, 8 (13.55%) events happen on Day 7, 5 event (8.47%) happens on Day 8, and 3 (5.08%) events happen on Day 9. This shows that the majority of the events take place between Days 4 and 7.

	Percentage of Days	Number (No.) of VAC Events
Day <3	0	0
Day 3	6.77	4
Day 4	16.94	10
Day 5	30.50	18
Day 6	18.64	11
Day 7	13.55	8
Day 8	8.47	5
Day 9	5.08	3
Day 10+	0	0

Table 11: Correlation between Percentage of Days and Number (No.) of VAC Events



Graph 1: Correlation between Percentage of Days and Number (No.) of IVAC Events

Criteria Used to Report IVACs:

Increase in Temperature (>38°C) and WBC (>12000):

In this study, 13 (22.03%) of the 59 patients with IVAC exhibit an increase in Temperature/Temp (>38°C), 42 (71.18%) cases show a rise in WBC (>12000), and 4 (6.77%) cases show an increase in both Temperature/Temp (>38°C) and WBC (>12000). This was depicted in the graph below. The accompanying diagram 1 depicts a rise in WBC (>12000) followed by an increase in temperature (>38°C) in the majority of instances.

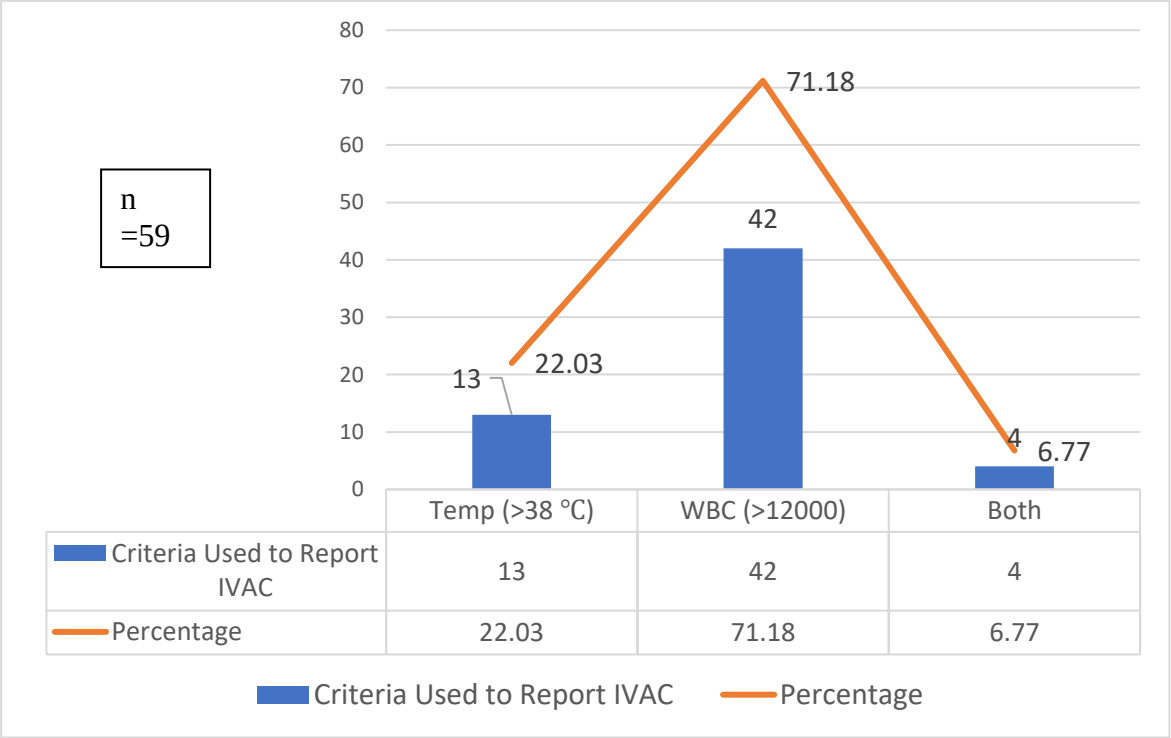
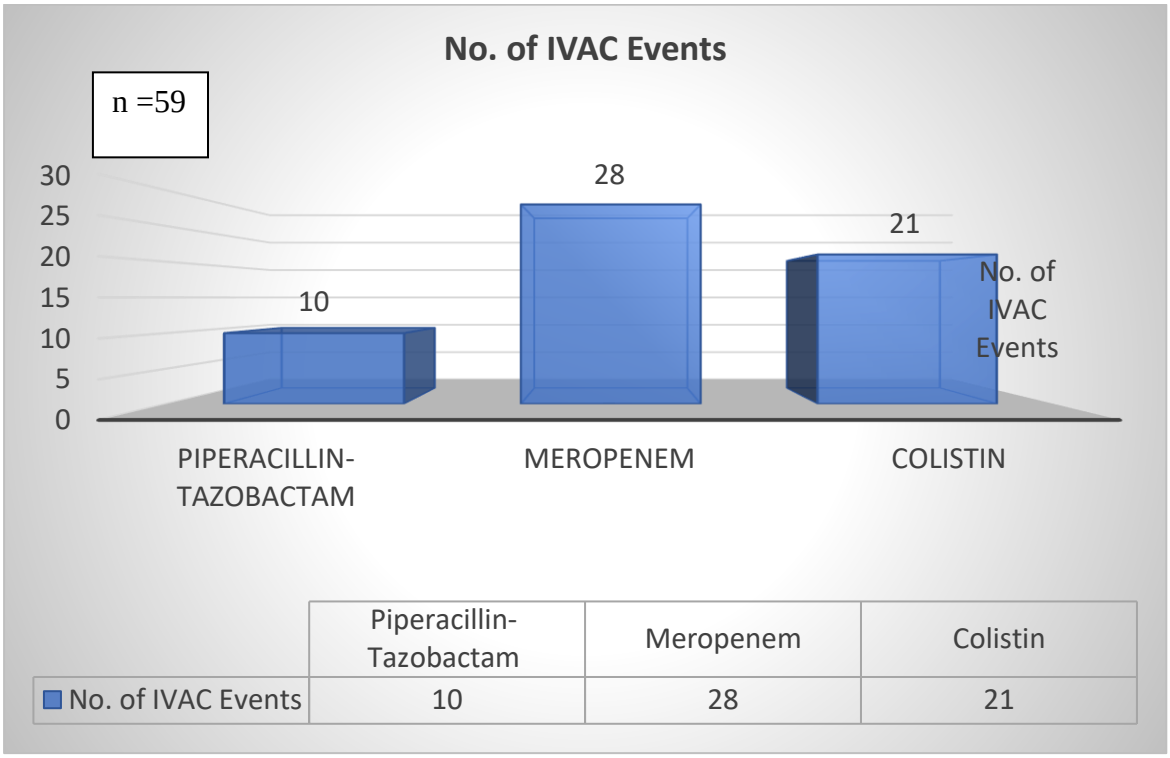


Diagram 1: Showing percentage correlation of Criteria used to Report IVAC

Change of antibiotics (>4 Qualifying antibiotics days):

There were 59 instances in this research that developed IVAC. In ten of the 59 instances, the antibiotic was switched from Ceftriaxone (which was used for two days) to Piperacillin-Tazobactam (which was taken for more than four days). The initial antibiotic used in the next 28 instances was Piperacillin-Tazobactam (2 days), which was then changed to Meropenem, which qualified >4 Qualifying antibiotics days to meet the IVAC Criteria. The antibiotics utilised in the remaining 21 instances were Piperacillin-Tazobactam (3 days), which was then changed to Meropenem for the following 3 days, and then the patients were put on Colistin, which qualified them for >4 Qualifying antibiotics days to meet the IVAC Criteria. The following graph 2 depicts the relationship between the number of IVAC events and the change in antibiotics (>4 Qualifying antibiotics days).

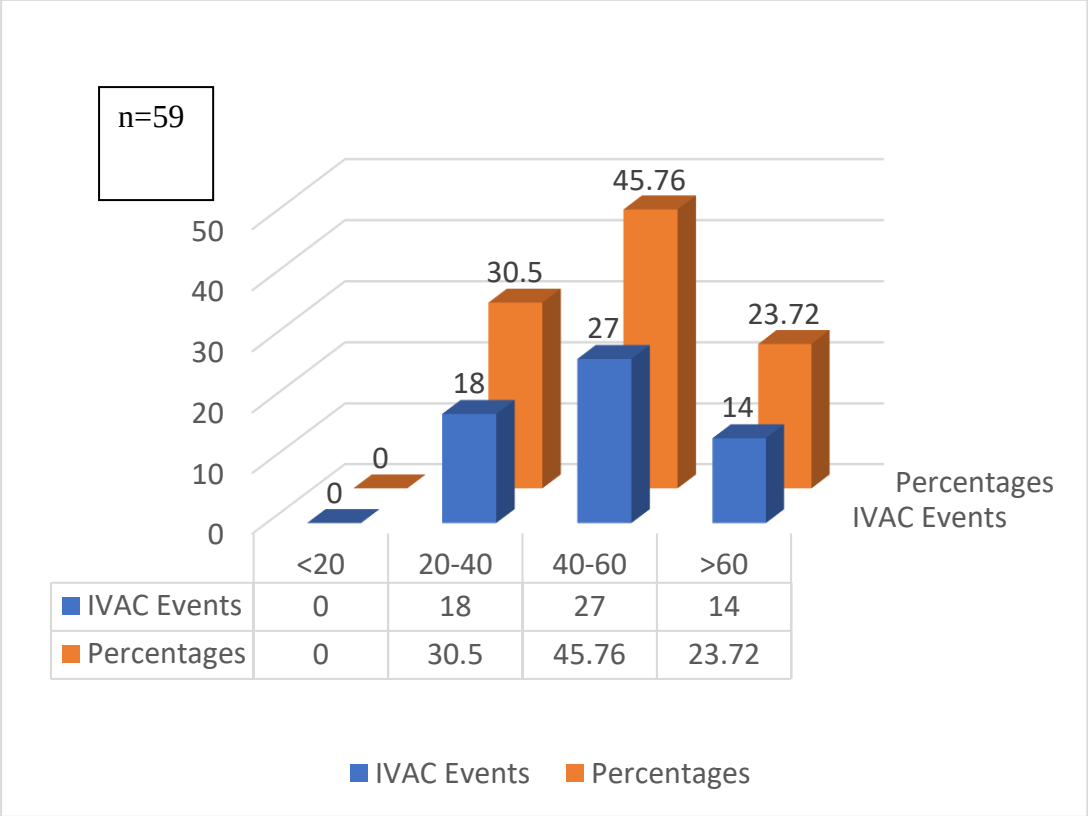


Graph 2: Association between No. of IVAC Events and Change of antibiotics (>4 Qualifying antibiotics days).

Age Association of IVAC Events (n=59):

The following graph 3 depicts the age group and its relationship with IVAC Events in this study. According to the graph, 18 (30.5%) individuals were between the ages of 20 and 40, 27 (45.76%) individuals were between the ages of 40 and 60, and 14 (23.72%) individuals were beyond the age of 60.

According to the graph below, the most prevalent age group associated with IVAC Events was 40-60 years, which was the same as the age group associated with VAC Events, followed by 20-40 years, and finally, age group > 60 years.



Graph 3: Age Association of IVAC Events.

Disease relation of IVAC Cases (n=59):

According to table 12 and figure 22, 5 (8.47 %) cases were related to basal ganglia bleed, 7 (11.86 %) cases were related to encephalitis, 5 (8.47 %) cases were related to meningitis (2 bacterial, 3 viral), 4 (6.77 %) cases were related to obstructive hydrocephalus, 6 (10.16 %) cases were related to subdural hematoma, 5 (8.47 %) cases were related to post-operative abdominal laparotomy, 4 (6.77%) cases were related to acute pancreatitis, 6 (10.16%) cases were CKD patients, 3 (5.08) cases were related to AKI, 4 (6.77%) cases were related to renal stenosis, 6 (10.16%) cases were related to septic shock, and 1 (1.69%) cases were related to each Acute liver failure and Cirrhosis patients. Finally, two instances (3.38 percent) were linked to Aspiration pneumoniae. The majority of cases are related with Central Nervous System manifestations, accompanied by Gastrointestinal, Liver manifestations, Kidney diseases, and septic shock, with a low predisposition to Aspiration pneumonia, as shown in the table and figure below.

Disorders	No. of VAC cases	Percentage relation (%)
Basal ganglia bleed	5	8.47
Encephalitis	7	11.86
Meningitis	5	8.47
Obstructive hydrocephalus	4	6.77
Subdural hematoma	6	10.16
P/o/c/o abdominal laparotomy	5	8.47
Acute pancreatitis	4	6.77
CKD	6	10.16
AKI	3	5.08
Renal stenosis	4	6.77
Septic Shock	6	10.16
Acute liver failure	1	1.69
Cirrhosis	1	1.69
Aspiration Pneumonia	2	3.38
Total	**59**	100

Table 12: Shows Disease relation of IVAC Cases (n=59)

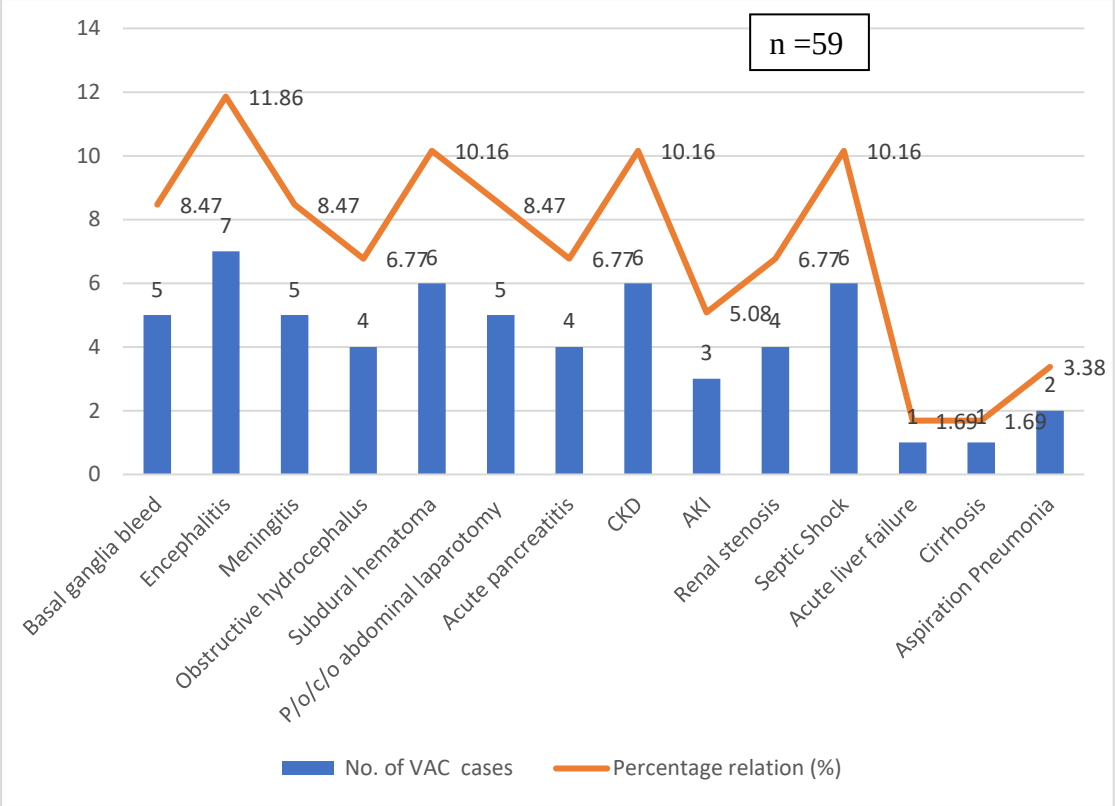


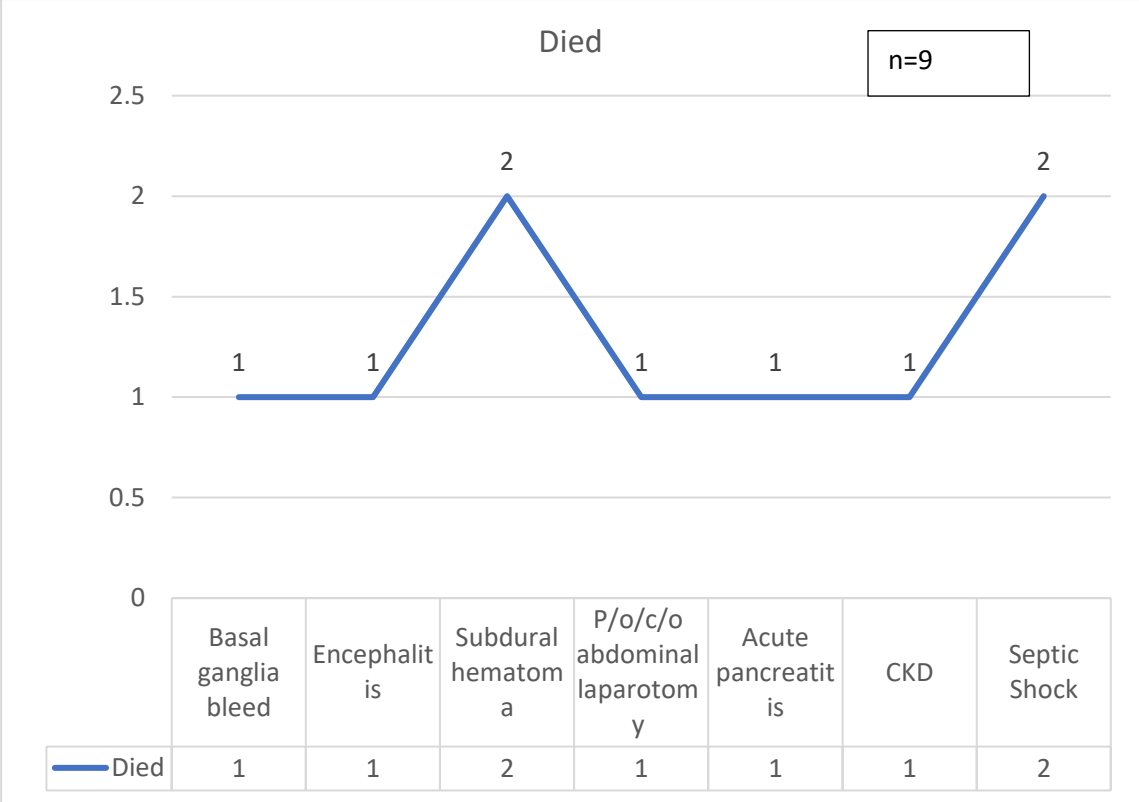
Figure 22: Graphical presentation of Disease relation of IVAC cases (n=59).

