"PREVALENCE AND CLINICAL PROFILE OF VENTILATOR ASSOCIATED PNEUMONIA IN PICU"

By

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Dissertation submitted to BLDE (Deemed to be University), Vijayapura.

In partial fulfillment of the requirements for the degree of

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IN

PEDIATRICS

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Date: 09.10.2020 **Dr. PRAJWAL KUMAR P. PATIL**

NEGLIGENCE is the start of an infection, that progresses to the disease,

VENTILATOR is the start of treatment and not the cure.

DR. PRAJWALKUMAR P. PATIL

LIST OF ABBREVIATIONS

PICU : PAEDIATRIC INTENSIVE CARE UNIT
VAP : VENTILATOR ASSOCIATED PNEUMONIA
HAI : HOSPITAL ACQUIRED INFECTION
NICU: NEONATAL INTENSIVE CARE UNIT
BAL: BRONCHOALVEOLAR LAVAGE
HFV: HIGH FREQUENCY VENTILATION
ET: ENDOTRACHEAL TUBE
MRSA: METHICILLIN RESISTANT STAPHYLOCOCCUS AUREUS
GCS: GLASCOW COMA SCALE
CFU: COLONY FORMING UNIT
OR: ODDS RATIO

ABSTRACT

Background and Objective:

Ventilator-associated pneumonia (VAP) is second most common hospital acquired infection in patients who are on mechanical ventilation, which develops more than 48 hours after start of the mechanical ventilation. This study is to determine the incidence rate, bacteriological profile, antibiotic sensitivity pattern of ventilator associated pneumonia in paediatric intensive care unit (PICU).

Materials and Methods:

This is a prospective cross-sectional study. The study was conducted on patients admitted in PICU of Shri B. M. Patil Medical College Hospital and Research Centre, Vijayapura, Karnataka, India, between November 2018 and July 2020. Patients diagnosed with VAP based on the defined criteria were included in the study and were studied determine the incidence rate, bacteriological profile, antibiotic sensitivity pattern of ventilator associated pneumonia in our paediatric intensive care unit.

Results:

The incidence of VAP was 11/81 (13.58%) in our hospital. 98.76 % of patients had a sterile blood culture and 1.24 % (n=1) showed the presence of gram-negative bacilli. A majority of patients (87.65 %, n=71) had a sterile ET Tube culture, while 3.70 % patients (n=3) showed the presence of *Klebsiella pneumoniae* in ET Tube culture. *Citrobacter frenudi* and *Staphylococcus aureus* was detected in 2.47 %(n=) of cultures, each. *Pseudomonas aeruginosa, Escherichia coli* and *Acinetobacter* was seen in 1.23 % (n=1) of neonates, each. Of the 81 enrolled patients, 76.54 % of the patients improved, while 9.88 % of patients were discharged against medical advice (n= 8). 13.58 % of patients (n= 11) had a fatal outcome. Of the patients who had VAP (n=11), 81.82 % improved with treatment, 9.09 % (n=1) were

discharged against medical advice and there was mortality of 9.09 % (n=1). The mortality in our study, attributable to VAP was 1/81 (1.23%). The ET tube isolates showed minimum resistance to Meropenem (30 %) and Vancomycin (20%) and maximum sensitivity to Meropenem (70 %) and Vancomycin (80%).

CONCLUSION:

Meropenem and Vancomycin were found to be the most appropriate antibiotics for the management of VAP in our hospital.

Keywords: Meropenem, Ventilator associated pneumonia, Vancomycin.

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INTRODUCTION

INTRODUCTION

Ventilator-associated pneumonia (VAP) is a pneumonia of hospital origin in patients who are on mechanical ventilation, which develops more than 48 hours after start of the mechanical ventilation. In the case of paediatric and neonatal intensive care units, VAP is the second most common hospital-acquired infection. Overall, the occurrence of VAP is 3 to 10 % of all ventilated Paediatric Intensive Care Unit patients. [1] A large portion of patients who develop VAP have serious adverse outcomes and increased length of hospital stay. The mortality rate for VAP ranges from 24-71% [2].

In order to manage VAP appropriately, it is vital to know the bacteriological profile or the chief Causative organisms of VAP in that particular environment or ICU. Based on that knowledge the sensitivity or resistance pattern of the primary causative organisms to the various available antibiotics can be studied in the laboratory in order to arrive at the ideal antibiotic for the treatment of VAP in that particular environment. Our study aimed to achieve just that in the environment of the PICU of our hospital.

AIMS & OBJECTIVES

AIMS AND OBJECTIVES

To determine the incidence rate, bacteriological profile, antibiotic sensitivity pattern of ventilator associated pneumonia in paediatric intensive care unit (PICU) of BLDE (Deemed to be University), Shri BM Patil medical college hospital and research centre.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

Historical Development

Neonatal respiratory failure has been treated with mechanical ventilation for almost half a century. The initial usage began as minor changes in adult ventilators used to treat babies of modest size and prematurity by today's standards. Most ventilators were time-cycled, and pressure limited in the early days. Ground-breaking developments in respiratory care took place in the 1970s. Antenatal corticosteroids were demonstrated to augment the maturity of the foetal lung, and development of the methods to monitor oxygen transcutaneously revealed the susceptibility of the preterm infant. The development of pulse oximetry and high-frequency ventilation (HFV) in the 1980s expanded the therapeutic armoury to a large extent. The technique of surfactant replacement began in the 1990s and was supplemented simultaneously by patient-triggered ventilation, real-time pulmonary graphics, and a multitude of pharmacologic agents. [3] The new millennium brought with it the microprocessor technology by the use of which the capabilities, monitoring, safety, and efficacy of neonatal ventilators was vastly enhanced thereby extending survival not only to infants born extremely prematurely but also those with a severe pulmonary disease that was heretofore lethal.

Definition

Ventilators can be life-saving. All the same, they can also increase the probability of a patient getting pneumonia by making it easier for microorganisms to reach the patient's lungs.

Ventilator-associated pneumonia (VAP) is defined by the Centre for Disease Control and Prevention (CDC) and National Healthcare Safety Network as "new and persistent radiographic infiltrates and worsening gas exchange in infants who are ventilated for at least

48 h and who exhibit at least 3 of the following criteria: temperature variability with no other known cause, leukopenia, change in the characteristic of respiratory secretions, respiratory distress and bradycardia or tachycardia."[4] This time window of 48 hours is vital in order to exclude any infection that might be incubating at the time of admission.[5]

Incidence

In spite of our increasing knowledge regarding the causes and prevention, hospital-associated pneumonia (HAP) and VAP account for 22% of all hospital-acquired infections (HAIs) in a multistate point-prevalence survey in the U.S. Although hospital-reported data from the National Healthcare Safety Network (NHSN) suggest that VAP rates have been declining, recently published data from a randomly selected national sample revealed that approximately 10% of patients who needed mechanical ventilation were diagnosed with VAP and that this rate has not declined over the past decade[1].

According to the surveillance report of European Centre for Disease Prevention and Control on Healthcare-associated infections acquired in intensive care units in 2017, in which 1192 hospitals and 1480 ICUs from 14 European countries provided data, 6 % of all ICU admissions presented with pneumonia. The incidence of pneumonia was 6.6 episodes per 1000 patient-days. However, the report did not specify the incidence of neonatal or paediatric patients separately[6].

In case of paediatric and neonatal intensive care units, VAP is the second most common hospital-acquired infection. Overall, the occurrence of VAP is 3 to 10 % of all ventilated Paediatric Intensive Care Unit patients in the U.S. Observation studies of hospital acquired infections indicate that pneumonia is responsible for 6.8 to 32.3 % of nosocomial infections in NICU patients[7].

PICU VAP rates have been reported from developed as well as developing countries. The National Healthcare Safety Network reported that VAP rate in level III NICUs of U.S. hospitals in 2010 were in the range 0.4-1.4/1000 MV days[8]. As per the data from International Nosocomial Infection Control Consortium, the average rate of VAP from 36 NICUs around the world between January 2004-December 2009 was 9.0/1000 MV days [9]. Data from the German Nosocomial Infection Surveillance System reports the average VAP rate to be 5.5/1000 MV days [10]. On the other hand, in 55 intensive care units of 8 developing countries between 2002-2005, the overall VAP rate was 24.1/1000 MV days ranging from 10.0-52.7/ 1000 MV days between units[11]. Data from Asian countries pointed to an incidence rate varying from 3.5- 46/1000 MV days in the new-born period[12].