Characterisation of Disease association, IVAC and Survival outcome/Died:

Table 13 and graph 4 demonstrate that 9 (15.25 percent) IVAC patients died whereas 50 (84.75 percent) survived. According to the following table and graph, one (11.11 percent) case was associated with Basal ganglia bleed, one (11.11 percent) case was associated with Encephalitis, two (22.22 percent) cases were related to Subdural hematoma, one (11.11 percent) case each was associated with post-operative abdominal laparotomy, acute pancreatitis, CKD, and finally two (22.22 percent) cases were related to septic shock. This clearly indicated that the majority of deaths were due to CNS manifestations, followed by GIT manifestations, Septic shock, and Kidney illness.

Disorders	No. of IVAC cases	Survived	Died
Basal ganglia bleed	5	4	1
Encephalitis	7	6	1
Meningitis	5	5	0
Obstructive hydrocephalus	4	4	0
Subdural hematoma	6	4	2
P/o/c/o abdominal laparotomy	5	4	1
Acute pancreatitis	4	3	1
CKD	6	5	1
AKI	3	3	0
Renal stenosis	4	4	0
Septic Shock	6	4	2
Acute liver failure	1	1	0
Cirrhosis	1	1	0
Aspiration Pneumonia	2	2	0
Total	59	50	9 (15.25%)

Table 13: Characterisation of Disease association, IVAC Events and Survival outcome/Died.



Graph 4: Disease correlation and Survival outcome/Died.

Cultural Characterization of IVAC:

According to the study and figure 23, 59 (n=59) people had IVAC, and their respiratory samples were taken. Out of the 59 IVAC cases, 56 (94.91%) endotracheal aspirate (ETA) and 3 (5.08%) bronchoalveolar lavage (BAL), both of which were taken and sent to the lab for microbiological diagnosis. In those 56 (ETA sample), 20 (35.714) samples show no microorganism growth, 15 (26.78) samples show insignificant growth (10 colony was NLF, 4 LF mucoid, and 1 LF flat colony), 21 (37.50 percent) samples showed more than 3 types of colonies (mixed microorganism growth), and those 3 BAL samples show no microorganism growth, all of which were not correlated with PVAP CDC criteria for VAE surveillance.

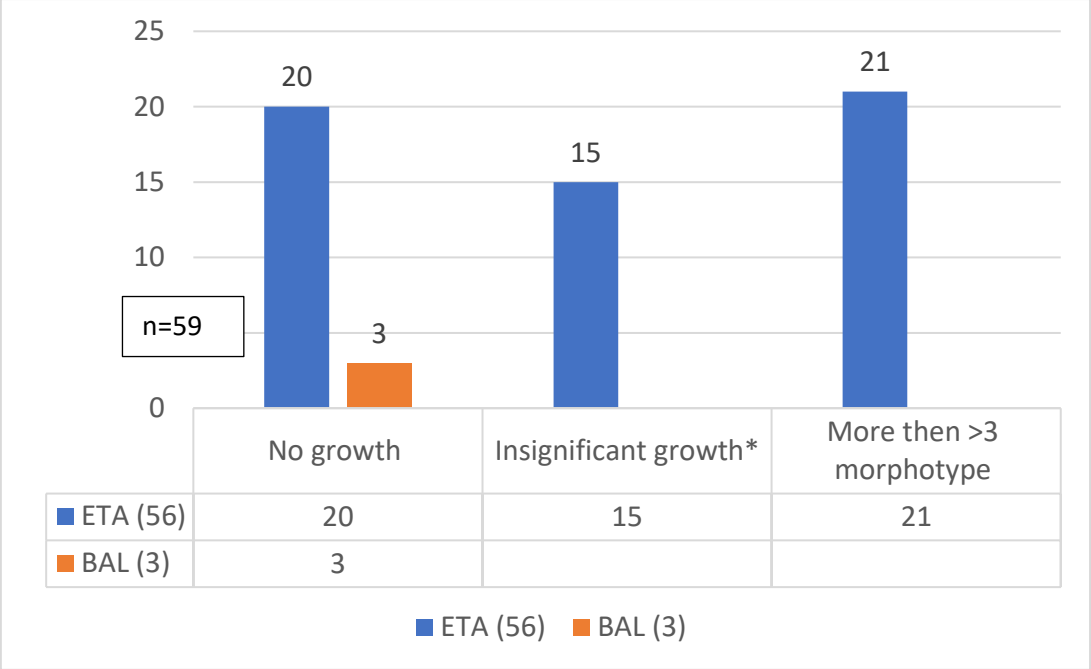


Figure 23: Cultural Characterisation of IVAC Events/Cases.
* (10 NLF colony, 4 LF mucoid and 1 LF Flat)

Possible Ventilator Associated Pneumonia (PVAP) Characteristics:

PVAP Incidence:

According to the research, 386 patients were on MV, 196 had VAE, and 125 (63.77 %) developed PVAP, compared to the other events, that were IVAC 59 (30.10 %), and VAC, 12 (6.12 %), as shown in diagram 2.

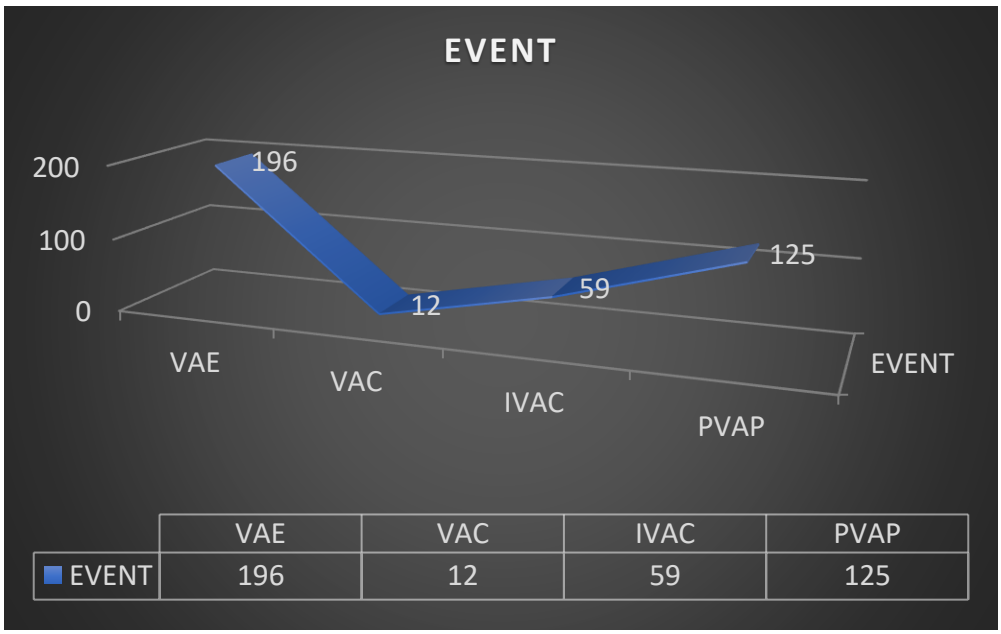


Diagram 2: Depicting correlation between total VAE, VAC Events, IVAC and PVAP

PVAP Rate:

PVAP is 35.39 VAE/1000 mechanical ventilation days in this study, compared to 16.7 VAE/1000 mechanical ventilation days for IVAC and 3.4 VAE/1000 mechanical ventilation days for VAC (Following figure 24 shows the correlation between the rate of VAC, IVAC and PVAP). PVAP had the highest rate, accompanied by IVAC and VAC, according to the study.

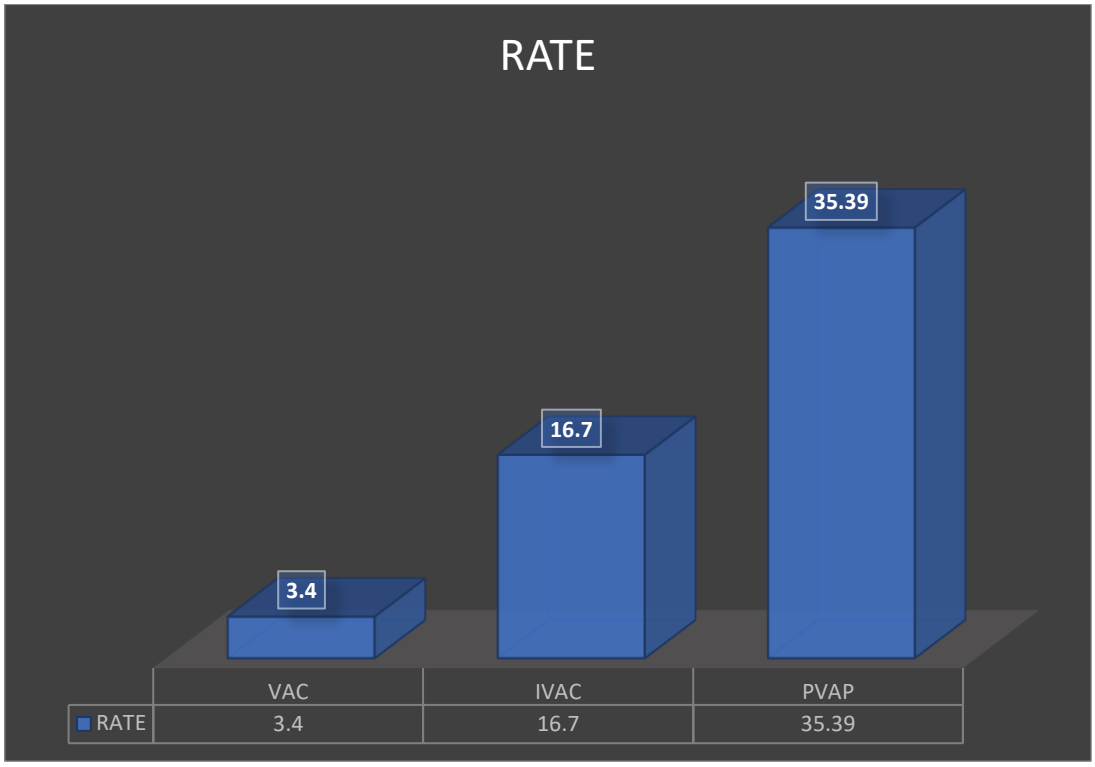
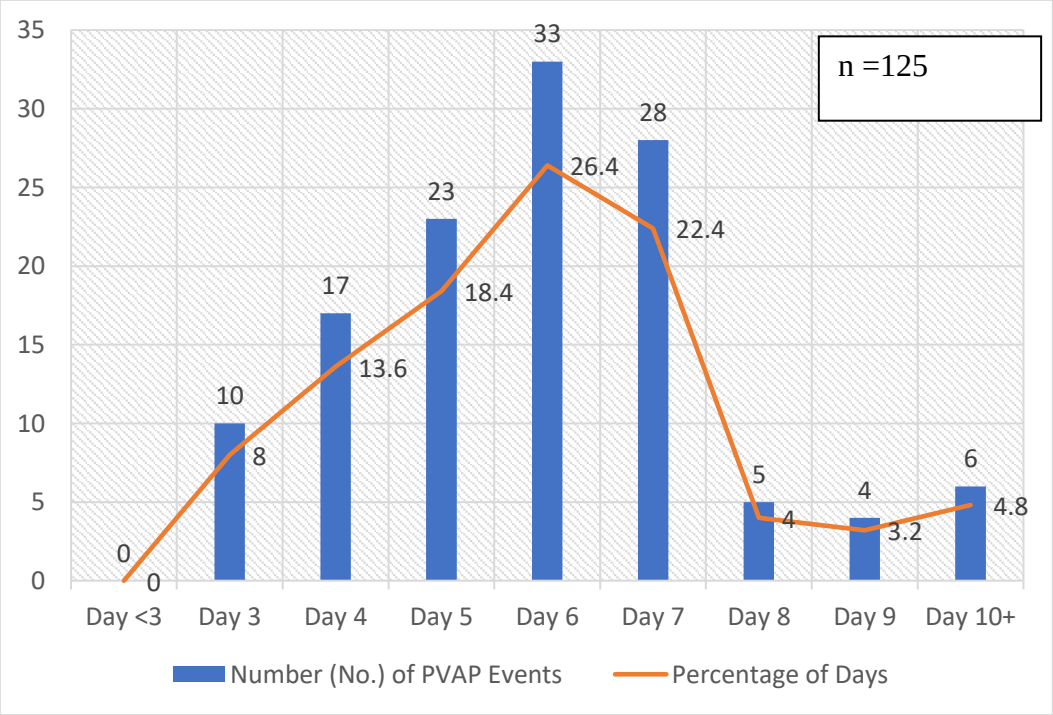


Figure 24: The Rate of PVAP in correlation with IVAC and VAC.

PVAP Event onset Correlation with Time from Intubation/Mechanical Ventilation:

According to Graph 5, out of 125 (n=125) cases that develop PVAP, 10 (8 %) events occur on Day 3, 17 (13.60 %) events occur on Day 4, 23 (18.4 %) events occur on Day 5, 33 (26.4 %) events occur on Day 6, 28 (22.4 %) events occur on Day 7, 5 event (4 %) events occur on Day 8, and 4 (%) events occur on Day 9 and 6. (1 event on 10th day of ventilation, 1 event on Day 11, 2 events on day 13 and 2 event on Day 15). According to the study, the majority of the events occur between Days 4 and 7.



Graph 5: Correlation between Percentage of Days and Number (No.) of PVAP Events.

Criteria Used to Report PVAP:

Increase in Temperature (>38°C) and WBC (>12000):

In this study, 19 (15.20 %) of the 125 (n=125) patients with PVAP showed an increase in Temperature/Temp (>38°C) and 94 (75.20 %) cases showed an increase in WBC (>12000), while 12 (9.60 %) cases had an increase in both Temperature/Temp (>38°C) and WBC (>12000). This was depicted in the diagram 3 below. The accompanying diagram 3 depicts a rise in WBC (>12000) followed by an increase in temperature (>38°C) in the majority of instances

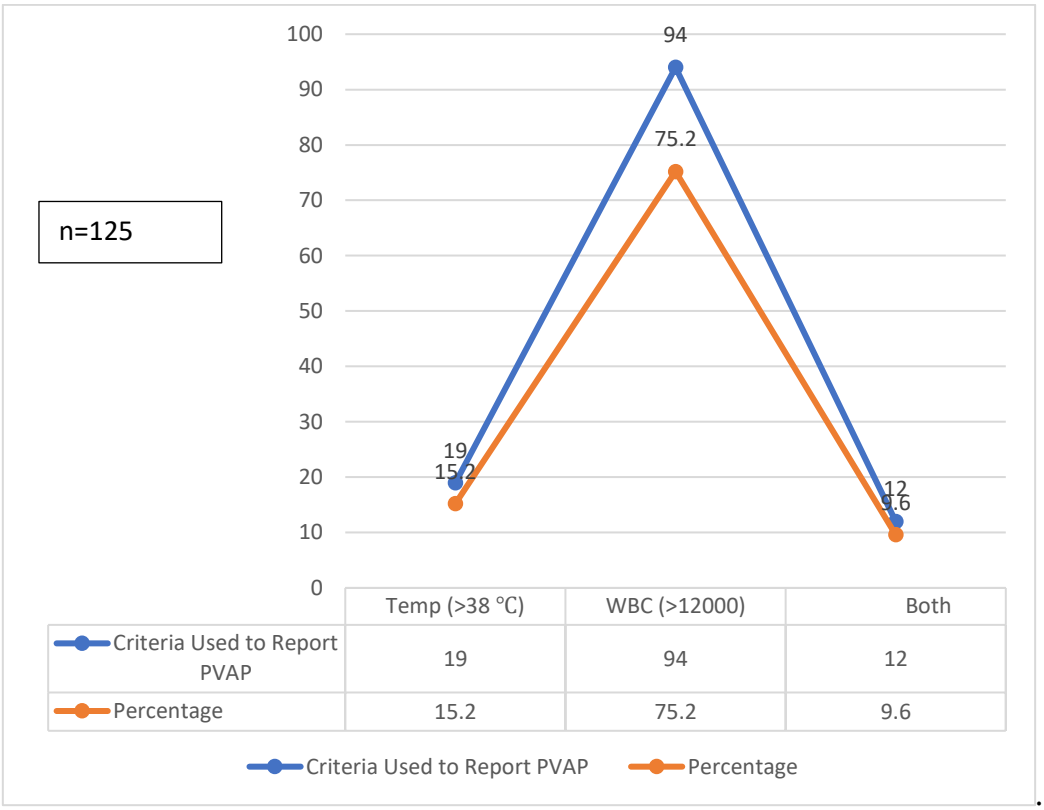


Diagram 3: Showing percentage correlation of Criteria used to Report PVAP

Change of antibiotics (>4 Qualifying antibiotics days):

PVAP occurs in 125 (n=125) patients in this research. In 16 of the 125 instances, the antibiotic was switched from Ceftriaxone (which was used for three days) to Piperacillin-Tazobactam (which was administered for more than four days). The first antibiotic n=125 following 68 instances was Piperacillin-Tazobactam (2 days), which was then changed to Meropenem, which qualified >4 Qualifying antibiotics days to meet the PVAP Criteria. The other 41 cases were treated with Piperacillin-Tazobactam for two days before being switched to Meropenem for another two days before being switched to Colistin to meet the PVAP criteria of >4 qualifying antibiotic days. F The diagram below depicts the relationship between the number of PVAP events and the change of antibiotics (>4 days of qualifying drugs). The following diagram 4 was used to illustrate this.