In a study in NICU in Tehran, Iran, VAP occurred in 17.3% infants, at the rate of 11.6 per 1000 days on the ventilator[13].

In a study from a PICU in Cairo, 31 % patients developed VAP and the incidence density was 21.3 per 1000 ventilator days[14].

A 30-month prospective surveillance study on VAP in a PICU in Saudi Arabia by Almuneef et al. [15] enrolled 361 patients with a mean age of 28.6 months. 37/361 acquired VAP. The mean VAP rate was 8.87 per 1,000 ventilation-days with a ventilation utilisation rate of 47%.

While pediatric studies across the globe report an incidence of 2–17% [16,17,18,15], there are very few studies from developing countries including India reporting the incidence of VAP in children. One study from North India reported incidence of VAP to be between 17 and 30% [19]. A study at AIIMS, New Delhi, reported a overall VAP rate of 11.9/1000 ventilator hours [20]. Another study by Balasubramanian and Tullu [21] in a PICU in Mumbai, India, the

median age of the subjects (N = 232) was 9 months with a male: female ratio being 1.3: 1. Of 232 infants enrolled in the study, there were 15 episodes of VAP in 14 infants (frequency of 6.03 %) with an average VAP rate of 6.3 per 1,000 ventilator days.

Variations in the methods used to study and the case mix can influence the stated incidence of VAP[6]. A 41-month long surveillance study in a children's hospital demonstrated the role of intensity of surveillance. For the first 24 months of the study, infection control surveillance was conducted twice a week and for the next 2 years it was conducted daily using a nursing sentinel sheet. It was observed that daily surveillance found a 50% rise in the incidence of reported hospital- acquired infections.[22]

With the amendment of NNIS definitions for VAP in 2002 a more stringent definition of VAP came into force. VAP studies centred on the amended definitions registered lower rates of VAP incidence, posing a difficulty in determining if VAP was over diagnosed earlier or is currently underdiagnosed. The altered definitions must also be taken into account when VAP rates are compared over time[7].

The U.S. Centers for Disease Control and Prevention (CDC) has definitions for VAP in infants<1 year of age, but criteria for low- or very-low birth-weight infants are unavailable, thereby complicating the scenario. Very frequently, the patients of these groups often have comorbidities such as bronchopulmonary dysplasia, hyaline membrane disease, bloodstream infections (BSIs), and necrotising enterocolitis that make clinical, laboratory, and radiographic evidence of VAP incomprehensible[7].

Outcomes

1. Morbidity and Mortality

VAP infections have an adverse effect on patient outcomes. The all-cause mortality associated with VAP has been reported to range from 20% to 50%, but it is difficult to precisely associate mortality directly related to VAP; a recent meta-analysis based on randomised VAP prevention studies estimated the attributable mortality at 13% [1].

Several studies reported only univariate analyses in order to compare mortality rates among patients with and with- out VAP. A multivariate analysis of predictors of mortality among a large number of PICU patients with VAP, adjusting for seriousness of illness at admission and at discharge as well as other likely predictors of death is vital to determine mortality in paediatric patients that is truly due to VAP[7].

In a study on extremely preterm neonates estimated gestational age (EGA) < 28 weeks) by Apisarnthanarak et al. [23] in Missouri, USA, (n= 229), Sixty-seven neonates (29%) had EGA <28 weeks. 19 occurrences of VAP occurred in 28.3% of mechanically ventilated patients. VAP rates were reported to be 6.5 per 1000 ventilator days for neonates with EGA <28 weeks and 4 per 1000 ventilator days for EGA ≥ 28 weeks. By multivariate analysis, bloodstream infection prior to VAP (adjusted odds ratio: 3.5; 95% confidence interval [CI]: 1.2-10.8) was an independent risk factor for VAP after controlling for the period of endotracheal intubation. Ventilator-associated pneumonia (adjusted odds ratio: 3.4; 95% CI: 1.2-12.3) was an independent predictor of mortality. A strong relationship between VAP and mortality was observed in neonates whose NICU stay was >30 days (relative risk: 8.0; 95% CI: 1.9-35.0). Neonates having VAP also had an extended NICU length of stay (median: 138 vs 82 days).

In a study in 2017 in a Thai NICU by Thatrimontrichai et al. [24], (n=128) the median (inter quartile range) gestational age was 35 weeks (30.2 weeks, 37.8 weeks and birthweight were and 2380 g(1323.8 g, 3020.0 g) . 17 patients had VAP (19 episodes) and 111 patients had no VAP. The VAP rate was 13.3% or 10.1 per 1000 ventilator days. As per the multivariate analysis, a birthweight less than 750 g (adjusted odds ratio (aOR)=10.75, 95% CI=2.35-49.16; P=0.002) and sedative medication use (aOR=4.00, 95% CI=1.23-12.50; P=0.021) were independent risk factors for VAP. In comparison to the non-VAP group, the median difference in the VAP group showed a significantly longer period of NICU stay (18 days, P=0.001), total duration of hospital stay (16 days, P=0.002) and higher hospital costs ($5113, P=0.001). The in-hospital mortality rate in the VAP group was 17.6 % and in the non-VAP group it was 15.3% (P=0.73).

However, Balasubramanian and Tullu [21] reported a mortality rate of VAP to be 42.8% in a hospital in Mumbai which was similar to that of subjects without VAP. Similarly, Almuneef et al. [15] also observed that there was no significant difference between VAP and non-VAP patients regarding mortality rate in a PICU in Saudi Arabia.

2. Increased intubation period

VAP rates increased drastically for patients intubated for extended periods of time. In the patients who were extubated within the first 3 days of surgery, only 4% developed VAP, as compared to 40% of postoperative cardiothoracic surgery patients intubated more than 30 days [25]. Of the 26 cases of VAP, 19 occurred within the first 3 to 6 days of surgery.

Almuneef et al. [15] reported the average duration of mechanical ventilation to be 21 days for patients whodeveloped VAP and 10 days for non-VAP patients in their study in a PICU in Saudi Arabia.

In a retrospective cohort study of children requiring invasive ventilation in the PICU in Amsterdam [26] between December 2006 and November 2014, PICU stay and mechanical ventilation lasted longer in children with co-infections than children with negative cultures (9.1 vs 7.7 days, p = 0.04 and 8.1vs 6.5 days, p = 0.02).

Fischer et al. [27] reported that VAP resulted in increased morbidity in PICU patients, specifically, a longer duration of mechanical ventilation. They undertook a prospective cohort study to evaluate the incidence of VAP due to the delayed extubation among neonates and children undergoing repair of congenital heart disease. 26/ 272 neonates developed VAP (9.6%) over a period of 22 months. Using a Cox proportional hazards model to control for complexity of surgery, other respiratory complications, and secondary surgeries, the researchers found that the median delay of extubation due to VAP was 3.7 days (mean of 5.2 days vs 1.5 days for patients with and without VAP, respectively).

Two studies in 2010 and 2012 estimated that VAP prolongs length of mechanical ventilation by 7.6 to 11.5 days [28,29].

3. Increased antibiotic utilisation

Presumed VAP is also related to increased resource utilisation in terms of antibiotic use. VAP is the most frequent reason for administration of empirical antibiotics among PICU patients. A prospective cohort study at a tertiary, multidisciplinary, neonatal, and paediatric intensive care unit of a university teaching hospital in Switzerland (n= 456) reported that over half (56.6%) of all patients received antibiotics [30] of which treatment for suspected VAP constituted 47% of the antibiotic treatment days. The study concluded that a mediation aimed at reducing antibiotic use for VAP would have the highest bearing on antibiotic use.

4. Increased length of PICU/NICU stay

In paediatric populations, the published data are univariate and unmatched for seriousness of illness but indicate that paediatric patients with VAP may have excess mortality and length of PICU and NICU stay. The European Multicentre Trial studied the epidemiology of nosocomial infections in 20 units (5 PICUs, 7 neonatal units, 2 haematology-oncology units, and 8 general paediatric units) in 8 countries, (n=14,675) [31]. The investigators observed that infected patients had a longer average duration of stay in the PICU (26.1 ± 17.3 days versus 10.6 ± 6 days; $p < 0.001$) as compared to uninfected patients. The mortality rate was 10 % for PICU patients with hospital-acquired infections. Though the mortality and duration of hospital stay related specifically with VAP were not reported, VAP constituted 53% of the nosocomial infections in PICU patients. The death rate among uninfected PICU patients was not stated.