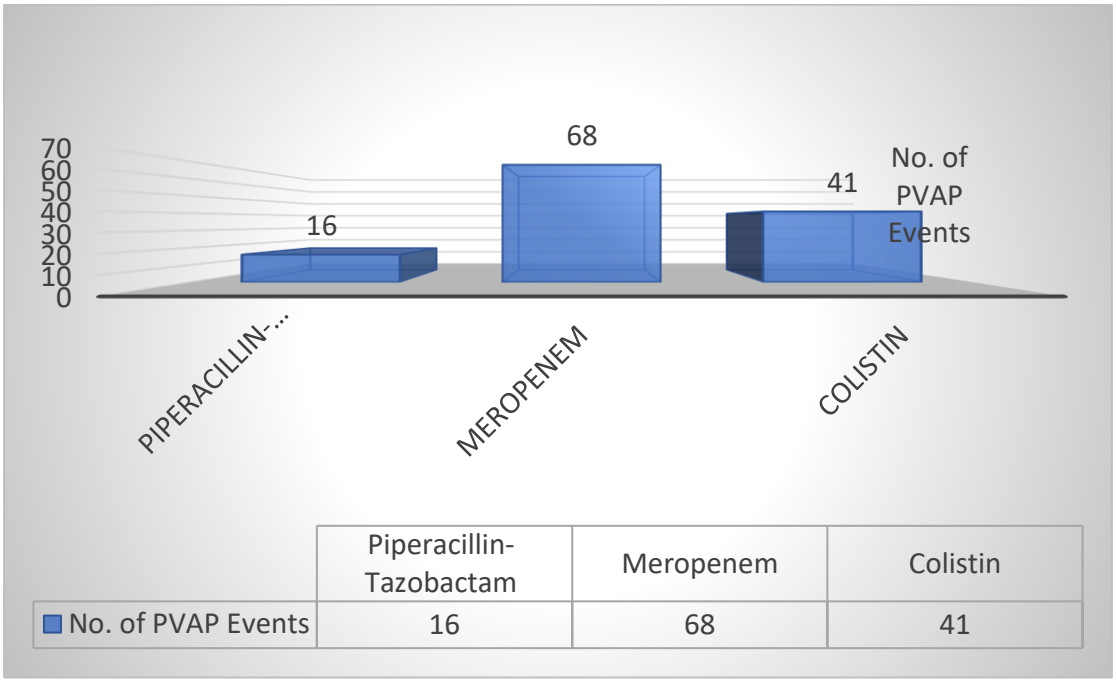


Diagram 4: Association between No. of PVAP Events and Change of antibiotics (>4 Qualifying antibiotics days)

Bacteriological Identification/Isolation of PVAP Cases:

According to the study, 120 (96%) ETA samples and 5 (4%) BAL samples were collected and analysed for microbiological identification. Bacteria were recovered from 124* of the 120 ETA samples tested (4 ETA samples shows growth of 2 organism each). Bacteria were recovered from 5** of the 5 BAL samples that were taken. There are 129 bacterial isolates in all. (*$\geq 10^5$ CFU/ml, **$\geq 10^4$ CFU/ml).

According to the following figure 25 and graph 6, 96 isolates were NLF and 33 were LF. Of the 96 NLF, 86 (66.66%) were *Acinetobacter baumannii* (84 isolated from ETA and 2 isolated from BAL), 29 (22.48%) were *Klebsiella pneumoniae* (28 isolated from ETA and 1 isolated from BAL), 10 (7.75%) were *Pseudomonas aeruginosa* (8 isolated from ETA and 2 isolated from Figure 24 and graph 6 show that *Acinetobacter baumannii* was the most often isolated organism (66.66 percent), followed by *Klebsiella pneumoniae* (22.48 %), *Pseudomonas aeruginosa* (7.75 %), and *Escherichia coli* (3.1 %).

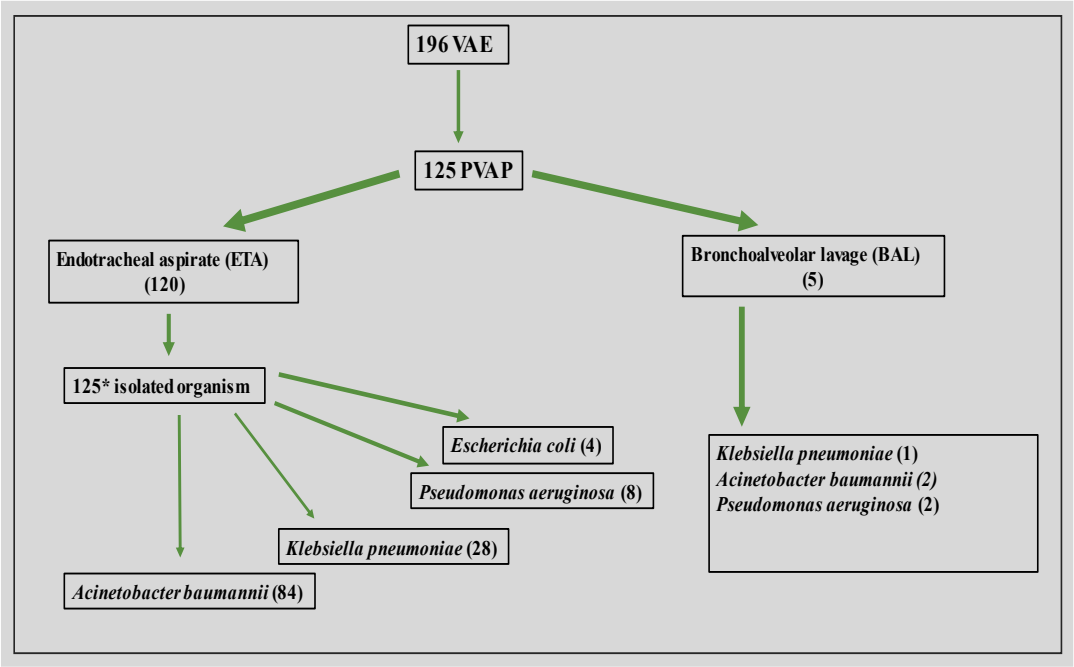
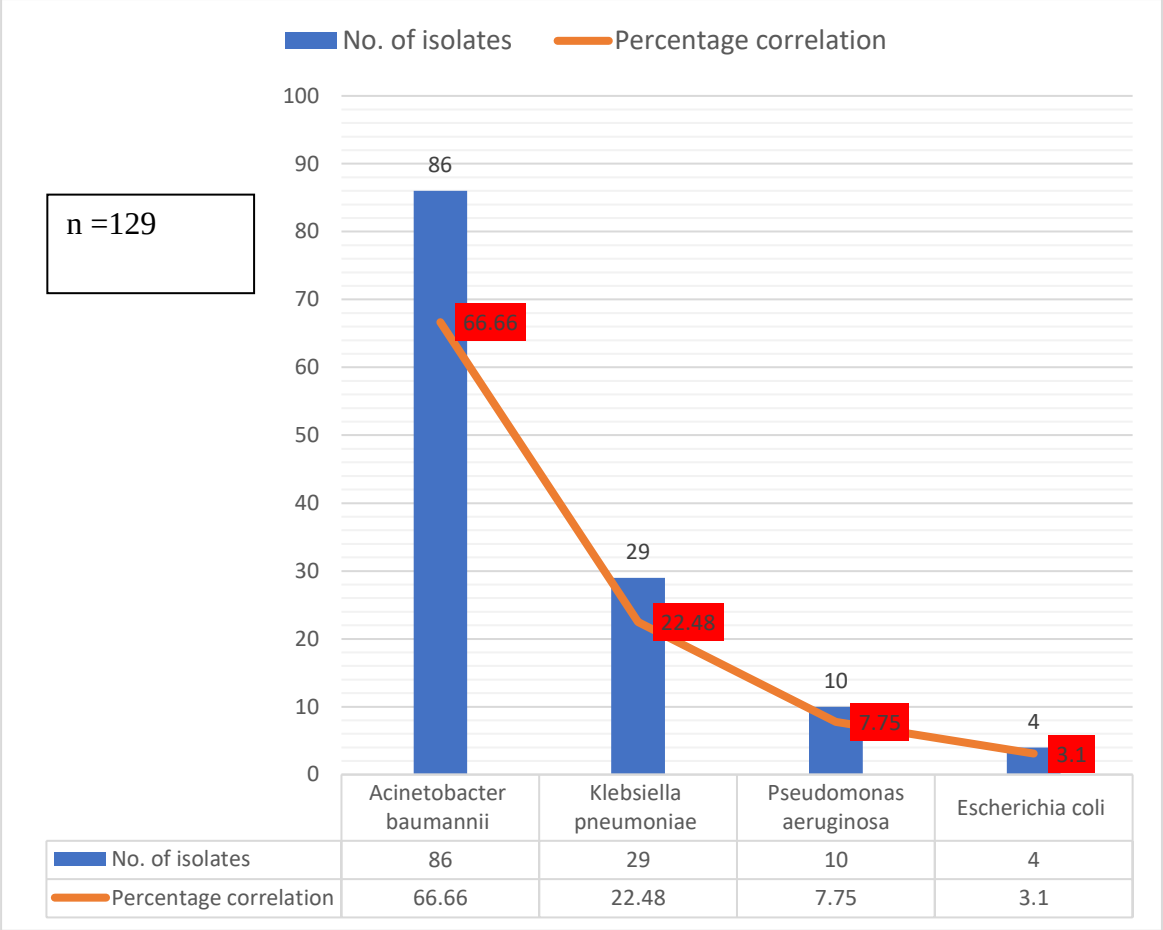


Figure 25: Bacterial isolation obtained from ETA and BAL

*4 ETA aspirate shows growth of 2 microorganism each, one was *Acinetobacter baumannii* and other was *Klebsiella pneumoniae each*.



Graph 6: Percentage association of number of bacterial isolates obtained.

Antibiotic susceptibility (AST) Profile of Individual Isolates:

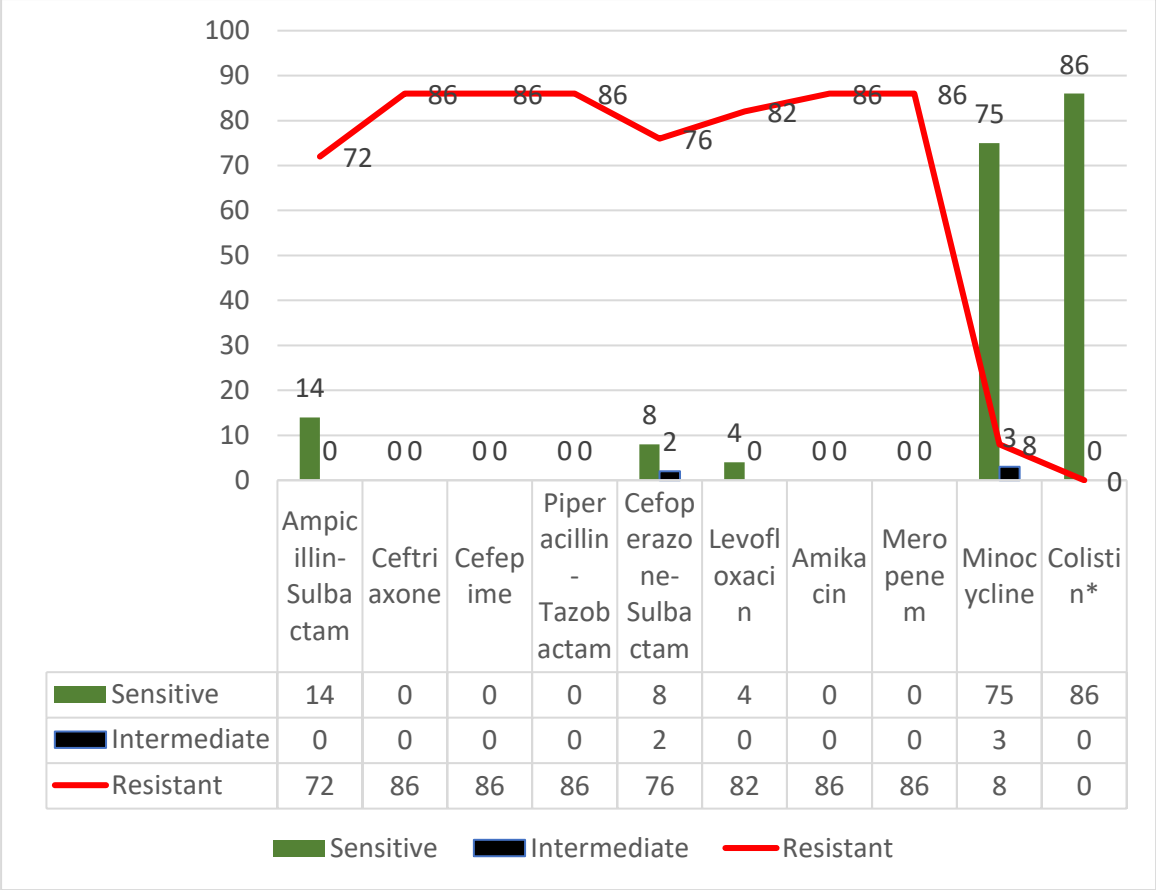
***Acinetobacter baumannii* (n=86)**:

According to table 14 and graph 7, 86 Acinetobacter baumannii isolates were found; 14 isolates were sensitive to Ampicillin-Sulbactam and 72 isolates were resistant; 8 isolates were sensitive, 2 isolates were intermediate, and 76 isolates were resistant to Cefoperazone-Sulbactam; 4 isolates were sensitive and 82 isolates were resistant to Levofloxacin; 75 isolates were sensitive, 3 isolates were intermediate, and 8 isolates were resistant to Minocycline, 86 isolates were sensitive to Colistin. Ceftriaxone, Cefepime Piperacillin-Tazobactam, Amikacin, and Meropenem resistance had been found in all isolates.

Antibiotics	Sensitive	Intermediate	Resistant
Ampicillin-Sulbactam	14	0	72
Ceftriaxone	0	0	86
Cefepime	0	0	86
Piperacillin-Tazobactam	0	0	86
Cefoperazone-Sulbactam	8	2	76
Levofloxacin	4	0	82
Amikacin	0	0	86
Meropenem	0	0	86
Minocycline	75	3	8
Colistin*	86	0	0

Table 14: Antibiotic susceptibility profile (AST) of *Acinetobacter baumannii.*

*By Colistin Disc Elution test



Graph 7: Graphical presentation of AST of *Acinetobacter baumannii* *By Colistin Disc Elution test.

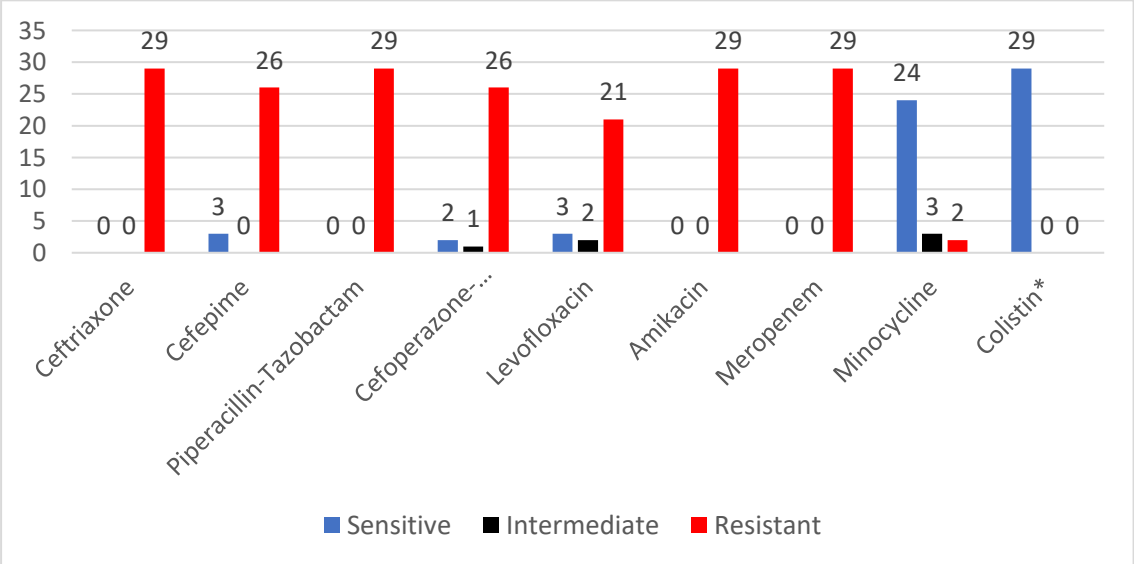
***Klebsiella pneumoniae* (n=29):**

According to table 15 and graph 8, two Klebsiella pneumoniae isolates were sensitive to Cefoperazone-Sulbactam, one isolate was intermediate, and 26 isolates were resistant to Cefoperazone-Sulbactam, three isolates were sensitive, two isolates were intermediate, and 24 isolates were resistant to Levofloxacin, 24 isolates were sensitive, three isolates were intermediate, and two isolates were resistant to Minocycline, and all 29 isolates were sensitive to Colistin. Ceftriaxone, Cefepime, Piperacillin-Tazobactam, Amikacin, and Meropenem resistance were found in all 29 isolates.

Antibiotics	Sensitive	Intermediate	Resistant
Ceftriaxone	0	0	29
Cefepime	0	0	29
Piperacillin-Tazobactam	0	0	29
Cefoperazone-Sulbactam	2	1	26
Levofloxacin	3	2	24
Amikacin	0	0	29
Meropenem	0	0	29
Minocycline	24	3	2
Colistin*	29	0	0

Table 15: Antibiotic susceptibility profile (AST) of *Klebsiella pneumoniae.*

*By Disc Elution test.



Graph 8: Graphical presentation of AST of *Klebsiella pneumoniae*

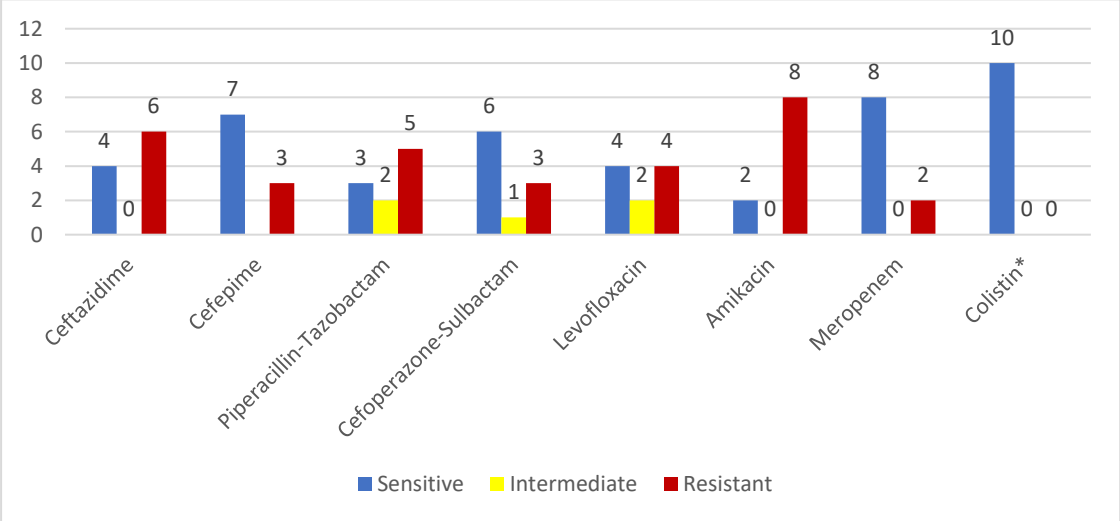
*By Colistin Disc Elution test.

***Pseudomonas aeruginosa* (n=10):**

According to table 16 and graph 9, ten Pseudomonas aeruginosa isolates were isolated; four isolates were sensitive and six isolates were resistant to Ceftazidime ; seven isolates were sensitive and three isolates were resistant to Cefepime; three isolates were sensitive, two isolates were intermediate, and five isolates were resistant to Piperacillin-Tazobactam; four isolates were sensitive, two isolates were intermediate, and four isolates were resistant to Levofloxacin, 2 isolates were susceptible to Amikacin and 6 isolates were resistant to it; 8 isolates were sensitive to Meropenem and 2 isolates were resistant to it; and all isolates were sensitive to Colistin.

Antibiotics	Sensitive	Intermediate	Resistant
Ceftazidime	4	0	6
Cefepime	7	0	3
Piperacillin-Tazobactam	3	2	5
Cefoperazone-Sulbactam	6	1	3
Levofloxacin	4	2	4
Amikacin	2	0	8
Meropenem	8	0	2
Colistin*	10	0	0

Table 16: Antibiotic susceptibility profile (AST) of *Pseudomonas aeruginosa.*
* By Colistin Disc Elution test.



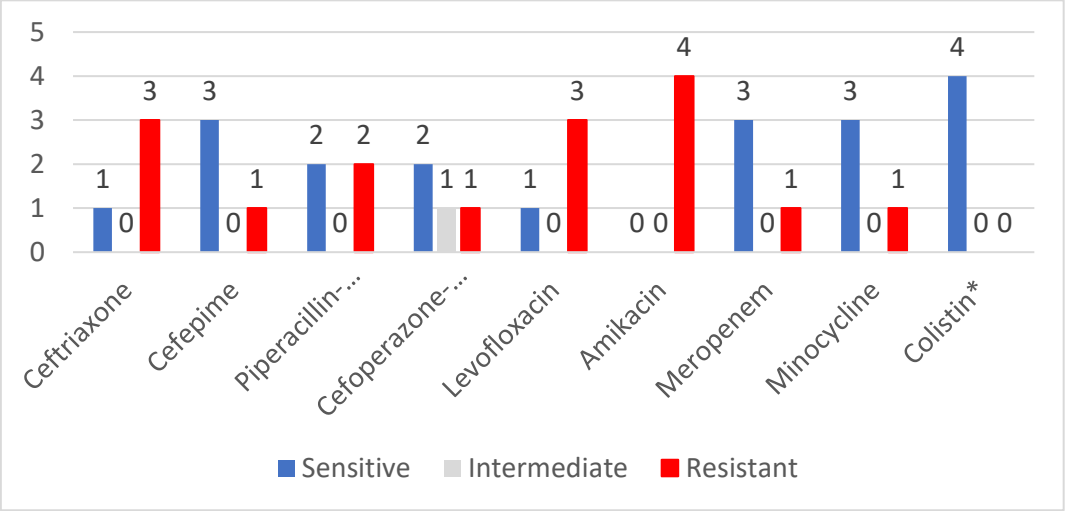
Graph 9: Graphical presentation of AST of *Pseudomonas aeruginosa*
*By Disc Elution test.

***Escherichia coli (n=4)* :**

According to the following table 17 and graph 10, 4 *Escherichia coli* were isolated, out of these 4 isolated organism, 1 isolate was sensitive and 3 isolate was resistant to Ceftriaxone, 3 isolate was sensitive and 1 isolate was resistant to Cefepime, 2 isolate was sensitive and 2 isolate are resistant to Piperacillin-Tazobactam, 2 isolate was sensitive, 1 isolate was intermediate and 1 isolate was resistant to Cefoperazone-Sulbactam, 1 isolate was sensitive and 3 isolate was resistant to Levofloxacin, 4 isolate was resistant to Amikacin, 3 isolate was sensitive and 1 isolate was resistant to Meropenem, 3 isolate was sensitive and 1 isolate was resistant to Minocycline and all 4 isolate was sensitive to Colistin.

Antibiotics	Sensitive	Intermediate	Resistant
Ceftriaxone	1	0	3
Cefepime	3	0	1
Piperacillin-Tazobactam	2	0	2
Cefoperazone-Sulbactam	2	1	1
Levofloxacin	1	0	3
Amikacin	0	0	4
Meropenem	3	0	1
Minocycline	3	0	1
Colistin*	4	0	0

Table 17: Antibiotic susceptibility profile (AST) of *Escherichia coli.*
* By Colistin Disc Elution test.



Graph10: Graphical presentation of AST of *Escherichia coli*
* By Disc Elution test.

Age Association of PVAP (n=125):

In this study, age group and its association with the PVAP Events are depicted in the following figure 26. According to the figure, 36 (28.8%) patients were between the age of 20-40 years, 57 (45.6%) patients were between 40-60 years, 32 (25.6%) patients were >60 years depicted.

According to the following figure, most common age associated with PVAP are 40-60 years same as with respect to IVAC , followed by 20-40 years age group and with age group > 60 years.

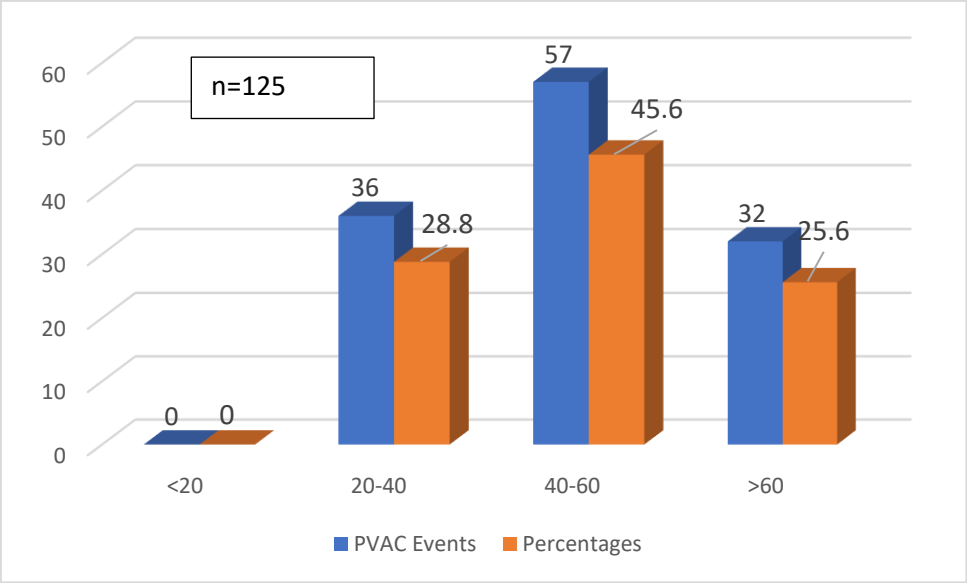


Figure 26: Percentage Characterisation of Age Association of PVAP Events

Disease relation of PVAP Cases (n=125):

According to the following table 18, 8 (6.4%) cases was related with Basal ganglia bleed, 11 (8.8%) case was associated with Encephalitis, 13 (10.4%) cases was associated with meningitis (3 bacterial, 10 viral), 7 (5.6%) cases was associated with obstructive hydrocephalus, 10 (8%) cases was associated with subdural hematoma, 8 (6.4%) cases were a post operative case of abdominal laparotomy, 3 (2.4%) cases of colon cancer, 3 (2.4%) case was associated with acute pancreatitis, 23 (18.4%) was CKD patients, 17 (13.6) was related to AKI, 3 (2.4%) cases was related to renal stenosis, 10 (8%) cases was related to septic shock, 2 (1.6%) cases each related to acute liver failure and cirrhosis patients. Lastly 5 (4%) cases were associated with aspiration

pneumoniae. As per the following table, most of the cases are associated with Central Nervous System manifestation followed by Gastrointestinal and Liver manifestation then followed by Kidney disorders and septic shock patient with low predisposition to aspiration pneumoniae patients.

Disorders	No. of PVAP cases	Percentage relation (%)
Basal ganglia bleed	8	6.4
Encephalitis	11	8.8
Meningitis	13	10.4
Obstructive hydrocephalus	7	5.6
Subdural hematoma P/o/c/o abdominal laparotomy	10 8	8 6.4
Colon carcinoma	3	2.4
Acute pancreatitis	3	2.4
CKD	23	18.4
AKI	17	13.6
Renal stenosis	3	2.4
Septic Shock	10	8
Acute liver failure	2	1.6
Cirrhosis	2	1.6
Aspiration Pneumonia	5	4
Total	125	100

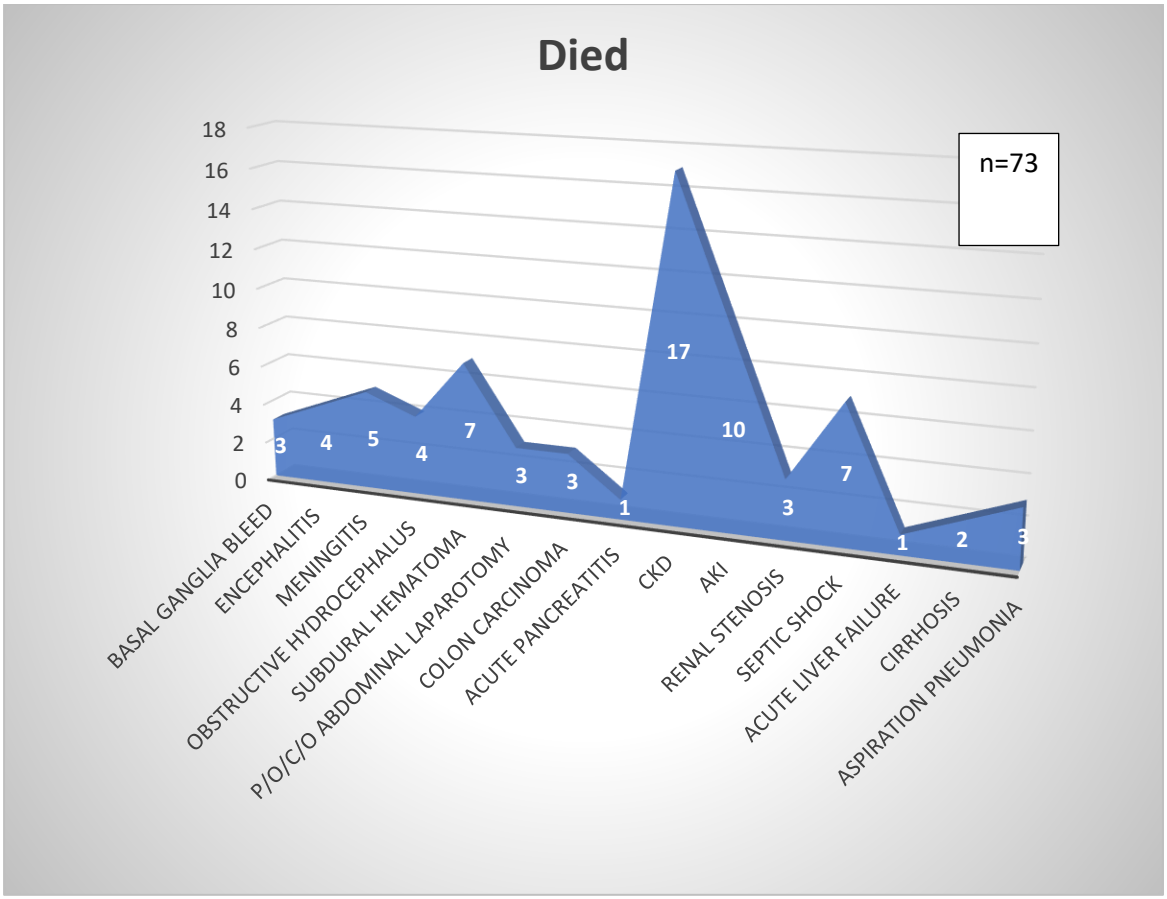
Table 18: Shows Disease relation of PVAP Cases (n=125)

Characterisation of Disease association, PVAP Events and Survival outcome/Died:

According to the following table 19 and graph 11, 73 PVAP Event patients (58.4 %) died. Out of the 73 PVAP cases, 3 (4.1 percent) were associated with Basal ganglia bleed, 4 (5.47 %) with Encephalitis, 5 (6.84 percent) and 4 (5.47 %) with Meningitis and Obstructive hydrocephalus, respectively, 7 (13.20 percent) with Subdural hematoma, 3 (4.1%) with post-operative abdominal laparotomy, 3 (4.1%) cases with colon carcinoma, 1 (1.36%) case of acute pancreatitis, 23 (31.50%), 10 (13.69%) was associated to CKD and AKI respectively. Finally, 3 (4.1 percent), 7 (9.58 percent), 1 (1.36 percent), 2 (2.73 percent), and 3 (4.1 percent) were related to septic shock, acute liver failure, cirrhosis, and aspiration pneumonia, respectively. The following table and graph clearly showed that the majority of cases who died were mostly related to Central Nervous System manifestation accompanied by CKD and AKI.

Disorders	No. of PVAP cases	Survived	Died
Basal ganglia bleed	8	5	3
Encephalitis	11	7	4
Meningitis	13	8	5
Obstructive hydrocephalus	7	3	4
Subdural hematoma	10	3	7
P/o/c/o abdominal laparotomy	8	5	3
Colon carcinoma	3	0	3
Acute pancreatitis	3	2	1
CKD	23	6	17
AKI	17	7	10
Renal stenosis	3	0	3
Septic Shock	10	3	7
Acute liver failure	2	1	1
Cirrhosis	2	0	2
Aspiration Pneumonia	5	2	3
Total	125	52	73

Table 19: Characterisation of Disease association, PVAP Events and Survival outcome/Died



Graph 11: Disease correlation and Survival outcome/Died

Isolated organisms relation (PVAP) with survival outcome/Died:

According to the study, a total of 82 patients died and 52 patients survived among 129 instances of isolated organism. Of the 82 patients who died, 73 (89.02 percent) were connected with PVAP events and 9 (10.97 percent) were related with IVAC events, as shown in Figure 27.

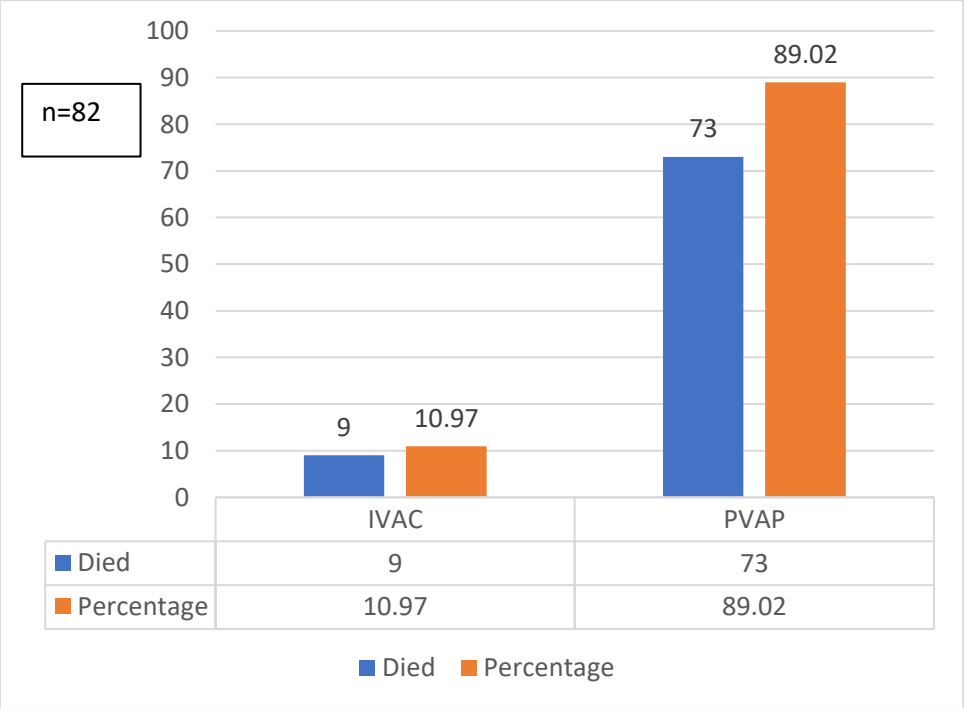


Figure 27: Percentage correlation of survival outcome with IVAC and PVAP

Acinetobacter baumannii was recovered in 51 (69.86%) of the 73 patients who died from PVAP, *Klebsiella pneumoniae* was found in 19 patients (26.02%), *Pseudomonas aeruginosa* was isolated in 2 (2.73%) patients, and *Escherichia coli* was isolated in 1 (1.37%) patient. According to the figure, *Acinetobacter baumannii* was the most prevalent bacteria linked to mortality, followed by *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Escherichia coli*. *Acinetobacter baumannii* was recovered in 31 (59.61 percent) of the 52 survivors, *Klebsiella pneumoniae* in 10 (19.23 percent), *Pseudomonas aeruginosa* in 8 (15.38 percent), and *Escherichia coli* in 3 (5.76 percent), as shown in figure 28.