Similarly, PICU length of stay in a prospective cohort study over a period of 9 months in an academic tertiary care centre by Elward et al. reported that patients with VAP (n = 30) had a mean PICU length of stay of 27 days vs 6 days for uninfected patients (n= 595) (p= 0.001) (16). Additionally, the mortality rates with VAP were 20 % and without VAP were 7% (p = 0.065). The outcomes between infants on mechanical ventilation for > 8 days with VAP (n= 30) and those without VAP (n = 62) were also compared. PICU duration of stay was longer for VAP patients (27.53 ± 20.09 days versus 18.72± 35 days). Hospital duration of stay was also longer forVAP patients (52.63 ±37.43 days versus 33.77 ± 49.51 days), but the mortality rates for VAP (20%) or uninfected patients (21%) were not significantly different.

In a prospective cohort study (n = 361) in Saudi Arabia, Almuneef et al. [15] reported that PICU duration of stay with (n= 37) and without (n = 324) VAP were longer for patients with VAP(33.70 ± 30.28 versus 14.66 ± 17.34 days; P = 0.001). Statistically significant differences in death rates between VAP patients and non- VAP patients were not found (P =0.362).

Balasubramanian and Tullu [21] reported that in their study, patients with VAP had a significantly longer period of mechanical ventilation (22.5 vs. 5 median days; $p < 0.001$), lengthier PICU stay (23.25 vs. 6.5 median days; $P < 0.001$) and lengthier hospital stay (43.75 vs. 13.25 median days; $p < 0.001$).

Two studies in 2010 and 2012 estimated that VAP prolongs length of hospitalisation by 11.5 days to 13.1 days as compared to similar patients without VAP [29,28].

5. Increased hospital costs

VAP has also been shown to be responsible for increased hospital costs. The cost of hospitalisation attributable to VAP was investigated in a 2-year study of PICU patients (n= 1919) with a single admission [25]. The direct cost for VAP patients (n = 56) was $38,614, and that for non- VAP patients was $7,682. In a multivariate analysis adjusting for other predictors of cost such as age, severity of illness, underlying disease, and ventilator days, VAP was independently associated with a direct cost of $30,931 (95% confidence interval, $18,349 to $82,638). Another study also reported that the excess cost associated with VAP was estimated to be approximately $40 000 per patient [28].

Types of VAP:

i) Early Onset VAP- VAP which occurs within first 4 days of ventilation; commonly caused by antibiotic sensitive organisms, community-acquired bacteria such as Haemophilus and Streptococcus.

ii) Late Onset VAP - VAP which occurs after 4 days of mechanical ventilation is more likely attributed to drug resistant organisms such as Pseudomonas aeruginosa [32].

Pathogenesis

The factors involved in the origin of respiratory infection include: immunodeficiency in the host; inoculation of microorganisms into the lower respiratory tract and a highly virulent organism.

Pneumonia is infection of the lung parenchyma. It ensues from proliferation of microbial pathogens at the alveolar level and host's response to those pathogens. The aero-digestive tract above the vocal cords has a high bacterial count but the lower respiratory tract is normally sterile. Only if the person has chronic bronchitis or has had respiratory tract instrumentation, bacteria are lodged in it [33]. Microorganisms enter the lower respiratory tract mainly by aspiration from the oropharynx. The pathogens enter by inhalation route as contaminated droplets, by haematogenous spread or by continuous extension from an infected pleura or mediastinum [34].

The following mechanical barriers of the host present the first line of defence against the invading pathogens:

i. Hair and turbinates of the nares capture large inhaled particles before reaching the lower respiratory tract.

ii. branching architecture of tracheobronchial tree traps microbes.

iii. Muco-ciliary clearance

iv. local antibacterial factors

v. Gag reflex and cough reflex

An endotracheal tube or tracheostomy interferes with the normal anatomy and physiology of the respiratory tract, especially the functional mechanisms involved in clearing secretions (cough and mucociliary action) [35].

Intubated patients have a reduced level of consciousness that impairs voluntary clearance of secretions, which may then pool in the oropharynx [36]. This leads to the macro aspiration and micro aspiration of contaminated oropharyngeal secretions that are rich in harmful pathogens. Normal oral flora start to multiply and are able to pass along the tracheal tube, forming a glycocalyx biofilm on the tube's surface that is resistant to both antibiotics and host defence mechanism [35]. In severely ill patients the normal flora in oropharynx is replaced by pathogenic microbes and almost all intubated patients experience micro aspiration and are transiently colonised with these pathogens. But only one third of colonised patients develop VAP. When the barriers are surpassed or when the pathogens are so small as to be inhaled, they reach the alveolar levels, where they are effectively cleared and killed by the alveolar macrophages present. The alveolar macrophages are assisted by the epithelial cells like surfactant proteins A and D which have opsonising properties and antibacterial and antiviral activity.

The pathogens, once engulfed are cleared by muco-ciliary elevator or lymphatics and are no longer harmful. When the capacity of alveolar macrophages to ingest or kill the microbes is exceeded clinical pneumonia manifests.

The alveolar macrophages also initiate the process of inflammatory response of the host. The host inflammatory response produces the clinical syndrome of pneumonia rather than proliferation of microbes. Inflammatory mediators like interleukin 1 and tumor necrosis factor are released giving rise to fever. The release of interleukin 8 results in peripheral Leukocytosis and purulent secretions. Granulocyte colony stimulating factor causes the release of neutrophils and their attraction to the lungs.

Inflammatory mediators cause the accumulation of new neutrophils and creates alveolar capillary leak similar to that seen in adult respiratory distress syndrome, but the leak is initially localised in pneumonia. Haemoptysis occurs when erythrocytes cross the alveolar-capillary membrane. The capillary leak is seen as infiltrate on a radiograph and rales on auscultation. Alveolar filling leads to hypoxemia. The interference of hypoxemic vasoconstriction by bacterial pathogens that normally occurs with fluid filled alveoli leads to severe hypoxaemia. Respiratory alkalosis results from increased respiratory drive caused by systemic inflammatory response. Dyspnoea is due to reduced compliance by capillary leak, hypoxemia, enhanced respiratory drive, secretions and infection related bronchospasm. If the alteration in lung mechanics are severe enough to decrease lung volume and compliance, respiratory failure and death may take place due to intrapulmonary shunting of blood.

In the mechanically ventilated patient, host defences are compromised due to several reasons: critical illness, comorbidities, and malnutrition impair the immune system, and, most importantly, endotracheal intubation thwarts the cough reflex, compromises mucociliary clearance, injures the tracheal epithelial surface, and provides a direct pathway for rapid entry of bacteria from above into the lower respiratory tract [33].

The series of pathologic changes in the evolution of classic pneumonia are as follows:

1) **Edema -** It is the initial phase due to proteinaceous exudate and bacteria in the alveoli.

2) **Red hepatisation phase** - It is due to erythrocytes in the cellular intra-alveolar exudate.

3) **Gray hepatisation phase** - no new erythrocytes extravasate and existing ones are being lysed and degraded. There is predominance of neutrophils with fibrin deposition and no bacteria. This phase indicates successful containment of infection and there is an improvement in gaseous exchange.

4) **Resolution -** It is the final phase; where macrophages again predominate with the clearance of inflammatory response; neutrophil debris and bacteria.

These stages of evolution are classically seen in pneumococcal lobar pneumonia. But in VAP the pattern is bronchopneumonia due to the mechanism of micro aspiration.

Risk factors for VAP

The Risk factors for VAP may be classified as : host related, device related or personnel related

Host related risk factors include: [7]

- Male sex
- Underlying medical condition
- Immunosuppression
- Chronic obstructive lung disease
- Adult respiratory distress syndrome

- Patient's body position
- Level of consciousness
- Number of intubations
- Medications
- Admission for trauma

Device related risk factors include:

- Endotracheal tube
- Ventilator circuit
- Nasogastric or orogastric tubes

Personnel related risk factors include:

- Improper hand washing
- Failure to change gloves between contact with patient
- Not using personal protective equipment when antibiotic resistant bacteria have been identified.