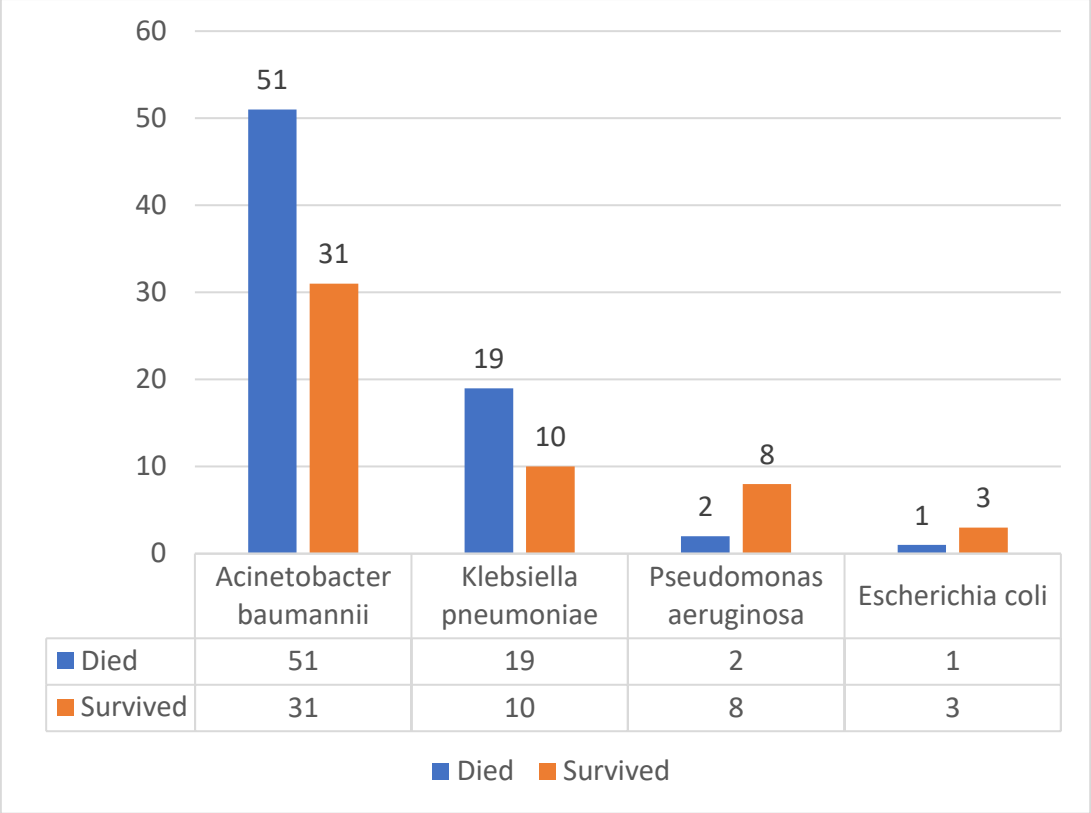


Figure 28: Showing Bacterial isolates and its relation with Survival /Outcome

Secondary Blood stream infection (BSI):

According with this research, 196 patients develop VAEs and 125 patients develop PVAP. Of the 125 PVAP events, 65 (52 percent) cause secondary BSI (same organism also isolated in blood culture). In those 65 cases, the most common organism isolated was Acinetobacter baumannii 46 (70.76%), followed by Klebsiella pneumoniae 15 (23.07%), Pseudomonas aeruginosa 3 (4.61%), and *Escherichia coli* 1 (1.53%).

Secondary BSI was found to be common in 33.16 percent of cases.

The percentage association between the organisms that cause BSI is shown in Figure 29.

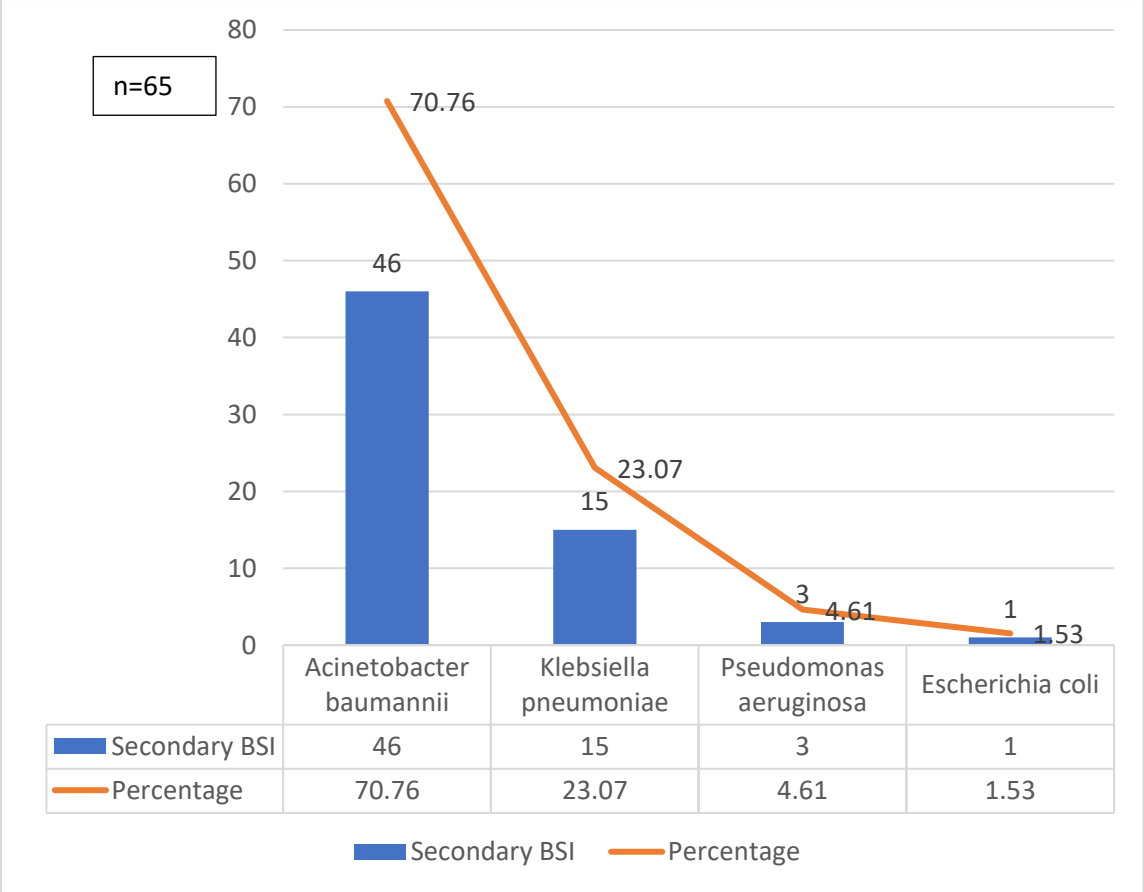


Figure 29: Percentage correlation between organism causing BSI

DISCUSSION

Classically, the most prevalent complexities of Mechanical Ventilation (MV) have been accounted for as ventilator-related respiratory infections (VARI) with unsatisfactory consequences [80]. The Centers for Disease Control and Prevention (CDC) categorised MV uncertainties in 2013, using FiO2 and PEEP as surrogate proportions of hypoxemia, avoiding the chest radiograph as symptomatic guidelines, and considering both infectious and non-infectious inconveniences for surveillance [81].

VAE rate/incidence among different studies and comparison with the present study

The rate/incidence of VAE, its microbiological isolation, and its antibiotic susceptibility are all detailed in this study. The majority of individuals transferred to ICUs needed MV, according to this research. When compared to other studies, the rate of VAEs among 386 patients on MV was quite high, with only 196 patients (50.7 %) meeting the criteria for VAE (55.49 per 1000 ventilator-days). According to He Q et al. [82], Pouly O et al. [83], Wolffers, O et al. [84], Sharma A et al. [85], the rate of VAE was 9.06 %, 21.43 %, 15.90 %, and 37% , respectively, which was comparatively low in contrast to the current study, as shown in figure 30.

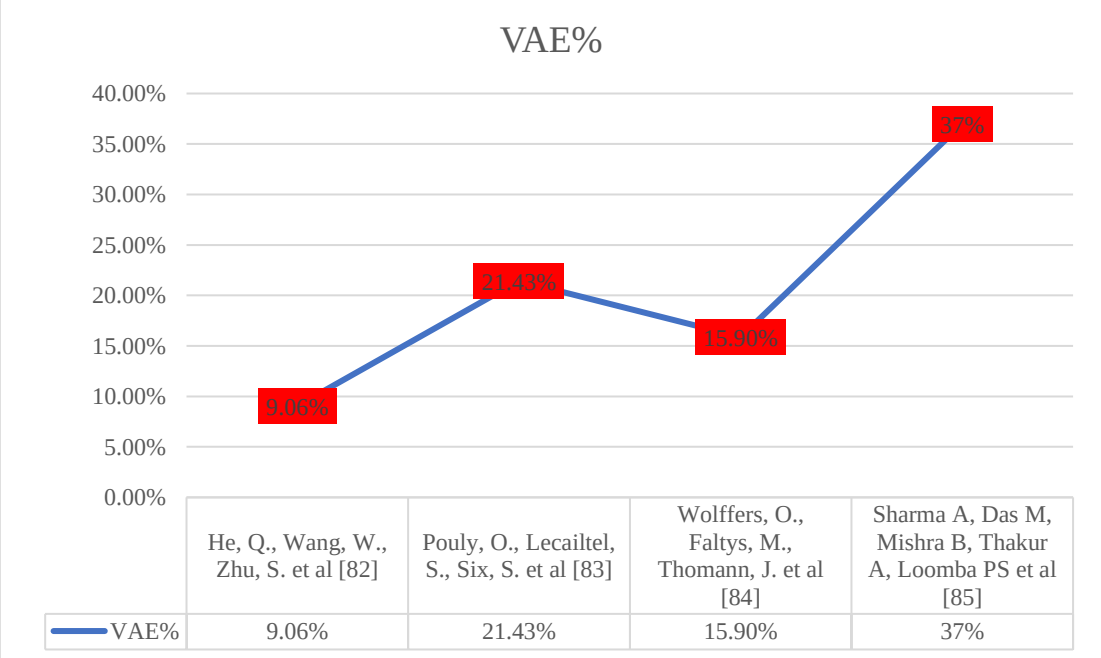


Figure 30: Percentage of the VAE events in other studies

When comparing the findings of this study to those of other researches, as per this research, we find that 3.1 % develops VAC (3.4 per 1000 ventilator days), 15.28 % develops IVAC (16.7 per 1000 ventilator days), and 32.38 % develops PVAP (35.39 per 1000 ventilator days). According to He Q et al. [82], the rate of VAC was 28.5 per 1000 ventilator-days, the rate of IVAC was 4 per 1000 ventilator-days, and the rate of PVAP was 1.64 per 1000 ventilator-days, and according to Wolffers O et al. [84], the rate of VAC was 16.7 per 1000 ventilator-days, the rate of IVAC was 6.4 per 1000 ventilator-days, and the rate of PVAP was 2.9 per 1000 ventilator-days, according to Sharma A et al. [85], the rate of VAC was 6.7 per 1000 ventilator-days, the rate of IVAC was 11.57 per 1000 ventilator-days, and the rate of PVAP was 5.7 per 1000 ventilator-days, in comparison to the current study, all of the aforementioned rates were quite low as depicted in following figure 31 and table 20. According to the study done in China [82] and Switzerland [84], there is indeed a lower rate of VAE and a lower percentage of VAE occurrences globally, as shown in China and Europe [82,84]. When we look at the situation in India, it appears that the rate of VAEs is higher, as evidenced by this study and previous studies done in India [85].

Because of the tenuous link between VAE and the traditional meaning of VAP, the new approach has been widely researched in the United States, followed by Europe, and is mostly used for observation. In any event, VAE isn't meant to be a stand-in for VAP; rather, it was created with the intention of broadening surveillance beyond pneumonia to include problems associated with mechanical ventilation in medical settings [82, 83, 84, 85].

This study was based on a routinely scheduled monitoring framework, which is up until this point is one of a important research in India regarding VAE. Through proper review and comparison, it is doubtful to miss VAE cases, and the analysis of VAE has been approved as somewhat accurate.

VAE is a relatively recent calculation that addresses difficulties connected to ventilation, including but not limited to VAP. This is quite different from the traditional approach of dealing with VAP alone, and subsequently deals difficulties for the long-standing reasoning example and practice schedules in tolerant consideration. More research is needed to demonstrate the preventability of VAE and its clinical impact on long-term outcomes in diverse countries and patient populations. These findings will

most likely result in a more effective, persuasive, and patient-centered (not just for surveillance purposes) tool to demonstrate the clinical relevance of VAE. In the meanwhile, because VAE is simple and straightforward to implement, we advise physicians to bring VAE concerns to light and consider the rate and impact of VAE on their patients.

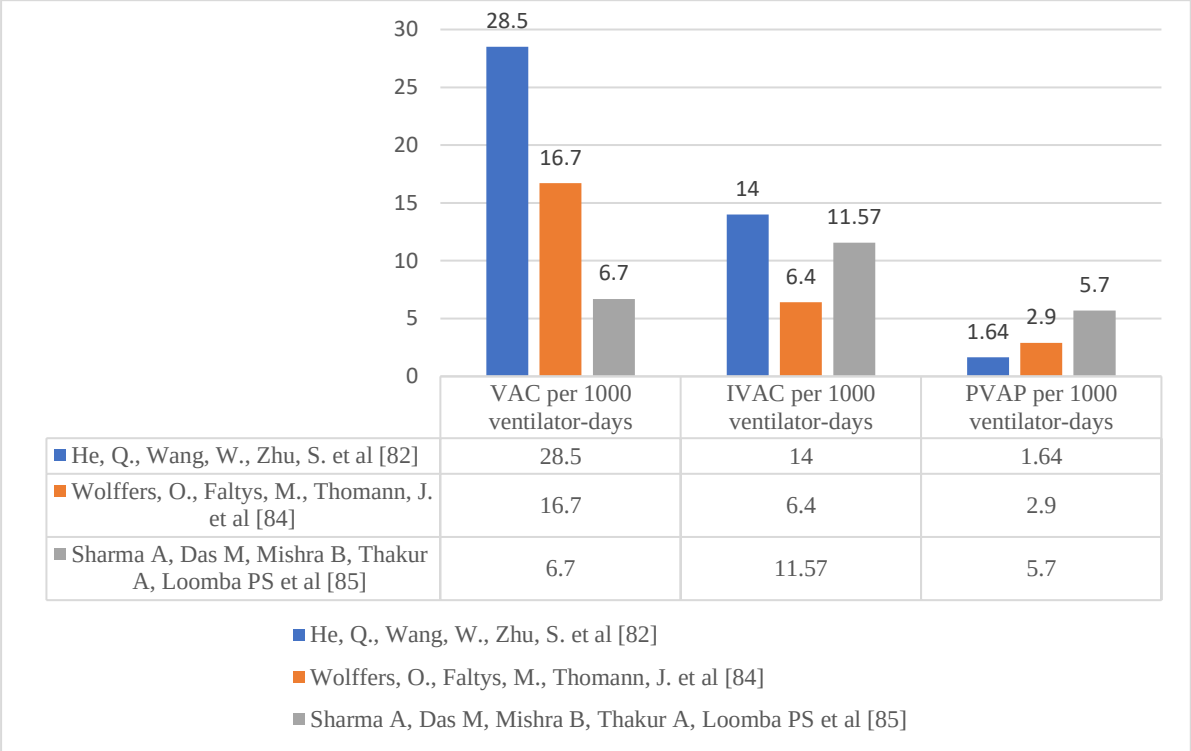


Figure 31: Correlating VAE rate in different studies

Study	VAC per 1000 ventilator-days	IVAC per 1000 ventilator-days	PVAP per 1000 ventilator-days
He, Q., Wang, W., Zhu, S. *et al.* [82]	28.5	14	1.64
Wolffers, O., Faltys, M., Thomann, J. *et al.* [84]	16.7	6.4	2.9
Sharma A, Das M, Mishra B, Thakur A, Loomba PS. e*t al.* [85]	6.7	11.57	5.7

Table 20: Correlating VAE rate in different studies

Mortality association with VAE Events and disease association:

In this study, 196 cases developed VAEs, with 125 (63.77%) developing PVAP. Among these PVAP cases, 73 (58.4%) cases died, indicating that the majority of PVAP victims perished. When we refer to the study by Sharma A et al. [85], we see that those cases with PVAP had a high death rate (77.7%), which is higher than the current study. Other studies by Thomas A et al. [86] and Rello. J et al. [87], the overall mortality rate of VAE cases was 25% and 30.7 %, respectively, when compared to our study, which showed 37.24 percent (73 died out of 196 VAEs), which was considerably greater than both [86, 87].

When we look at this review, it is clear that those patients who developed IVAC died primarily from Central Nervous System manifestations, followed by GIT manifestations, Septic shock, and Kidney issue, while those who developed PVAP died primarily from Central Nervous System manifestations, followed by Kidney failure, and GIT manifestation.

In patients with CNS manifestation, GIT manifestation, Renal failure and Septic shock that results can be a predisposing factor for VAE. Patients with CNS manifestations were routinely given powerful anaesthetic medicines for long periods of time, which might be a contributing factor to VAE.

When compared to other research throughout the world, there is a paucity of data linkage between mortality and VAE Events and illness relationship [85, 86, 87].

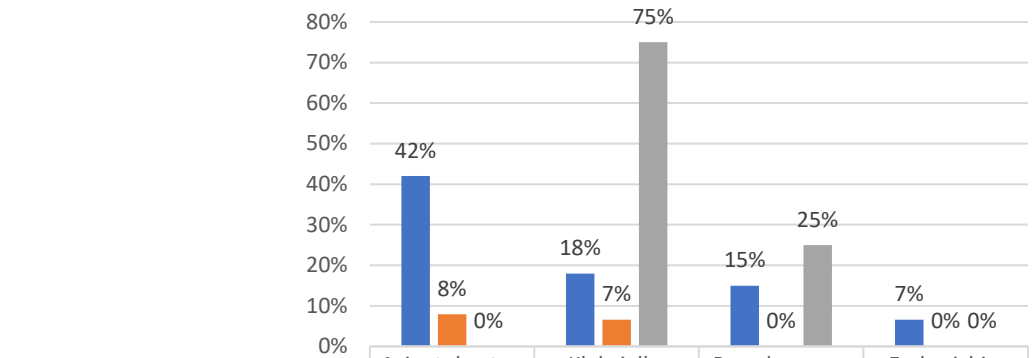
Age association of events:

According to this study, the most prevalent age group related with VAE Events is 40-60 years, next 20-40 years, and finally > 60 years. When we compare this study to Rello. J et al. [87], we find that the most common age group linked was > 60 years, followed by 40-60 years, and 40 years.

Bacteriological isolation and its AST profile of different species among different studies and its comparison with the present study:

Bacteriological isolation:

According to this research work, *Acinetobacter baumannii* was the most prevalent isolate (66.66 percent), followed by *Klebsiella pneumoniae* (22.48 percent), *Pseudomonas aeruginosa* (7.75 percent), and *Escherichia coli* (7.75 percent) (3.1 percent). The findings of the study were contrasted to those of other studies in the figure 32 below. According to figure 31, *Acinetobacter baumannii* was recovered in 42 percent of the cases studied by Wu VKS et al. [78], followed by *Klebsiella pneumoniae* (18 percent), *Pseudomonas aeruginosa* (15 percent), and *Escherichia coli* (7 percent). According to He Q et al. [82], *Acinetobacter baumannii* was identified in 8% of cases, followed by *Klebsiella pneumoniae* in 7% of cases. Another research by Thomas A et al. [86] found that *Klebsiella pneumoniae* was isolated 75% of the total and *Pseudomonas aeruginosa* was isolated 25% of the total. According to this and previous studies, *Acinetobacter baumannii* was the most prevalent organism identified in the present and other studies, followed by *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Escherichia coli*. In this study, there was a genuine difference in the increasing prevalence of one specific organic entity over another in patients with VAE, compared to Wu VKS et al. [78], who found no significant link between the different organisms identified. The highest death rate was seen in *Acinetobacter baumannii*, followed by *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Escherichia coli*. Interestingly, we really want to comprehend the pathophysiology and seclusion of microorganisms' that in all the above studies what we talked about there was a specific order of bacterial affiliation which was *Acinetobacter baumannii*, trailed by *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Escherichia coli*.



	Acinetobacter baumannii	Klebsiella pneumoniae	Pseudomonas aeruginosa	Escherichia coli
Wu, V.K.S., Fong, C., Walters, A.M. et al [78]	42%	18%	15%	7%
He, Q., Wang, W., Zhu, S. et al [82]	8%	7%	0%	0%
86.Thomas A, Jitendranath A, Vishwamohanan I, Bhai G, Sarika et al [86]	0%	75%	25%	0%

Figure 32: Bacteriological isolation in different studies

Antibiotic resistance is becoming more common, posing a threat to human health, particularly among vulnerable patients in emergency departments and intensive care units. Medical costs, morbidity, and death all rise as a result of this. Microorganisms are fast to create new restriction mechanisms and antimicrobial self-protection methods (develops resistance). *Acinetobacter baumannii*, *Klebsiella pneumoniae*, *Escherichia coli*, and *Pseudomonas aeruginosa* have all been identified as microorganisms that have a very high rate of antibiotic resistance, resulting in a shrinking pool of available antibiotics for these organisms. To effectively combat this problem, both preventive and responsive actions are required. Decreasing the spread of resistant microbes, just as lessening the pace of development of resistance is complicated. To effectively combat this problem, both preventive and responsive actions are required. It's difficult to slow the progression of resistant microorganisms while also slowing the development of resistance. Such a task necessitates a more prudent use of antibiotics based on a better understanding of illness, including the research of disease transmission, resistance patterns, and treatment protocols. These goals can best be met by implementing ASP and the subsequent turn of events, as well as the presentation of potential drugs capable of eradicating MDR microorganisms.

AST profile of different species among different studies and its comparison with the present study

In the present study, *Acinetobacter baumannii* showed maximum susceptibility to colistin (100%) same as compared with other study [86]. Carbapenem susceptibility was 9.32 % in this study, compared to 47 % and 50% sensitivity to carbapenems in other studies [88, 89], which were significantly high carbapenem sensitivity when contrasted to this study. In all Indian publications [88, 89, 90], this species exhibited reduced susceptibility to aminoglycosides (around 18%), but only 1.5 percent of isolates were sensitive (98.5 percent resistance) in our study, which was a very low proportion of sensitivity in comparison to previous studies [88, 89, 90]. Ciprofloxacin susceptibility have reduced drastically to < 15% in other studies with 13.5% (87.59%) resistance in this study which was approximately similar with other studies [88, 89, 90].

The susceptibility of *Klebsiella pneumoniae* to amikacin ranges from 28.5 percent to 66.7 percent, however the isolate in this investigation was 100% resistant, which was a relatively low degree of sensitivity in contrast to other studies [90, 91]. Although susceptibility to ciprofloxacin has been reported as high as 33% [88, 89], Rajasekhar T et al. [90] reported 100 percent resistance, and the isolate in this study was 10.34 percent sensitive, which was far less sensitive than the other research [88, 89] and more sensitive over the other study [90]. Despite the fact that imipenem susceptibility in Klebsiella pneumoniae has been reported to be between 85 and 100 percent [86, 90, 91], it was 100 percent resistant in the current research, which is by far the most resistant correlation with other studies [90, 91, 92]. The Colistin susceptibility of *Klebsiella pneumoniae* in this investigation was same (100%) to previous reported susceptibilities [86, 90, 91, 92].

Pseudomonas aeruginosa was completely sensitive to colistin in this investigation, and the same susceptibility was seen in Thomas A et al. [86]. Carbapenem susceptibility was found to be 80%, which is identical to what Gupta et al. observed. [89] Though earlier investigations have demonstrated imipenem susceptibility in *Pseudomonas* species ranging from 50% to 78 percent [90, 91, 92], Rajasekhar T et al. [90] found it to be just 25% [90]. Ceftazidime susceptibility ranges from 31% to 50% in different studies [91, 92, 93], but in this study, susceptibility was 40%, which was roughly in

line with other studies [91, 92, 93]. *Pseudomonas aeruginosa* susceptibility to aminoglycosides has decreased in recent years, ranging from 16 to 40% [90, 91, 92, 93], and amikacin susceptibility was just 20% in our investigation. Piperacillin-tazobactam susceptibility ranges from 50% to 70% in several Indian research [90, 91, 92, 93], but it was 30% susceptible in our investigation, which was low in contrast to the above studies. According to the previous explanation, the organisms that we isolated were all multidrug resistant pathogens with low susceptibility to all first line medications such as 3 generation cephalosporins, blactam/blactamase inhibitors, fluoroquinolones, and aminoglycosides. It has now been shown that they have developed higher resistance to all higher order antibiotics such as carbapenems [90, 91, 92, 93].

This time is an excellent moment to implement proper and stringent AMS, which may also reduce the density of Multiple Drug Resistant microbes. The direct antibiotic susceptibility testing approach provides critical data for the rapid resolution of adequate antibiotic therapy. To really be clear, this strategy can significantly impact the best antibiotic treatment option (more effective or appropriate drugs) and encourages decreased mortality, a lower number of unnecessary lab and radiology symptomatic tests, and a shorter ICU stay. In terms of VAE, it supports specialists in directing a specific antibiotic therapy within 24 hours after clinical suspicion of VAP. Recent evidence for healthcare professionals who rely on direct AST has also been linked to less antibiotic overuse, shorter days on mechanical ventilation, and decreased mortality.

The therapy of Multiple Drug Resistant GNB illnesses in critically ill patients offers several challenges. Because a viable therapy should be administered as soon as possible, the use of several antimicrobials diminishes the possibility of successful trial inclusion, with potentially disastrous effects. In this light, timely access to a patient's clinical history and recent data on the microbiological study of disease transmission remain critical for characterising the pattern risk of Multiple Drug Resistant GNB disease and firmly guiding inferential treatment recommendations, with the goal of avoiding both under and over management. Immediate diagnostics and specialized research centre work methods are also critical, both for anticipating detecting and rapidly limiting the antimicrobial range, for de-acceleration objectives and in line with antimicrobial stewardship regulations.

CRE, *Acinetobacter baumannii*, *Kliebsiella pneumoniae*, and *Pseudomonas aeruginosa* are all increasing in frequency over the world, despite substantial variation among localities, emergency clinics, and particular wards. New treatment options, including as Meropenem, Ceftazidime-Avibactam, and Colistin, have emerged in the last few years, and more will emerge soon, providing some much-anticipated assets to viably balance serious disorders caused by these above MDR organisms. Regardless, their (AMR) optimal utilisation appears to be secured in the long run; however, deferring these steps should fairly be predicted to raise and disperse the density of MDR pathogen. However, key contributions such as the pk/pd problem and management protocol in critically ill patients have a few gaps that need to be addressed, which should be viewed as an extra impediment that might be identified as a significant endpoint. Treatment of severe Multiple Drug Resistant GNB diseases in sick patients will sooner or later necessitate a specialist and complex clinical thinking, taking into account the characteristics of the target population, but nevertheless likewise suggested the necessity for satisfactory empirical inclusion and the increasingly explicit enzyme level resistance of new therapeutic antimicrobials raises the various obstruction components of Multiple Drug Resistant GNB.

CONCLUSION

Mechanical ventilation (MV) was necessary for the majority of ICU patients. VAEs were usual in individuals who had more than four ventilator days, and they can happen very quickly in the case of MV. All levels of VAE were associated with poor clinical outcomes, including longer hospitalizations in the emergency unit and ICU, as well as a higher risk of mortality. The infections involved were multidrug-resistant microorganisms with extremely high morbidity and death rates. These findings highlight the need of VAE surveillance and the development of strategies to prevent VAEs. According to various literatures, there is a scarcity of data available in India based on current CDC recommendations for VAE, and most studies have only focused on one of the components, such as VAP and their incidence, or bacteriological profiling. The term "ventilator associated events" is used to describe the surveillance of infections and problems caused by mechanical ventilation. It covers both clinicopathological indicators. This research addresses the concerns identified with parts of VAEs distinguished in chosen (Critical Care Unit) clinical circumstances. It can guide the Interventionist and clinicians to pick the fitting Antimicrobials according to bacteriological profiling and provide a guidance about secondary blood stream infection began in view of VAEs which could moreover reduces the morbidity and mortality of patients. This research provided rationale for why organisms failed to response to prescribed medication (due to multidrug resistance), subsequently increasing the degree of therapy and expanding hospitalisation expenses, which will escalate the problem of those who cannot manage such expenditures. We need to understand, the threat of rapidly increasing antibiotic resistance is reinforced by the fact that there are very few new antibiotic agents in development. As a neutralizing procedure, minimization of wide range anti-microbial use with short and proper course of antimicrobial drug management will support and decreases the incidence of MDR pathogens. More comprehensive pharmacological monitoring will aid in medication reconciliation management and promote a patient-centred paradigm. Research into the multiplicity of intensive care units and the need for new antibiotic pharmaceutical research are key areas in which more study is needed.

BIBLIOGRAPHY

1. Muscedere J, Sinuff T, Heyland DK, Dodek PM, Keenan SP, Wood G, et al. The clinical impact and preventability of ventilator-associated conditions in critically ill patients who are mechanically ventilated. *Chest*. 2013 Nov;144(5):1453–60. Available from: doi:10.1378/chest.13-0853.
2. Klompas M. Ventilator-Associated Events: What They Are and What They Are Not. *Respir Care*. 2019 Aug;64(8):953–61. Available from: doi:10.4187/respcare.07059.
3. Klompas M. Complications of Mechanical Ventilation — The CDC's New Surveillance Paradigm. *N Engl J Med*. 2013 Apr 18;368(16):1472–5. Available from: http://www3.med.unipmn.it/papers/2013/NEJM/2013-04-18_nejm/nejmp1300633.pdf [Accessed 10 Dec 2021].
4. Magill SS, Klompas M, Balk R, Burns SM, Deutschman CS, Diekema D, et al. Developing a new, national approach to surveillance for ventilator-associated events. *Am J Crit Care*. 2013 Nov;22(6):469–73. Available from: doi:10.4037/ajcc2013893.
5. Klompas M, Kleinman K, Murphy MV. Descriptive epidemiology and attributable morbidity of ventilator-associated events. *Infect Control Hosp Epidemiol*. 2014 May;35(5):502–10. Available from: doi:10.1086/675834.
6. Khurana S, Mathur P, Kumar S, Soni KD, Aggrawal R, Batra P, et al. Incidence of ventilator-associated pneumonia and impact of multidrug-resistant infections on patient's outcome: Experience at an Apex Trauma Centre in North India. *Indian J Med Microbiol*. 2017 Dec;35(4):504–10. Available from: doi:10.4103/ijmm.IJMM_16_186.
7. Mathai AS, Phillips A, Kaur P, Isaac R. Incidence and attributable costs of ventilator-associated pneumonia (VAP) in a tertiary-level intensive care unit (ICU) in northern India. *J Infect Public Health*. 2015 Apr;8(2):127–35. Available from: doi:10.1016/j.jiph.2014.07.005.
8. Patil HV, Patil VC. Incidence, bacteriology, and clinical outcome of ventilator-associated pneumonia at tertiary care hospital. *J Nat Sci Biol Med*. 2017;8(1):46-55. doi:10.4103/0976-9668.198360.

9. Raoof S, Baumann MH, on behalf of the Critical Care Societies Collaborative consisting of the leadership of the AA of C-CN the American College of Chest Physicians, the American Thoracic Society, and the Society of Critical Care Medicine. Ventilator-Associated Events: The New Definition. *American Journal of Critical Care*. 2014 Jan; 23(1):7–9. Available from: https://doi.org/10.4037/ajcc2014469 [Accessed 10 Dec 2021].
10. Patrick R Murray; Ellen Jo Baron. *Manual of clinical microbiology*. 9th ed. Washington, D.C.: ASM Press; 2007.
11. Meyer KC, Raghu G, Baughman RP, Brown KK, Costabel U, du Bois RM, et al. An official American Thoracic Society clinical practice guideline: the clinical utility of bronchoalveolar lavage cellular analysis in interstitial lung disease. *Am J Respir Crit Care Med*. 2012 May 1;185(9):1004–14. Available from: doi:10.1164/rccm.201202-0320ST.
12. Bartholomew JW, Mittwer T. The Gram stain. *Bacteriol Rev*. 1952;16(1):1-29. doi:10.1128/br.16.1.1-29.1952.
13. Albers AC, Fletcher RD. Accuracy of calibrated-loop transfer. *J Clin Microbiol*. 1983 Jul;18(1):40–2. Available from: doi:10.1128/jcm.18.1.40-42.1983.
14. Melvin P. Weinstein *Performance Standards for Antimicrobial Susceptibility Testing.* 31st ed. USA: Clinical & Laboratory Standards Institute: 2021. Available from: https://clsi.org/standards/products/microbiology/companion/using-m100 [Accessed 10 Dec 2021].
15. American Thoracic Society, Infectious Diseases Society of America. Guidelines for the management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia. *Am J Respir Crit Care Med*. 2005 Feb 15;171(4):388–416. Available from: doi:10.1164/rccm.200405-644ST.
16. Respiratory System Anatomy - Major Zones & Divisions *GetBodySmart*. 2017 Dec 12]. Available from: https://www.getbodysmart.com/respiratory-system/respiratory-system-anatomy [Accessed 10 Dec 2021].
17. Bartlett JG, Dowell SF, Mandell LA, File TM, Musher DM, Fine MJ. et al. Practice guidelines for the management of community-acquired pneumonia in

adults. Infectious Diseases Society of America. *Clin Infect Dis*. 2000 Aug;31(2):347–82.

Available from: doi:10.1086/313954.

18. Boivin G, Abed Y, Pelletier G, Ruel L, Moisan D, Côté S, et al. Virological features and clinical manifestations associated with human metapneumovirus: a new paramyxovirus responsible for acute respiratory-tract infections in all age groups. *J Infect Dis*. 2002 Nov 1;186(9):1330–4. Available from: doi:10.1086/344319.
19. Broughton WA, Middleton RM, Kirkpatrick MB, Bass JB. Bronchoscopic protected specimen brush and bronchoalveolar lavage in the diagnosis of bacterial pneumonia. *Infect Dis Clin North Am*. 1991 Sep;5(3):437–52. Available from: https://pubmed.ncbi.nlm.nih.gov/1955692 [Accessed 10 Dec 2021].
20. Caliendo AM. Enhanced diagnosis of Pneumocystis carinii: Promises and problems. *Clinical Microbiology* 1996 Aug 1;18(15):113–6. Available from: https://www.sciencedirect.com/science/article/pii/0196439996889379 [Accessed 10 Dec 2021].
21. Campbell S, Forbes BA. The Clinical Microbiology Laboratory in the Diagnosis of Lower Respiratory Tract Infections. *J Clin Microbiol*. 2011;49:S30-S33. Available from: doi:10.1128/JCM.00789-11.
22. Cantral DE, Tape TG, Reed EC, Spurzem JR, Rennard SI, Thompson AB et al. Quantitative culture of bronchoalveolar lavage fluid for the diagnosis of bacterial pneumonia. *Am J Med*. 1993 Dec;95(6):601–7. Available from: doi:10.1016/0002-9343(93)90356-t.
23. Carroll KC. Laboratory diagnosis of lower respiratory tract infections: controversy and conundrums. *J Clin Microbiol*. 2002 Sep;40(9):3115–20. Available from: doi:10.1128/JCM.40.9.3115-3120.2002.
24. National Nosocomial Infections Surveillance System. National Nosocomial Infections Surveillance (NNIS) System Report, data summary from January 1992 through June 2004, issued October 2004. *Am J Infect Control*. 2004 Dec;32(8):470–85. Available from: doi:10.1016/S0196655304005425.

25. Kim JE, Kim UJ, Kim HK, Cho SK, An JH, Kang SJ, Park KH, Jung SI, Jang HC et al. Predictors of viral pneumonia in patients with community-acquired pneumonia. *PLoS One*. 2014 Dec 22;9(12):e114710. Available from: doi: 10.1371/journal.pone.0114710.

26. Fang GD, Fine M, Orloff J, Arisumi D, Yu VL, Kapoor W, et al. New and emerging etiologies for community-acquired pneumonia with implications for therapy. A prospective multicenter study of 359 cases. *Medicine (Baltimore)*. 1990 Sep;69(5):307–16. Available from: doi:10.1097/00005792-199009000-00004.