In a meta-analysis of risk factors for VAP in PICU conducted by Liu et al. [37] from the year 1950 to 2013, 205 articles were initially retrieved from literature of which 9 were included for the analysis. These 9 studies had 4,564 patients of which 213 patients had VAP and 4,351 patients were without VAP. Among 14 risk factors, 6 factors statistical significant as shown in the table:

Table 1: Risk factors for VAP		
Risk factor	Odds Ratio	95% Confidence Interval
Genetic syndrome	2.04	1.08-3.86
Steroids	1.87	1.07-3.27
Reintubation or self-extubation	3.16	2.10-4.74
Blood stream Infection	4.42	2.12-9.22
Prior antibiotic therapy	2.89	1.41-5.94
Bronchoscopy	4.48	2.31-8.71

Another meta-analysis by Tan et al. [38] collated data from databases of Embase, Pubmed, Cochrane Central Register of Controlled Trials, and Web of Science upto July 2013. In a total of eight studies, 370 cases and 1,071 controls were identified. Ten risk factors were found to be related to neonatal VAP which were listed as follows:

Table 2: Odds ratios for risk factors for VAP	
Risk factor	**Odds Ratio**
Duration of stay in NICU	23.45
Reintubation	9.18
Enteral feeding	5.59
Mechanical ventilation	4.04
Transfusion	3.3
Low birth weight	3.16
Prematurity	2.66
Parenteral nutrition	2.30
Bronchopulmonary dysplasia	2.21
Tracheal intubation	1.12

Kawanishi et al. [39] examined the frequency and risk factors associated with VAP, especially in ventilator circuit changes every 7-day versus every 14-day, in a neonatal intensive care unit (NICU) in Japan. Seventy-one neonates hospitalised in the NICU were enrolled and divided into two groups: with VAP and without VAP. Using univariate logistic regression analyses, significant risk factors for the development of VAP were identified which included: prolonged mechanical ventilation, frequent re-intubation, low gestational age, and low birth weight. After controlling for other variables, only BW < 626 g was a significant independent predictor for VAP in NICU infants. Further, in one group circuit changes were made every 7-days and compared with the group in which circuit changes were made every 14-days. In the every 7-day ventilator change group, the incidence of VAP was 9.66/ 1000 ventilator days and slightly but not significantly lower at 8.08/1000 ventilator day for the every 14-day change group. The study concluded that BW < 626 g was a significant independent predictor of VAP. Decreasing the number of days after which ventilator circuit changes are made from every 7 days to 14 days had no contrary effect on the VAP rate in the NICU.

A case- control study in Spain in 2015 by Izelo-Flores et al. [40] to pinpoint risk factors for the development of VAP in a NICU included 45 cases and 90 matched controls. The risk factors found to be statistically significant in the univariate analysis were: previous episode of sepsis, reintubation, airway malformation, exclusive parenteral nutrition, and duration of mechanical ventilation. In the logistic regression analysis, the following were found to be independent risk factors for VAP:

Table 3: Independent risk factors for VAP			
Risk factor	Odds Ratio	C I 95%	P value
Reintubation	41.26	11.9 – 158.41	0.001
Airway malformation	19.5	1.34- 282.3	0.029
Days of mechanical ventilation	8.9	1.9-40.8	0.005

The authors concluded that of the significant risk factors, it was feasible to intervene in reintubation events, by tightening the endotracheal cannula with an adequate fixation, be extra-careful while shifting the patient, and follow a decannulation protocol to reduce the number of days the patient is on ventilation.

Lee et al. [41] conducted a retrospective observational study to establish the clinical characteristics and risk factors for the development of VAP in intubated low birth weight (< 2.5 Kg) neonates in a Chinese neonatal intensive care unit. Six hundred and five low birth weight infants were analysed. Of the 114 infants who were intubated for >48 hours, 15 (13.2%) developed VAP. Of these 15 patients, the average age at onset of VAP was 24.0 days ± 11.2 days and the mean gestational age was 27.1weeks ± 2.3 weeks, which was significantly lower than the mean gestational age in the group without VAP (30.2 weeks ± 3.5 weeks). The average birth weight was 944.4 ± 268.4 g in the VAP group and 1340.1 g ± 455.4 g in the non- VAP group ($p < 0.001$). Longer time of intubation (odds ratio: 1.35, 95% confidence interval: 1.12-1.62) and parenteral nutrition (odds ratio: 1.32, 95% confidence interval: 1.14-1.51) were found to be risk factors in the VAP group after correcting for gestational age and birth weight. The authors concluded that early removal of the endotracheal tube and sufficient enteral nutrition may reduce the incidence of VAP in low birth weight infants.

Another study in China from 2003 to 2005 by Zhu et al. [42] included 106 neonates, of whom 84 received mechanical ventilation for ≥ 48 hours. Thirty-five (41.7%) out of the 84 patients developed VAP. Univariate analysis showed that gestational age, duration of mechanical ventilation, reintubation, birth weights, primary lung disease and gamma globulin administration were associated with the development of VAP (P <0.05). Multivariate stepwise logistic regression analysis predicted the following risk factors for the development of VAP.

Table 4: Risk factors for development of VAP

Risk factor	Odds Ratio	95% CI	P value
Primary lung disease	3.671	1.0-13.45	< 0.05
Duration of mechanical ventilation	4.945	1.51-16.21	<0.01
Re- intubation	7.721	2.31 – 25.85	<0.01
High dose gamma globulin administration	5.520	2.08 – 16.26	<0.01

In the study, the detection rate of gram-negative bacilli (76.9%) was the highest, followed by gram positive coccus (17.9%) in VAP patients.

A retrospective cohort study [43] in a NICU in China included 259 patients who were ventilated > 48 hours. There were 52 occurrences of VAP (20.1%). The main pathogens were gram negative bacterium (82.1%, 23/28). The duration of stay in the hospital in the VAP group was 19.9 ± 5.9 vs. 16.7± 7.2 days in controls (p<0.01). The mortality rate of the VAP group was 13.5% (7/52) vs. 12.1% in controls (p>0.05). By logistic regression analysis the following independently predicted VAP:

Table 5: Independent risk factors for VAP		
Risk factor	**Odds Ratio**	**95% CI**
Re-intubation	5.3	2.0 - 14.0
Duration of mechanical ventilation	4.8	2.2 - 10.4
Treatment with opiates	3.8	1.8 - 8.5
Endotracheal suctioning	3.5	1.6 - 7.4

Petdachai [12] conducted a prospective observational study in a neonatal intensive care unit to pinpoint factors associated with the development of ventilator-associated pneumonia (VAP) in 170 infants aged less than 30 days who required mechanical ventilation for more than 48 hours. VAP occurred in 85 infants (50 cases per 100 mechanically-ventilated infants) or 70.3 cases per 1,000 ventilator days. Stepwise logistic regression analysis identified 3 factors independently associated with VAP:

Table 6: Independent risk factors for VAP			
Risk factor	**Adjusted odds ratio**	**95% CI**	**P value**
Umbilical catheterisation	2.5	1.3 – 4.7	P=0.007
Respiratory distress syndrome	2.0	1.0 to 3.9	P=0.03
Insertion of orogastric tube	3.0	1.3 – 7.2	P=0.01

Infants with VAP had longer duration on ventilator (14.2 days vs 5.9 days; $p<0.001$) and longer hospital stay (28.2 days vs 13.8 days; $p<0.001$). Organisms were isolated in 42 specimens (49.4%) from endotracheal aspirate culture and in 17 specimens (20.0%) from hemoculture; Pseudomonas aeruginosa, Klebsiella pneumoniae and Acinetobacter spp were predominant. Polymicrobial infection was found in 11 specimens (12.9%) from endotracheal aspirate culture. Leukocytosis and blood gas values could not predict the presence of VAP.

The mortality of infants with VAP (29.4%) did not differ significantly from that of infants without VAP (30.6%) (p=0.87). Certain clinical interventions might potentially affect the incidence of VAP and outcome associated with VAP.

In an Iranian study [13] the only VAP predictor was sputum (odds ratio (OR) = 5.11, p = 0.02). Death rate for VAP was 2/14 (14.3%). Length of mechanical ventilation (hazard ratio (HR) = 0.96, P = 0.01, birth weight (HR = 0.81, P < 0.001), and purulent tracheal aspirate (HR = 0.25, P < 0.006) were independent forecasters of overall survival.

Almuneef et al. [15] reported that witnessed aspiration, reintubation, prior antibiotic therapy, continuous enteral feeding, and bronchoscopy were associated with VAP in univariate analysis in their study. On multiple logistic regression analysis, only prior antibiotic therapy, continuous enteral feeding, and bronchoscopy were independent predictors of VAP.

A study by Sharma et al. [44] in Punjab, India, implicated the use of H (2) blocker (Ranitidine) to be associated with higher incidence of VAP in children.

Another Indian study by Patra et al. [19] in a PICU reported Re-intubation, prolonged duration of intubation and mechanical ventilation as significant risk factors on univariate analysis for development of nosocomial pneumonia. On multiple regression analysis, reintubation was the only independent risk factor for nosocomial pneumonia (OR 0.72, 95% CI 0.55-0.94).

Balasubramanian and Tullu [21] reported neuromuscular disease (p = 0.005), histamine-2 receptor blockers (p = 0.0001), tracheostomy (p = 0.0001), and positive blood culture growth (p = 0.0008) to be significantly associated with VAP in univariate analysis.

However, on multivariate analysis, only positive blood culture growth was a risk factor for VAP.

Diagnosis

There is no gold standard for the diagnosis of VAP in both adults and children thereby increasing the complexity of interpretation of the literature. The clinical conditions for the diagnosis of VAP have been set by the NNIS [45] and the CDC [22]. The following table summarises the clinical criteria for diagnosis of VAP for infants < 1 year, children between 1 to 12 years of age and children above 12 years. NNIS/CDC criteria do not require microbiologic confirmation to diagnose pneumonia.

Table 7: NNIS/CDC criteria for diagnosis of VAP			
Criteria	Infants ≤ 1 year of age	Children > 1 year and ≤ 12 years of age	Children > 12 years of age
Common criteria	Patients who are mechanically ventilated for more than or equal to 48 h		
Common criteria	two or more abnormal chest radiographs with at least one of the following symptoms: new or progressive and persistent infiltrate, consolidation, cavitation, and/or pneumatoceles		
	at least three of the following criteria: - temperature instability with no other recognised cause; -new onset of purulent sputum, -change in character of sputum, -increased respiratory secretions, or increased suctioning requirements; -apnea, tachypnea, nasal flaring with retraction of chest wall, or grunting; -wheezing, rales, or rhonchi; cough; -bradycardia (<100 beats/ min) or tachycardia (>170 beats/min).	at least three of the following criteria: fever (>38.4°C or>101.1°F) or hypothermia (<37°C or 97.7°F) with no other recognised cause; - leukopenia (<4,000 WBC/mm^3) or leucocytosis (≥15,000 WBC/mm^3); -new onset of purulent sputum -change in character of sputum - increased respiratory secretions, or increased suctioning requirements; -rales or bronchial breath sounds;	at least one of the following symptoms: fever (>38°C) with no other recognized cause, - leukopenia (<4,000 WBC/mm^3) or leukocytosis (≥12,000 WBC/mm^3), At least two of the following: -new onset of purulent sputum, -change in character of sputum, -increased respiratory secretions, or increased suctioning requirements; -new onset of or Worsening cough, dyspnea, or tachypnea; rales or bronchial breath sounds;
	worsening gas exchange (oxygen desaturations, increased oxygen requirements, or increased ventilator demand)	worsening gas exchange (O2 desaturations [pulse oximetry of <94%], increased oxygen requirements, or increased ventilation demand).	worsening gas exchange (e.g., O2 desaturations [e.g., PaO2/FiO2 levels of ≤240], increased oxygen requirements, or increased ventilation demand)

Challenges in diagnosis of VAP

VAP definitions were developed for supervision purposes, but they are inappropriate to apply in neonates, since they have not been validated as clinical diagnostic criteria. Overlap of signs and symptoms and radiographic findings with underlying respiratory conditions poses difficulty in the diagnosis of VAP in neonates and may be a cause of overdiagnosis [46]. Fever and leukocytosis are highly non-specific and can occur due to any condition that causes release of cytokines. The alternative causes are antibiotic associated diarrhoea, sinusitis, UTI, pancreatitis, drug fever. Chest X-ray suspicious of VAP may also point to the differentials of pulmonary edema, pulmonary infarction, atelectasis or acute respiratory distress syndrome [47].

Microbiologic testing such as respiratory cultures does not reliably differentiate bacteria colonising the respiratory tract from the true infections. Gram stain of respiratory secretions may show an inflammatory infiltrate with neutrophils, but this may indicate a tracheitis or pneumonia. When the Gram stain and culture identify the same organism, the likelihood of its causal role in VAP is enhanced. Furthermore, the use of chest X rays as a criterion for the diagnosis of VAP has raised questions of reliability and reproducibility [48]. Finally, it is painstaking to obtain true samples of lower respiratory tract secretions from infants. Because of these challenges with defining VAP accurately in the neonatal population, in 2014 the NHSN discontinued accepting and analysing VAP identified in the NICU. However, many NICUs and collaboratives continue surveillance and internal benchmarking of this condition.

The lack of a gold standard for diagnosis of VAP is the major culprit for poor outcome. Hence the **differential diagnosis** of VAP includes:

- Atypical pulmonary edema
- Pulmonary contusion
- Alveolar hemorrhage
- Hypersensitivity pneumonitis
- Acute respiratory distress syndrome
- Pulmonary embolism

In conditions mimicking pneumonia the diagnosis of VAP can be ruled out by accurate diagnostic techniques. The clinical approach enhanced by principles learned from quantitative culture studies is valid according to recent IDSA / ATS guidelines for diagnosis of HAP / VAP. The lack of specificity in clinical diagnosis has led to the betterment in diagnostic criteria.

The Clinical Pulmonary Infection Score (CPIS) was thus developed by Pugin et al. [49] which includes clinical, physiological, microbiological and radiographic evidence to allow a numerical value to predict the presence or absence of VAP.

Table 8: Clinical Pulmonary Infection Score (CPIS)		
Sr. No.	Criteria	Score
1	Fever (°C) ≥ 38.5 but ≤ 38.9 ≥ 39 or ≤ 36	1 2
2	Leukocytosis<4000 or >11000/μL Bands >50%	1 1 (additional)
3	Oxygenation (mmHg) PaO2 / FiO2 <250 / no ARDs	2
4	Chest radiograph - localized infiltrate - Patchy / diffuse infiltrate - Progression of infiltrate (no ARDs / CHF)	2 1 2
5	Tracheal aspirate -moderate / heavy growth -same morphology on Gram's stain	 1 1 (additional)
	Maximum score	12

Scores vary between 0 and 12.

At the time of original diagnosis, progression of infiltrate is unknown and tracheal aspirate cultures are unavailable, so the initial maximal score is8-10. Score > 6 shows good correlation with presence of VAP [49].

The sensitivity of CPIS is 93% and specificity is 100%. Despite the popularity of CPIS there is still a debate on its validity. The inter observer variation in CPIS calculation jeopardises its use in clinical practice [50].

Samples for culture and microbiology

NNIS/CDC criteria for VAP do not mandate a microbiologic confirmation. But due to the growing frequency of VAP being caused by Multi Drug Resistant organisms, along with the risks of initial ineffective therapy, experts suggest that cultures of respiratory secretions should be obtained from virtually all patients with suspected VAP. The American Thoracic Society (ATS) and Infectious Diseases Society of America (IDSA) guidelines for adults (2016) suggests lower respiratory samples for culture and microbiology [1]. However, there is no clarity on whether the adult experience can be extrapolated to children. The Guidelines suggest non-invasive sampling with semiquantitative cultures to diagnose VAP, rather than invasive or non-invasive sampling with quantitative cultures .

Invasive respiratory sampling includes bronchoscopic techniques (ie, bronchoalveolar lavage [BAL], protected specimen brush [PSB]) and blind bronchial sampling (ie, mini-BAL). Non-invasive respiratory sampling refers to endotracheal aspiration.

Once samples are collected, they are sent for Gram stain, culture and sensitivity. Gram stain helps to identify the type of organism and also whether the material is purulent or not. Purulence is defined as > 25 neutrophils and < 10 squamous epithelial cells per low power field [19]. Culture results are reported as semi-quantitative and or quantitative values. The samples are inoculated in blood agar, Mac Conkey agar and chocolate agar. Semi quantitative values obtained are considered positive when the agar growth is moderate (+++) or heavy (++++) while quantitative positivity is > 105 cfu/ml.