27. Dasaraju PV, Liu C, Baron S ED. *Infections of the Respiratory System*. 4th ed. Galveston (TX): University of Texas Medical Branch 1996 Available from: http://www.ncbi.nlm.nih.gov/books/NBK8142/ [Accessed 10 Dec 2021].

28. Bosch AATM, Biesbroek G, Trzcinski K, Sanders EAM, Bogaert D. Viral and Bacterial Interactions in the Upper Respiratory Tract. *PLOS Pathogens*. 2013 Jan 10; 9(1): e1003057. Available from: https://journals.plos.org/plospathogens/article?id=10.1371/journal.ppat.1003057 [Accessed 10Dec 2021].

29. James Versalovic, Karen C Carroll; Guido Funke; James H Jorgensen; Marie L Land *Manua*l *of clinical microbiology*, 10th ed., Washington, DC: ASM Press; 2011. Available from: https://www.worldcat.org/title/manual-of-clinical-microbiology/oclc/855372297 [Accessed 10 Dec 2021].

30. Hedges JR, Lowe RA. Approach to acute pharyngitis. *Emerg Med Clin North Am*. 1987 May;5(2):335–51. Available from: https://pubmed.ncbi.nlm.nih.gov/3325277. [Accessed 10 Dec 2021].

31. Albahout KS, Lopez RA. Anatomy, Head and Neck, Pharynx. *Treasure Island (FL): Stat pearls* 2021. Available from: http://www.ncbi.nlm.nih.gov/books/NBK544271/ [Accessed 10 Dec 2021].

32. Abdallah C Acute epiglottitis: Trends, diagnosis and management. *Saudi J Anaesth* 2012; 6:3: 279-281 [cited 2021 Dec 12]. Available from: DOI**:** 10.4103/1658-354X.101222.

33. Gottlieb M, Long B, Koyfman A. Clinical Mimics: An Emergency Medicine-Focused Review of Streptococcal Pharyngitis Mimics. *J Emerg Med*. 2018 May;54(5):619–29. Available from: doi:10.1016/j.jemermed.2018.01.031.

34. Brennan-Krohn T, Ozonoff A, Sandora TJ. Adherence to guidelines for testing and treatment of children with pharyngitis: a retrospective study. *BMC Pediatrics*. 2018 Feb 9 ;18(1):43. Available from: doi.org/10.1186/s12887-018-0988-z.

35. Dunmire SK, Hogquist KA, Balfour HH. Infectious Mononucleosis. *Curr Top Microbiol Immunol*. 2015;390(Pt 1):211–40. Available from: doi:10.1007/978-3-319-22822-8_9.

36. Yamamoto S, Gu Y, Fujitomo Y, Kanai N, Yamahata Y, Saito H, Hashimoto T, Ohmagari et al Development and efficacy of a clinician-targeted refresher course for treating nonpneumonia respiratory tract infections. *J Gen Fam Med*. 2018 Jul;19(4):127-132. Available from: doi:10.1002/jgf2.183.

37. Akhtar M, Van Heukelom PG, Ahmed A, Tranter RD, White E, Shekem N, Walz D, Fairfield C, Vakkalanka JP, Mohr NM et al. Telemedicine Physical Examination Utilizing a Consumer Device Demonstrates Poor Concordance with In-Person Physical Examination in Emergency Department Patients with Sore Throat: A Prospective Blinded Study. *Telemed J E Health*. 2018 Oct;24(10):790-796. Available from: doi.org/10.1101/2021.05.31.21258110.

38. Singh A, Avula A, Zahn E. Acute Bronchitis. In : *StatPearls* Treasure Island (FL): StatPearls ; 2021. Available from: http://www.ncbi.nlm.nih.gov/books/NBK448067/ [Accessed 10 Dec 2021].

39. Widysanto A, Mathew G Chronic Bronchitis. In : *StatPearls* Treasure Island (FL): StatPearls ; 2021 Jan-. Available from: https://pubmed.ncbi.nlm.nih.gov/29494044/ [Accessed 10 Dec 2021].

40. Friedman JN, Rieder MJ, Walton JM, Canadian Paediatric Society, Acute Care Committee, Drug Therapy and Hazardous Substances Committee. Bronchiolitis: Recommendations for diagnosis, monitoring and management of children one to 24 months of age. *Paediatr Child Health*. 2014 Nov;19(9):485–98. Available from: doi:10.1093/pch/19.9.485.

41. Sattar SBA, Sharma S Bacterial Pneumonia. In *StatPearls* Treasure Island (FL): StatPearls Publishing; 2021 Jan. Available from: https://www.ncbi.nlm.nih.gov/books/NBK513321 [Accessed 10 Dec 2021].

42. Van der Poll T, Opal SM. Pathogenesis, treatment, and prevention of pneumococcal pneumonia. *The Lancet* . 2009; 374(9700):1543–56. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0140673609611144 [Accessed 10 Dec 2021].

43. Metlay JP, Waterer GW, Long AC, Anzueto A, Brozek J, Crothers K, et al. Diagnosis and Treatment of Adults with Community-acquired Pneumonia. An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America. *Am J Respir Crit Care Med*. 2019 Oct;200(7):e45–67. Available from: https://www.atsjournals.org/doi/full/10.1164/rccm.201908-1581ST [Accessed 10 Dec 2021].

44. File TM. Community-acquired pneumonia. *Lancet*. 2003 Dec 13;362(9400):1991–2001. Available from: doi:10.1016/S0140-6736(03)15021-0.

45. Wunderink RG, Waterer GW. Clinical practice. Community-acquired pneumonia. *N Engl J Med*. 2014;370(6):543-551. Available from: doi:10.1056/NEJMcp121486.

46. Klapdor B, Ewig S, Pletz MW, Rohde G, Schütte H, Schaberg T, et al. Community-acquired pneumonia in younger patients is an entity on its own. *European Respiratory Journal*. 2012 May 1 ;39(5):1156–61. Available from: https://erj.ersjournals.com/content/39/5/1156 [Accessed 10 Dec 2021].

47. Freeman AM, Leigh, Jr TR. Viral Pneumonia. In: *StatPearls*. Treasure Island (FL): StatPearls 2021. Available from: https://pubmed.ncbi.nlm.nih.gov/30020658 [Accessed 10 Dec 2021].

48. Li Z, Lu G, Meng G. Pathogenic Fungal Infection in the Lung. *Front Immunol* . 2019 Jul 3 ;10:1524. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6616198/ [Accessed 10 Dec 2021].

49. Pahal P, Rajasurya V, Sharma S Typical Bacterial Pneumonia In: *StatPearls*. Treasure Island (FL): StatPearls 2021 Jan. Available from: https://www.ncbi.nlm.nih.gov/books/NBK534295/ [Accessed 10 Dec 2021].

50. Mortensen EM, Copeland LA, Pugh MJ, Fine MJ, Nakashima B, Restrepo MI, et al. Diagnosis of pulmonary malignancy after hospitalization for pneumonia. *Am J Med*. 2010 Jan;123(1):66–71. Available from: doi:10.1016/j.amjmed.2009.08.009.

51. Kim JE, Han A, Lee H, Ha J, Kim YS, Han SS et al. Impact of Pneumocystis jirovecii pneumonia on kidney transplant outcome. *BMC Nephrology*. 2019 Jun 10 ;20(1):212. Available from: https://doi.org/10.1186/s12882-019-1407-x [Accessed 10 Dec 2021].

52. Huang L, Crothers K. HIV-associated opportunistic pneumonias. *Respirology*. 2009 May;14(4):474–85. Available from: doi:10.1111/j.1440-1843.2009.01534.x

53. Rosenstengel A. Pleural infection-current diagnosis and management. *J Thorac Dis*. 2012;4(2):186-193. Available from: doi:10.3978/j.issn.2072-1439.2012.01.12.

54. Girard R, Perraud M, Herriot HE, Prüss A, Savey A, Tikhomirov E, et al. *Prevention of hospital-acquired infection* 2nd ed Malta WORLD HEALTH ORGANIZATION 2002. Available from: https://apps.who.int/iris/bitstream/handle/10665/67350/WHO_CDS_CSR_EPH_2002.12.pdf?sequence=1&isAllowed=y [Accessed 10 Dec 2021].

55. Benenson AS. Control of communicable diseases manual, 16th ed. Washington: American Public Health Association;1995. Available from: https://www.worldcat.org/title/control-of-communicable-diseases-manual/oclc/55167024 [Accessed 10 Dec 2021].

56. Nosocomial infection rates for interhospital comparison: limitations and possible solutions. A Report from the National Nosocomial Infections Surveillance (NNIS) System. *Infect Control Hosp Epidemiol*. 1991 Oct;12(10):609–21. Available from: https://pubmed.ncbi.nlm.nih.gov/1664844/ [Accessed 10 Dec 2021].

57. Chalmers JD, Rother C, Salih W, Ewig S. Healthcare-Associated Pneumonia Does Not Accurately Identify Potentially Resistant Pathogens: A Systematic Review and Meta-Analysis. *Clinical Infectious Diseases* . 2014 Feb 1 ;58(3):330–9. Available from: https://doi.org/10.1093/cid/cit734 [Accessed 10 Dec 2021].

58. Magill SS, O'Leary E, Janelle SJ, Thompson DL, Dumyati G, Nadle J, et al. Changes in Prevalence of Health Care-Associated Infections in U.S. Hospitals. *N Engl J Med*. 2018 Nov 1;379(18):1732–44. Available from: doi:10.1056/NEJMoa1801550 .

59. Edwards JR, Peterson KD, Andrus ML, Dudeck MA, Pollock DA, Horan TC, et al. National Healthcare Safety Network (NHSN) Report, data summary for 2006 through 2007, issued November 2008. *Am J Infect Control*. 2008 Nov;36(9):609–26. Available from: doi:10.1016/j.ajic.2008.08.001.

60. Muscedere JG, Day A, Heyland DK. Mortality, attributable mortality, and clinical events as end points for clinical trials of ventilator-associated pneumonia and hospital-acquired pneumonia. *Clin Infect Dis*. 2010;51 Suppl 1:S120-S125. Available from doi:10.1086/653060.

61. Bhadade R, Harde M, deSouza R, More A, Bharmal R. Emerging trends of nosocomial pneumonia in intensive care unit of a tertiary care public teaching hospital in Western India. *Ann Afr Med*. 2017;16(3):107-113. Available from: doi:10.4103/aam.aam_7_17

62. Scheld WM. Developments in the pathogenesis, diagnosis and treatment of nosocomial pneumonia. *Surg Gynecol Obstet*. 1991;172 Suppl:42–53. Available from: https://pubmed.ncbi.nlm.nih.gov/2024226/ [Accessed 10 Dec 2021].

63. Jaillette E, Girault C, Brunin G, Zerimech F, Behal H, Chiche A, et al. Impact of tapered-cuff tracheal tube on microaspiration of gastric contents in intubated critically ill patients: a multicenter cluster-randomized cross-over controlled trial. *Intensive Care Med*. 2017 Nov;43(11):1562–71. Available from: doi:10.1007/s00134-017-4736-x.

64. Safdar N, Crnich CJ, Maki DG. The pathogenesis of ventilator-associated pneumonia: its relevance to developing effective strategies for

prevention. *Respir Care*. 2005;50(6):725-741. Available from: https://pubmed.ncbi.nlm.nih.gov/15913465/. [Accessed 10 Dec 2021].

65. Nseir S, Di Pompeo C, Pronnier P, Beague S, Onimus T, Saulnier F, et al. Nosocomial tracheobronchitis in mechanically ventilated patients: incidence, aetiology and outcome. *Eur Respir J*. 2002 Dec;20(6):1483–9. Available from: doi:10.1183/09031936.02.00012902.

66. Huang HB, Jiang W, Wang CY, Qin HY, Du B. Stress ulcer prophylaxis in intensive care unit patients receiving enteral nutrition: a systematic review and meta-analysis. *Crit Care*. 2018;22(1):20. Available from: doi:10.1186/s13054-017-1937-.

67. Weiner LM, Webb AK, Limbago B, Dudeck MA, Patel J, Kallen AJ, et al. Antimicrobial-Resistant Pathogens Associated With Healthcare-Associated Infections: Summary of Data Reported to the National Healthcare Safety Network at the Centers for Disease Control and Prevention, 2011-2014. *Infect Control Hosp Epidemiol*. 2016 Nov;37(11):1288–301. Available from: doi:10.1017/ice.2016.174.

68. Magill SS, Klompas M, Balk R "Developing a new, national approach to surveillance for ventilator associated events". *Critical Care Medicine* 2013;41:2467-75. Available from: https://manuals.plus/m/b315db.pdf [Accessed 10 Dec 2021].

69. Kalil AC, Metersky ML, Klompas M, Muscedere J, Sweeney DA, Palmer LB, et al. Management of Adults With Hospital-acquired and Ventilator-associated Pneumonia: 2016 Clinical Practice Guidelines by the Infectious Diseases Society of America and the American Thoracic Society. *Clin Infect Dis*. 2016 Sep 1;63(5):e61–111. Available from: doi:10.1093/cid/ciw353.

70. National Healthcare safety Network (NHSN), *Ventilator-associated Event (VAE)*: *NHSN Guideline* 2021. Available from: https://www.cdc.gov/nhsn/pdfs/pscmanual/10-vae_final.pdf [Accessed 10th Dec 2021].

71. Magill SS, Li Q, Gross C, Dudeck M, Allen-Bridson K, Edwards JR et al. Incidence and Characteristics of Ventilator-Associated Events Reported to the National Healthcare Safety Network in 2014. *Crit Care Med*. 2016 Dec ;44(12):2154–62. Available from:

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5113232/ [Accessed 10 Dec 2021].

72. Klompas M, Khan Y, Kleinman K, Evans RS, Lloyd JF, Stevenson K, et al. Multicenter evaluation of a novel surveillance paradigm for complications of mechanical ventilation. *PLoS One*. 2011 Mar 22;6(3):e18062. Available from: doi:10.1371/journal.pone.0018062.

73. Fan Y, Gao F, Wu Y, Zhang J, Zhu M, Xiong L. et al. Does ventilator-associated event surveillance detect ventilator-associated pneumonia in intensive care units? A systematic review and meta-analysis. *Crit Care*. 2016;20(1):338. Published 2016 Oct 24. Available from: doi:10.1186/s13054-016-1506-z.

74. Klompas M, Platt R. Ventilator-associated pneumonia--the wrong quality measure for benchmarking. *Ann Intern Med*. 2007;147(11):803-805. Available from: doi:10.7326/0003-4819-147-11-200712040-00013.

75. Angus DC, Seymour CW, Coopersmith CM, et al. A Framework for the Development and Interpretation of Different Sepsis Definitions and Clinical Criteria. *Crit Care Med*. 2016;44(3):e113-e121. Available from: doi:10.1097/CCM.0000000000001730.

76. Ji Liu, Shenglei Zhang, Jiaxuan Chen, Yiping Mao, Xiaoqing Shao, Yang Li, Jianmei Cao, Wei Zheng, Bing Zhang, Zhiyong Zong et al. Risk factors for ventilator-associated events: A prospective cohort study, *American Journal of Infection Control*, 2019;47(7), 744-749 Available from: https://doi.org/10.1016/j.ajic.2018.09.032.

77. Tablan OC, Anderson LJ, Arden NH, Breiman RF, Butler JC, McNeil MM. et al. Guideline for prevention of nosocomial pneumonia. The Hospital Infection Control Practices Advisory Committee, Centers for Disease Control and Prevention. *Am J Infect Control*. 1994;22(4):247-292. Available from: doi:10.1016/0196-6553(94)90079-5.

78. Centers for Disease Control and Prevention, *National and State Healthcare-Associated Infections Progress Report*. CDC ; 2016.

79. Wu VKS, Fong C, Walters AM, Lele AV. Prevalence, Clinical Characteristics, and Outcomes Related to Ventilator-Associated Events in Neurocritically Ill

Patients. *Neurocrit Care*. 2020;33(2):499-507. Available from doi:10.1007/s12028-019-00910-5.

80. Ramirez-Estrada , Ventilator-associated events versus ventilator-associated respiratory infections—moving into a new paradigm or merging both concepts, instead?. *Annals of Translational Medicine* Available from: https://atm.amegroups.com/article/view/22208/html [Accessed 10 Dec 2021].

81. Macht M, Robinson JC, Graham BB. Updated approach for the assessment of ventilator-associated pneumonia. *Crit Care Med.* 2013;41(11):2641-2642. Available from: doi:10.1097/CCM.0b013e3182a84be1.

82. He Q, Wang W, Zhu S, Wang M, Kang Y, Zhang R, et al. The epidemiology and clinical outcomes of ventilator-associated events among 20,769 mechanically ventilated patients at intensive care units: an observational study. *Critical Care* . 2021 Feb 2;25(1):44. Available from: https://doi.org/10.1186/s13054-021-03484-x. [Accessed 10 Dec 2021].

83. Pouly O, Lecailtel S, Six S, Préau S, Wallet F, Nseir S, et al. Accuracy of ventilator-associated events for the diagnosis of ventilator-associated lower respiratory tract infections. *Annals of Intensive Care* . 2020 Jan 13 ;10(1):6. Available from: https://doi.org/10.1186/s13613-020-0624-6 [Accessed 10 Dec 2021].

84. Wolffers, O., Faltys, M., Thomann, J. Jonas Marschall & Rami Sommerstein Stephan M. Jakob & Tobias M. Merz et al. An automated retrospective VAE-surveillance tool for future quality improvement studies. *Sci Rep* 2021 ;**11:**22264. Available from: https://doi.org/10.1038/s41598-021-01402-3 [Accessed 10 Dec 2021].

85. Sharma A, Das M, Mishra B, Thakur A, Loomba PS. Ventilator-associated events:Incidence and mortality in intensive care unit of a superspecialty hospital of North India. *Int J Health Allied Sc*i 2019;9:62-6. Available from: https://www.ijhas.in/article.asp?issn=2278344X;year=2020;volume=9;issue=1;spage=62;epage=66;aulast=Sharma [Accessed 10 Dec 2021].