The exact speciation of the organism and their antibiotic susceptibility takes a few days, but provides invaluable information.

Microbiology

Knowledge about the causative microorganisms of VAP is critical for guiding decisions regarding empirical antibiotic therapy.

The natural flora of the oropharynx in the non-intubated patient without severe illness consists majorly of viridans streptococci, *Haemophilus* species, and anaerobes. Salivary flow and content (immunoglobulin, fibronectin) are the main host factors maintaining the normal flora of the mouth (and dental plaque). Aerobic Gram-negative bacilli are usually not found in the oral secretions of healthy patients. During severe illness, especially in ICU patients, the oral flora shifts dramatically to a predominance of aerobic Gram-negative bacilli and *Staphylococcus aureus*. Bacteria sticks to the orotracheal mucosa of the mechanically ventilated patient due to the reduced mucosal immunoglobin A and increased protease production, exposed and denuded mucous membranes, elevated airway pH, and increased numbers of airway receptors for bacteria, due to acute illness and antimicrobial use [51].

The known and suspected microbiologic causes of VAP are reproduced here from an article by Park [51]as follows:

Table 9: Known and suspected microbiologic causes of VAP	
Gram-positive cocci	**Anaerobic bacteria**
Staphylococcus aureus	**Bacilli**
Streptococcus pneumoniae	*Bacteroides* species
Other streptococci	*Fusobacterium* species
Coagulase-negative staphylococci	*Prevotella* species
Enterococci	*Actinomyces* species
Gram-positive rods	**Cocci**
Corynebacterium species (diptheroids)	*Veillonella* species
Listeria monocytogenes	Peptostreptococci
*Nocardia*species	
Aerobic Gram-negative bacilli	**"Atypical bacteria"**
Haemophilus influenzae	Legionella species
	Legionella-like amoebal pathogens
	Mycoplasma pneumoniae
	Chlamydia pneumoniae
Lactose fermenting Gram-negative bacilli	**Fungi**
Enterobacteriaceae	*Candida* species and other yeasts
Escherichia coli	*Aspergillus* species and other molds
Klebsiella species	Pneumocystis carinii
Enterobacter species	
Proteus species	
Serratia species	
Citrobacter species	
Hafnia alvei	
Non-lactose fermenting Gram-negative bacilli	**Viruses**
Acinetobacter calcoaceticus and baumannii	Influenza and other respiratory viruses
Stenotrophomonasmaltophilia	Herpes simplex virus
Burkholderia cepacia	Cytomegalovirus
Pseudomonas aeruginosa	
Gram-negative cocci	**Miscellaneous causes**
Neisseria species	Mycobacterium tuberculosis
Moraxella species	*Strongyloides stercoralis*

The organism that causes VAP depends on the duration of mechanical ventilation. The causative organism for early onset VAP is usually one of the following:

- Staphylococcus aureus
- Streptococcus pneumoniae
- Hemophilus influenzae
- Proteus species
- Serratiam arcescens
- Klebsiella pneumoniae
- Escherichia coli

The causative organism for late onset VAP is usually one of the following:

- Pseudomonas aeruginosa
- Methicillin resistant staphylococcus aureus (MRSA)
- Acinetobacter species
- Enterobacter species

Treatment

When selecting an appropriate therapy for VAP it is essential to know the organisms likely to be present, local resistance patterns within the ICU, a rational antibiotic regimen, and a rationale for antibiotic de-escalation or stoppage [52].

Treatment of suspected VAP is centred on an approach of initial empirical therapy with broad-spectrum antibiotics followed by de-escalation to specific antimicrobial therapy once culture results are known or discontinuation of antibiotics if VAP is no longer suspected. The American Thoracic Society and Infectious Disease Society of America updated their evidence-based guidelines for the management of VAP in adults in 2005 [35]. Major suggestions in the new document include the use of early, appropriate, and broad-spectrum antibiotics for empirical therapy; utilisation of empirical antibiotics from a different class than antibiotics that the patient has recently received; well-judged use of combination therapy in nosocomial pneumonia; the likely use of linezolid as an alternative to vancomycin for VAP caused by methicillin-resistant *Staphylococcus aureus* (MRSA); the use of colistin for patients with VAP caused by carbapenem-resistant *Acinetobacter* species; the potential use of aerosolised antibiotics as adjunctive therapy for patients with VAP due to certain antibiotic-resistant organisms; scaling down of antibiotics depending on patients' culture results and clinical improvement; and a shorter duration of antibiotics regimen for patients with uncomplicated nosocomial pneumonia from bacteria other than non-fermenting gram-negative bacilli. These guidelines are arrived at on data from clinical trials of nosocomial pneumonia in adult patients. There is insufficient data to recommend the optimal treatment for VAP in children [7].

Empirical Therapy

Table 10: Comparison of recommended initial empiric therapy for ventilator associated pneumonia according to time of onset [53,54]	
Early onset VAP	**Late onset VAP**
Second or third generation **Cephalosporin:** i) Ceftriaxone ii) Cefuroxime iii) Cefotaxime or **Fluoroquinolones:** i) Levofloxacin ii) Moxifloxacin or **Aminopencillin + B lactamase inhibitor:** Ampicillin + Sulbactam or Ertapenem	**Cephalosporin** e.g. Cefepime Ceftazidime Or **Carbapenems:** Eg: Imipenem cilastatin or Meropenem Or **B lactam / B-lactamase inhibitor** Eg. Piperacillin + tazobactam **Plus Aminoglycoside:** Amikacin Gentamycin Tobramycin or **Antipseudomonal fluoroquinolone** Ciprofloxacin Levofloxacin **Plus coverage for MRSA** Vancomycin or Linezolid 600mg B.D.

Table 11: Recommended therapy for suspected or confirmed MDR organisms and fungal VAP [22, 23, 24]	
Pathogen	**Treatment**
MRSA Pseudomonas aeruginosa Acinetobacter species ESBL positive Enterobacteriaceae	**Carbapenams** Eg : Imipenam + Cilastin Meropenem Or **B lactam / B lactamase inhibitor** Ampicillin + Sulbactam Or Tigecycline **Carbapenem** Imipenem + Cilastatin Meropenem
Fungi Legionella	Fluconazole Caspofungin or Voriconazole Macrolides (eg : Azithromycin) or Fluoroquinolones (eg.Levofloxacin)

If the CPIS decreases over the first 3 days, antibiotics should be stopped after 8 days. An 8 day course is as effective as a 2 week course and is associated with less frequent emergence of antibiotic – resistant strains.

There is a lot of controversy regarding monotherapy versus combination therapy for patients with VAP. The major reasons in favour of combination therapy are to prevent the development of resistance, improve outcomes, provide synergy, and provide sufficient antibiotic coverage should the pathogen be resistant to the agent that would have been chosen as single therapy.

Though the former two arguments are logical, they are not yet proven. In fact, a meta-analysis pointed out that clinical failure was more common with combination therapy, as was nephrotoxicity; aminoglycosides were the second agent, and combination therapy did not stop new resistance pattern. Since mortality is higher when therapy is inappropriate during the first 48 h, Koenig and Truwit [52] favoured initiating combination therapy for patients at risk for multidrug-resistant organisms until sensitivities were known. This was consistent with an approach suggested by Gruson et al. [55].

Prevention

Clinicians must focus on eliminating or minimising the incidence of VAP through preventive techniques. The incidence of early-onset VAP can be reduced by simple measures[52]. Several suggestions have been given to decrease VAP which are as follows:

1. Using orotracheal tubes (instead of nasotracheal tubes) in patients requiring mechanical ventilation and minimise its duration [56]. Non-invasive ventilation through a nasal or full-face mask is an alternative to endotracheal intubation when possible. The presence of endotracheal tube is the main culprit for VAP development. So, patients should be assessed

on a daily basis for potential weaning and early extubation. The methods used for assessing readiness for extubation include T-piece trials, weaning intermittent mandatory ventilation and pressure support ventilation[57].

2. Changing breathing circuits of ventilators only if they are found to be faulty or if they are apparently contaminated[56].

3. Using endotracheal tubes having dorsal lumens to enable respiratory secretions to drain [56].

4. Hand hygiene is most important tool to reduce interpersonal transmission of bacteria in order to reduce the rate of hospital-acquired infections. Considerable bacterial contamination of hospital staff hands during normal patient care has been established. Proper hand washing for 10 seconds should be performed before and after contact with patients. Gloves should be worn while on contact with oral or endotracheal secretions.

5. Oral hygiene - Oral decontamination by both mechanical and pharmacological methods reduce the number of bacteria within the patient's oral cavity. Mechanical interventions are brushing the tooth and rinsing of oral cavity to remove dental plaque. Suctioning also removes dental plaque. Pharmacological interventions involve use of antimicrobial agent like chlorhexidine oral rinse twice a day[58]. VAP prevention can also be accomplished by the use of solution containing gentamycin, colistin and vancomycin every 6 hours[59].

6. Stress ulcer prophylaxis - Patients on mechanical ventilation for more than 48 hours are at a 16-fold increased risk for gastro intestinal bleeding[60]. Almost all patients receiving mechanical ventilation are given stress ulcer prophylaxis which increase gastric pH. Pathogens multiply in the alkaline gastric environment and bacterial colonisation of the stomach can lead to aspiration and colonisation of the respiratory tract [61]. Ranitidine an H2 receptor blocker significantly reduced the risk of bleeding without increasing the risk of

VAP or mortality [62].However, in another study, VAP rates did not differ between patients receiving ranitidine, omeprazole or sucralfate for stress ulcer prophylaxis [63]. Stress ulcer prophylaxis does not play a pivotal role in the development of VAP but prevents serious gastro intestinal bleeding according to the studies done so far.

7. In line suctioning - Endotracheal suctioning is used for removing bronchopulmonary secretions from the airway[7]. It is mandatory while on mechanical ventilation to prevent contamination of airways. Mucus can become stagnant in the airways and become a medium for bacterial growth. Maintaining adequate cuff pressure is necessary to prevent leakage of secretions and aspiration. Pressure in the cuff should be maintained at no less than 20cm H2O [64] and using tubes with ports for continuous suctioning reduces the incidence of VAP by 50% [65].However, currently CDC does not offer any recommendations pertaining to the preferential use of either closed or open suction systems, nor are there any recommendations regarding the frequency of replacement for multiuse closed suctioning systems in a particular patient[56].

8. Turning of patients every 2 hours increases pulmonary drainage and reduces the development of VAP. Using beds capable of continuous lateral rotation reduced the incidence of pneumonia but not mortality or duration of mechanical ventilation. So these beds are not routinely used for prevention of VAP[66].

9. Head-of-Bed Elevation - Supine body position is thought to have some correlation with VAP in adult patients, probably due to enhanced gastroesophageal reflux and aspiration. Semirecumbent positioning has been shown to advantageous in lowering surrogate outcomes such as aspiration and gastroesophageal reflux in adults. One clinical trial demonstrated a substantial decrease in the occurance of confirmed VAP in patients with head-of-bed elevation (5% versus 23%; OR, 6.8; 95% CI, 1.7 to 26.7)[67]. As per the

practice statements given by AACN, simple elevation of the head end of bed by 30° reduces VAP by 34% [68]. However, there is insufficient data to recommend semi recumbent positioning in decreasing VAP in children. One age- and sex-matched case control study of hospital acquired pneumonia in children pointed out that there was no difference between cases and controls with different head-of-bed elevation. However, the limitation of the study was its small sample size (n = 9 for each group)[69]. Additionally, practical issues pose a problem in using semi recumbent positioning in children. For example, elevating the head >30° is logistically difficult for small pediatric patients such as infants and toddlers[7].

10. Minimising usage of narcotic agents prevents aspiration of gastric contents[70]. Cautious reduction in the use of narcotics and sedatives must be done as pain limits deep breathing and impairs oxygenation. Daily interruption of continuous sedative infusions reduces the duration of mechanical ventilation by more than 2 days and duration of ICU stay by 3.5 days[71].

11. Gastric overdistension should be avoided by monitoring gastric residual volumes and administration of agents that enhance gastric motility as a measure to prevent VAP (70).

12. Educational Interventions - The effects of VAP on the morbidity, mortality, duration of hospital stay and cost are immense. So education plays a vital role in the management of VAP. After Identifying effective measures for preventing VAP, they need to be properly implemented in the hospital setting. Several studies have shown a decrease in VAP rates after courses to educate hospital care staff about the epidemiology of VAP and the preventive measures needed to control VAP [72,56,73,74].

13. The Bundle Approach - In December 2004, the Institute for Healthcare Improvement (IHI) threw a challenge to hospitals to save 100,000 lives by June 2006 [21]. One of the six

evidence-based guidelines to be implemented for achieving this goal was the VAP Bundle for prevention of VAP. Bundles of care are evidenced-based practices that are grouped together to encourage the consistent delivery of these practices [75]. These involve the simultaneous application of several preventive strategies for all patients, often aided by tools such as checklist[76].

The VAP bundle for adults is to

i. Whenever possibly, to avoid/decrease endotracheal intubation and duration of mechanical ventilation.

ii. Use orotracheal and orogastric tubes to lower the risk of hospital-acquired sinusitis,

iii. Avoid heavy sedation and neuromuscular blockade with depression of cough reflexes,

iv. Keep endotracheal cuff pressures to greater than 20 cm water,

v. Stop condensate in tubing from entering the lower respiratory tract,

vi. Maintain head-of-bed elevation at 30° to 45°,

vii. Preserve oral hygiene, and

viii. Maintain hand hygiene [77]

This tactic using the IHI bundle has been shown to give good results in reducing VAP [76,77].

MATERIALS

AND

METHODS

MATERIALS AND METHODS

Source of data:

All babies Satisfying Inclusion criteria. Cases on mechanical ventilation admitted in PICU of Shri BM Patil Medical College & Research Centre. Minimum of 81 cases or more of mechanical ventilation.

Duration of study:

Study period was from Nov-2018 to July-2020.

Method of collection of Data

Children between 1month -12 yrs fulfilling selection criteria will be included after obtaining the written informed consent from parents.

Method of study:

A Prospective cross-sectional study involving 1 mnth -12 yr babies admitted in PICU. For the diagnosis of VAP Criteria of Centers for Disease Control and Prevention is used (CDC)[9]

Radiology signs: Two or more serial chest radiograph with atleast one of the following:

- New or progressive infiltrate
- Consolidation
- Cavitation

Clinical signs - At least one of the following

- fever (temperature >38 C)
- leukopenia (<4000 WBC) or leucocytosis (>12000)

Plus atleast 2 of the following:

- new onset of purulent sputum or changing character of sputum
- increased respiratory secretions or increased sectioning requirements or worsening of cough or dyspnea or tachypnea
- rales or bronchial sounds
- worsening gas exchange
- increased oxygen requirement

Microbiological criteria: At least one the following

- Positive growth in blood culture not related to any other source of infection.
- Positive quantitative culture from broncho alveolar lavage.
- Histopathological evidence of pneumonia.

As for the diagnosis we are following CDC guidelines clinical criteria are satisfied and after than evaluation of microbiological criteria is done .After hand washing and wearing sterile gloves before suctioning , Endotracheal aspirates were collected from endotracheal tube. Endotracheal aspirate culture were collected before putting the patient on ventilator and also after 48 hrs of ventilation.

Data analysis:

Determination of sample size (n):

With 95% confidence level and margin of error of ±7%, a sample size of 81 subjects will allow the study to determine the Incidence rate of Ventilator Associated Pneumonia with finite population correction (N=200)[10]

By using the formula:

$$n = \frac{z^2 p(1-p)}{d^2}$$

where

Z= z statistic at 5% level of significance

d is margin of error

p is anticipated prevalence rate (22.9%)

Statistical analysis

All characteristics will be summarized descriptively. For continuous variables, the summary statistics of N, mean, standard deviation (SD) will be used. For categorical data, the number and percentage will be used in the data summaries and data will be analysed by Chi square test for association, comparison of means using t test, ANOVA and diagrammatic presentation.