86. Thomas A, Jitendranath A, Vishwamohanan I, Bhai G, Sarika. Incidence of ventilator associated events among intubated patients in neurosurgery

ICU of a tertiary health centre in India. *Indian J Microbiol Res* 2019;6(2):150-2. Available from: doi: 10.18231/j.ijmr.2019.032

87. Rello J, Ramírez-Estrada S, Romero A, Arvaniti K, Koulenti D, Nseir S, et al. Factors associated with ventilator-associated events: an international multicenter prospective cohort study. *Eur J Clin Microbiol Infect Dis*. 2019 Sep;38(9):1693–9.Available from: https://doi.org/10.1007/s10096-019-03596-x [Accessed 10 Dec 2021].

88. Anuradha De, Arghadip Samaddar, Salma Patwegar, Sujata Baveja. Antibiotic Susceptibility Pattern of Bacteria Isolated from Adult Patients with Ventilator Associated Pneumonia (VAP) in Intensive Care Units in a Tertiary Care Hospital, *JMSCR* 2018 ; 6:4. Available from: DOI**:** https://dx.doi.org/10.18535/jmscr/v6i4.181**.**

89. Gupta A, Agrawal A, Mehrotra S, Singh A, Malik S, Khanna A. et al. Incidence, risk stratification, antibiogram of pathogens isolated and clinical outcome of ventilator associated pneumonia. *Indian J Crit Care Med*. 2011;15(2):96-101. Available from: doi:10.4103/0972-5229.83015.

90. Rajasekhar T, Anuradha K, Suhasini T, Lakshmi V. The role of quantitative cultures of non-bronchoscopic samples in ventilator associated pneumonia. *Indian J Med Microbiol*. 2006;24(2):107-113. Available from: doi:10.4103/0255-0857.2522

91. Dey A, Bairy I. Incidence of multidrug-resistant organisms causing ventilator-associated pneumonia in a tertiary care hospital: a nine months' prospective study. *Ann Thorac Med*. 2007;2(2):52-57. Available from: doi:10.4103/1817-1737.32230.

92. Goel N, Chaudhary U, Aggarwal R, Bala K. Antibiotic sensitivity pattern of gram negative bacilli isolated from the lower respiratory tract of ventilated patients in the Intensive care unit. *Indian J Crit Care Med*. 2009;13(3):148-151. Available from: doi:10.4103/0972-5229.58540.

93. Mukhopadhyay C, Krishna S, Shenoy A, Prakashini K. Clinical, radiological and microbiological corroboration to assess the role of endotracheal aspirate in diagnosing ventilator-associated pneumonia in an intensive care unit of a tertiary care hospital, India. *IJIC* 2009Dec 22;6(2). Available from: https://www.ijic.info/article/view/4104 [Accessed 10 Dec 2021].

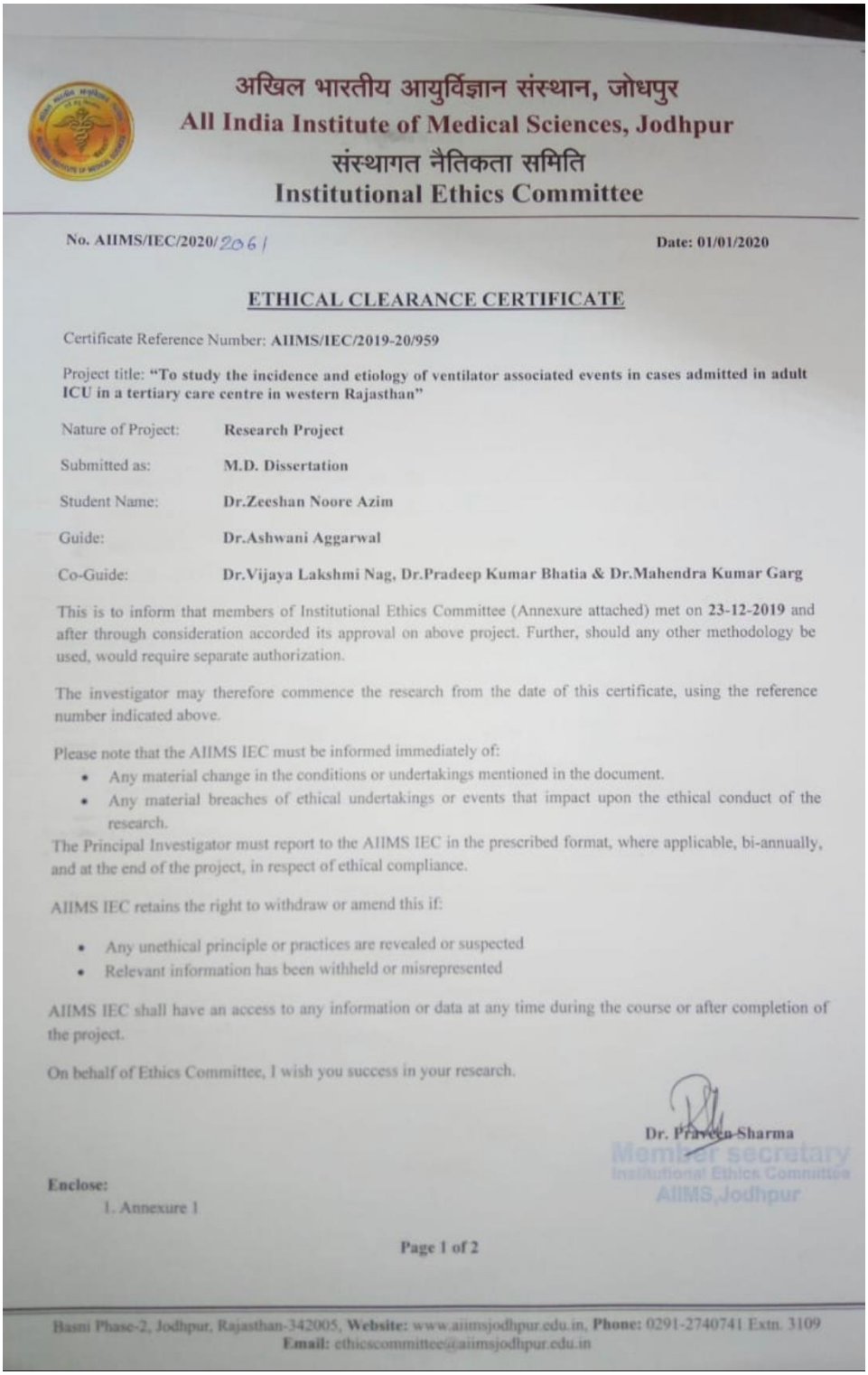
Annexure 1

Case performa sheet:

AIIMS ID			Name			Age Sex
Date of Admision			Date of Discharge			Total MV Days
Diagnosis						
Day 1	**PEEP**	**FiO2**	**WBC10*3u/L**	**Temp**	**Antibiotics**	**Organism**
Day 2						
Day 3						
Day 4						
Day 5						
Day 6						
Day 7						
Day 8						
Day 9						
Day 10						
Day 11						
Day 12						
Day 13						
Day 14						
Day 15						
Day 16						
Day 17						
Day 18						
Day 19						
Day 20						
Day 21						
Day 22						

Annexure 2

Ethical Clearance Certificate:



अखिल भारतीय आयुर्विज्ञान संस्थान, जोधपुर
All India Institute of Medical Sciences, Jodhpur
संस्थागत नैतिकता समिति
Institutional Ethics Committee

No. AIIMS/IEC/2020/2061 Date: 01/01/2020

ETHICAL CLEARANCE CERTIFICATE

Certificate Reference Number: **AIIMS/IEC/2019-20/959**

Project title: **"To study the incidence and etiology of ventilator associated events in cases admitted in adult ICU in a tertiary care centre in western Rajasthan"**

Nature of Project:	**Research Project**
Submitted as:	**M.D. Dissertation**
Student Name:	**Dr.Zeeshan Noore Azim**
Guide:	**Dr.Ashwani Aggarwal**
Co-Guide:	**Dr.Vijaya Lakshmi Nag, Dr.Pradeep Kumar Bhatia & Dr.Mahendra Kumar Garg**

This is to inform that members of Institutional Ethics Committee (Annexure attached) met on **23-12-2019** and after through consideration accorded its approval on above project. Further, should any other methodology be used, would require separate authorization.

The investigator may therefore commence the research from the date of this certificate, using the reference number indicated above.

Please note that the AIIMS IEC must be informed immediately of:

- Any material change in the conditions or undertakings mentioned in the document.
- Any material breaches of ethical undertakings or events that impact upon the ethical conduct of the research.

The Principal Investigator must report to the AIIMS IEC in the prescribed format, where applicable, bi-annually, and at the end of the project, in respect of ethical compliance.

AIIMS IEC retains the right to withdraw or amend this if:

- Any unethical principle or practices are revealed or suspected
- Relevant information has been withheld or misrepresented

AIIMS IEC shall have an access to any information or data at any time during the course or after completion of the project.

On behalf of Ethics Committee, I wish you success in your research.

Dr. Praveen Sharma
Member secretary
Institutional Ethics Committee
AIIMS,Jodhpur

Enclose:
1. Annexure 1

Page 1 of 2

Basni Phase-2, Jodhpur, Rajasthan-342005, **Website:** www.aiimsjodhpur.edu.in, **Phone:** 0291-2740741 Extn. 3109
Email: ethicscommittee@aiimsjodhpur.edu.in

Annexure 3

Abstract MICRO-D-CON 2021 (Oral Presentation)

To study the rate and bacteriological profile of ventilator associated events in cases admitted in icu in a tertiary care centre in western Rajasthan

Introduction

The components of Ventilator Associated events are 1) Ventilator Associated Condition **(VAC)** 2) Infection related to Ventricular Associated Complications (**IVAC**) 3) Possible Ventilator associated Pneumonia (**PVAC**).

Aims and Objectives: To study the rate and bacteriological profile with Antimicrobial Susceptibility Testing of Ventilator Associated Events in cases admitted in ICU in a tertiary care centre in western rajasthan.

Materials and Methods: It is a prospective observational study carried out in cases of patients (>18 yr) on mechanical ventilation in adult ICU (Dept of Anesthesiology and Critical Care). The samples collected from cases and processed at Department of Microbiology, All India Institute of Medical Sciences, Jodhpur.

Results: A total of **130 cases** who were on mechanical ventilation were studied, in which **47 cases** develop Ventilator Associated Events in that **47** develops VAC and **46** IVAC, **32 cases** develops PVAP. The incidence of VAC is **41.33** and IVAC is **40.45** VAE/1000 mechanical ventilation days, and PVAP is **28.14** VAE/1000 mechanical ventilation days.The organism isolated is predominantly Gram negative bacteria, especially the *Acinetobacter baumannii* (21 isolates), followed by *Klebsiella pneumoniae* (10 isolates), *Pseudomonas aeruginosa* (2 isolates) and *Escherichia coli* (1 isolates). Most isolates are multidrug resistant, mostly sensitive to Colistin and Minocycline.

Conclusion: VAEs remain the major threat to patients on mechanical ventilation in ICUs. It is to emphasize that an urgent need is required to have a proper and strict infection control measures to cut down the VAE rate which leads to the overall reduction in patient expenses, morbidity and mortality.

Annexure 4

Abstract MYCOCON 2021 (Poster Presentation)

To study the profile of fungal isolates from skin/nail/hair samples in a tertiary care centre in western Rajasthan

Introduction: Dermatophytoses are the most common types of superficial cutaneous fungal infections seen globally. It is a major public health problem because of its contagious nature and incidence of the disease is increasing steadily in India.

Aim: To study the profile of fungal isolates obtained from Skin/Nail/Hair samples received in the mycology lab over a period of 14 months.

Materials and Methods: It is a retrospective cross sectional study carried out in the mycology laboratory of the Department of Microbiology, AIIMS Jodhpur over 14 months from November 2019 to December 2020. All Skin/Nail/Hair samples received were screened for fungal elements by KOH wet mount microscopy. Then they were inoculated on Sabouraud's Dextrose agar at 25 ℃ and 37 ℃, for 4 -6 weeks. Culture positives were further processed by conventional methods for fungal identification.

Results: A total of 580 specimens of skin 522 (90%), Nail 55 (9.5%) and Hair 3 (0.5%) were received in the mycology lab during the study period. Of them, 181 (31.2%) samples were positive for fungal elements on microscopy. Only 69 (11.89%) specimens of skin were positive on culture, all yielding *Trichophyton spp*. The commonest species isolated was *Trichophyton mentagrophytes* 35 (50.72) followed by *Trichophyton tonsurans* 27(39.13%), *Trichophyton violaceum* 4(5.79%) and *Trichophyton rubrum* 3(4.34%). All nail and hair samples were sterile on culture.

Conclusion: Microscopy remains critical for rapid diagnosis of dermatophytosis and one third of our study specimens were successfully diagnosed by microscopy alone. However, Culture positivity was poor, only 11.89%. The most likely reason for the same could be empirical antifungal prescription prior to sample collection. We urge the clinicians to collect Skin/Nail/Hair samples prior to antifungal therapy. This will encourage a culture-driven selection of antifungals and promote anti-fungal stewardship in Western Rajasthan.

Annexure 5

All India Institute of Medical Sciences, Jodhpur

PATIENT INFORMATION SHEET

Ventilator Associated Events are associated with infection like Ventilator Associated Pneumonia which has major threat to patient who is on mechanical ventilation worldwide.

PURPOSE OF STUDY: TO STUDY THE INCIDENCE AND PROFILE OF VENTILATOR ASSOCIATED EVENTS(VAEs) IN A TERTIARY CARE CENTRE

METHODS INVOLVED: relevant sample will be collected from patient with Ventilator Associated Condition and will transport for proper bacteriological profiling and AST.

BENEFIT OF STUDY TO THE PATIENT: It will be helpful in the proper diagnosis and treatment to the patient and will helpful in selecting antimicrobial drugs.

RISK INVOLED TO THE PATIENT: There is no risk of any kind to the patient in this study. No drug or vaccines are being tested in the study.

CONFIDENTIALITY OF RECORDS: The patient's records/reports/ shall be kept confidential.

अखिल भारतीय आयुर्विज्ञान संस्थान, जोधपुर

रोगी की सूचना पत्र

वेंटीलेटर एसोसिएटेड इवेंट वेंटिलेटर एसोसिएटेड न्यूमोनिया जैसे संक्रमण से जुड़े होते हैं, जो रोगी के लिए बड़ा खतरा है जो दुनिया भर में मैकेनिकल वेंटिलेशन पर है।

अध्ययन का अधिकार: एक सहायक देखभाल केंद्र में वेंटिलेटर एसोसिएटेड इवेन्ट्स (VAE) के रेट और बैकेरियोलॉजिकल प्रोफ़ेसर का अध्ययन करना

विधि इनवॉल्ड: प्रासंगिक नमूना वेंटिलेटर एसोसिएटेड स्थिति के साथ रोगी से एकत्र किया जाएगा और उचित बैक्टीरियलोलॉजिकल प्रोफाइलिंग और एएसटी के लिए परिवहन करेगा।

रोगी को अध्ययन का लाभ: यह रोगी को उचित निदान और उपचार में मददगार होगा और रोगाणुरोधी दवाओं का चयन करने में सहायक होगा।

रोगी के लिए आमंत्रित जोखिम: इस अध्ययन में रोगी को किसी भी प्रकार का कोई खतरा नहीं है। अध्ययन में किसी भी दवा या टीके का परीक्षण नहीं किया जा रहा है।

रिकॉर्ड की मान्यता: रोगी के रिकॉर्ड / रिपोर्ट / गोपनीय रखे जाएंगे

Annexure - 6

All India Institute of Medical Sciences, Jodhpur

Informed Consent Form

Title of the project: study and correlation of results determining Rate and Bacteriological Profiling of Ventilator Associated Events in cases admitted in ICU in a Tertiary Care Centre in western Rajasthan.

Name of the Principal Investigator: Dr. Zeeshan Noore Azim

Tel. No. (Mobile): - 8210390449

Patient ID No: _____

I, _____S/o or D/o_____

R/o _____give my full, free, voluntary consent to be a part of the study and correlation of results determining incidence and etiology of Ventilator Associated Events the procedure and nature of which has been explained to me in my own language to my full satisfaction. I confirm that I have had the opportunity to ask questions.

I understand that my participation is voluntary and I am aware of my right to opt out of the study at any time without giving any reason.

I understand that the information collected about me and any of my medical records may be looked at by responsible individual from AIIMS Jodhpur or from regulatory authorities. I give permission for these individuals to have access to my records.

Date: _____ _____

Place: _____ Signature/Left thumb impression (Patient/Caregiver)

This to certify that the above consent has been obtained in my presence.

Date: _____ _____

Place: _____ Signature of Principal Investigator

1. Witness 1
2. _____
   Signature

2. Witness

_____

Signature

अखिल भारतीय चिकित्सा विज्ञान संस्थान

सूचित सहमति प्रपत्र

अन्वेषक का नाम : डॉ जीशान नूरे अज़ीम मोबाइल न 8210390449 रोगी आईडी

नं._____ मैं. _____ एस / ओ या डी / ओ._____अध्ययन का हिस्सा बनने के लिए मेरी पूर्ण, स्वतंत्र, स्वैच्छिक सहमति पश्चिमी राजस्थानी में तृतीयक देखभाल अस्पताल के आईसीयू के मामलों में वेंटिलेटर संबंधित घटनाओं के बैक्टीरियोलॉजिकल प्रोफाइल का अध्ययन करने के लिए जिस प्रक्रिया और प्रकृति,को मैंने अपनी भाषा में अपनी पूर्ण संतुष्टि के लिए मुझे समझाया है। मैं पुष्टि करता हूं कि मुझे सवाल पूछने का अवसर मिला है।

मैं समझता हूं कि मेरी भागीदारी स्वैच्छिक है और मुझे बिना कोई कारण बताए किसी भी समय अध्ययन से बाहर निकलने के मेरे अधिकार के बारे में पता है।

मैं समझता हूं कि मेरे और मेरे किसी भी मेडिकल रिकॉर्ड के बारे में एकत्रित जानकारी को एम्स, जोधपुर के जिम्मेदार व्यक्ति या नियामक अधिकारियों से देखा जा सकता है।

दिनांक.

स्थान. प्रिंसिपल जांचकर्ता के हस्ताक्षर

1.साक्षी. 2.साक्षी