Selection criteria

Inclusion criteria:

- Patient aged between 1 Month-12 years
- Patient admitted in paediatric intensive care unit
- Patient kept on mechanical ventilator for >48hr

Exclusion criteria:

- Patient already having pneumonia at the time of PICU admission
- Patients having congenital airway abnormalities
- Patients with immunodeficiency disorders

Ethical Clearance:

Institutional ethical committee clearance was undertaken for the study.

RESULTS

RESULTS

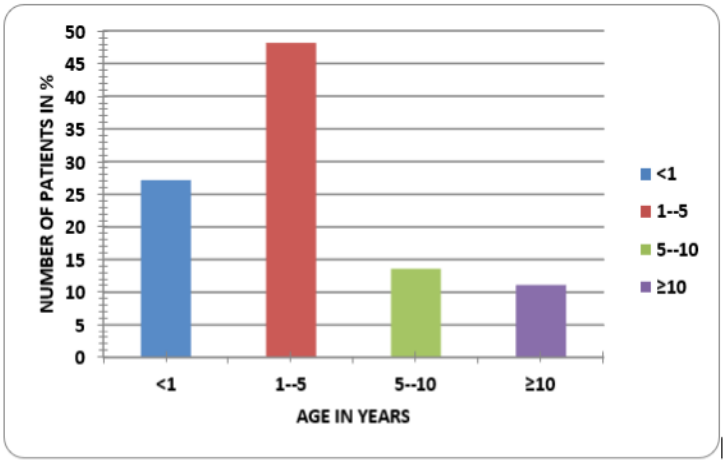
Distribution of patients according to Age (Years):

Maximum number of patients (48.15 %) were in the age group 1 to 5 years. 27.1 %patients were aged less than 1 year. 13.58% patients were in the age group of 5 to 10 years and 11.11 % of patients were more than 10years of age. The mean age of the patients was 5.50 years ± 4.18 years.

Table 12: Distribution of patients according to Age (Years)

Age (Years)	No. of patients	Percentage
<1	22	27.16
1-5	39	48.15
5 – 10	11	13.58
≥10	9	11.11
Total	81	100.0
Mean±SD	5.50±4.18	

Figure 1: Distribution of patients according to Age (Years)



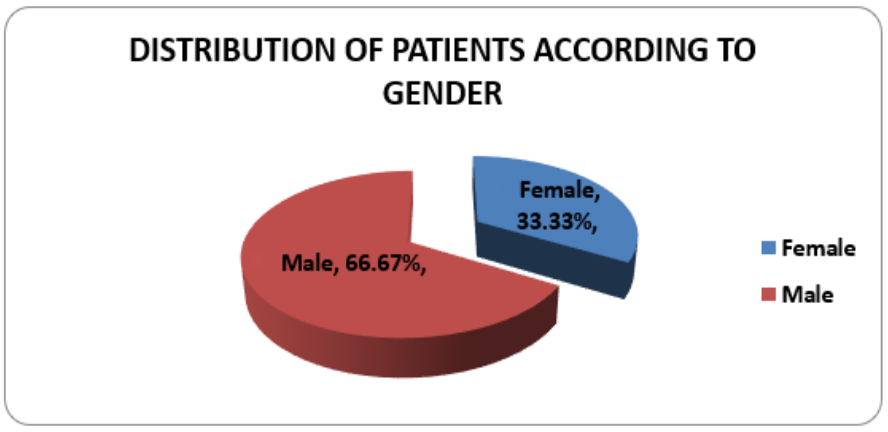
Distribution of patients according to Gender:

Male patients (66.67 %) were predominant in the study compared to female patients (33.33%). The male: female ratio was 2:1.

Table 13: Distribution of patients according to Gender

Gender	No. of patients	Percentage
Female	27	33.33
Male	54	66.67
Total	81	100.0

Figure 2: Distribution of patients according to Gender



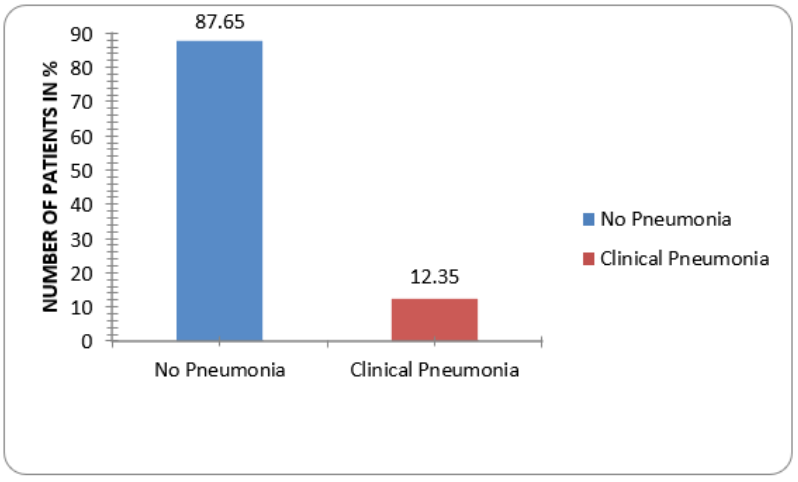
Distribution of patients according to Clinical suspicion of Pneumonia after Ventilation:

12.35 % of patients had a clinical suspicion of pneumonia.

Table 14: Distribution of patients according to Clinical suspicion of Pneumonia after Ventilation

RS	No. of patients	Percentage
No Pneumonia	71	87.65
Clinical Pneumonia	10	12.35
Total	81	100

Figure 3: Distribution of patients according to Clinical suspicion of Pneumonia after Ventilation



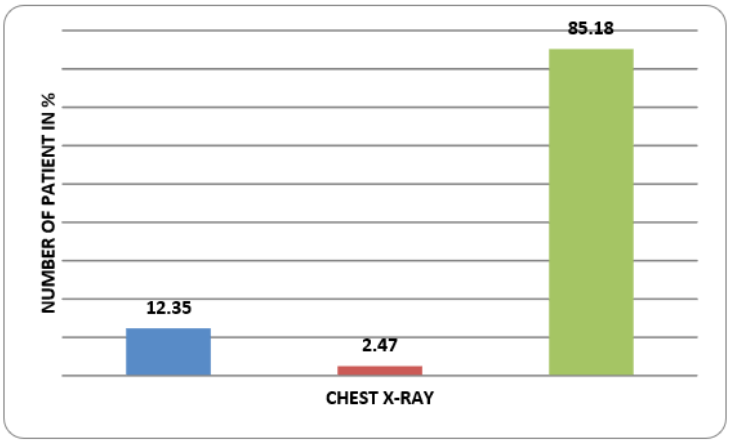
Distribution of patients according to Chest X- ray:

85.18% of patients showed a normal chest X-ray. 12.35 % of patients (n=10) showed a Chest X-ray suggestive of B/L progressive infiltrate, while 2.4% of patients (n= 2) showed a Chest X-ray suggestive of B/L progressive infiltrate with right side consolidation.

Table 15: Distribution of patients according to Chest X- ray

Chest X-ray	No. of patients	Percentage
B/L progressive infiltrate	10	12.35
B/L progressive infiltrate with Right side Consolidation	2	2.47
Normal	69	85.18
Total	81	100.0

Figure 4: Distribution of patients according to Chest X- ray



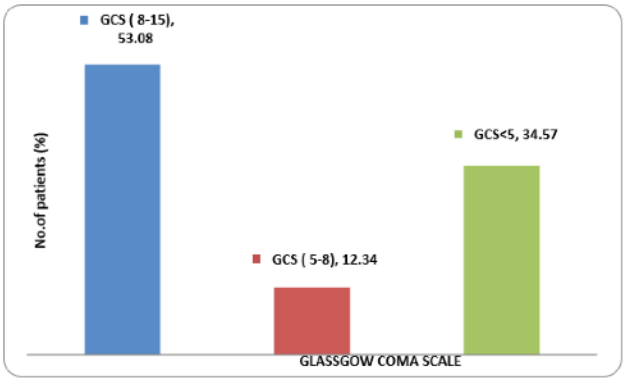
Distribution of patients according to CNS:

53.08 % of patients had a GCS between 8 to 15, 12.34 % had a GCS between 5 to 8, while 34.57 % had a GCS less than 5.

Table 16: Distribution of patients according to CNS

CNS	No. of patients	Percentage
GCS (8-15)	43	53.08
GCS (5-8)	10	12.34
GCS<5	28	34.57
Total	81	100.0

Figure 5: Distribution of patients according to CNS



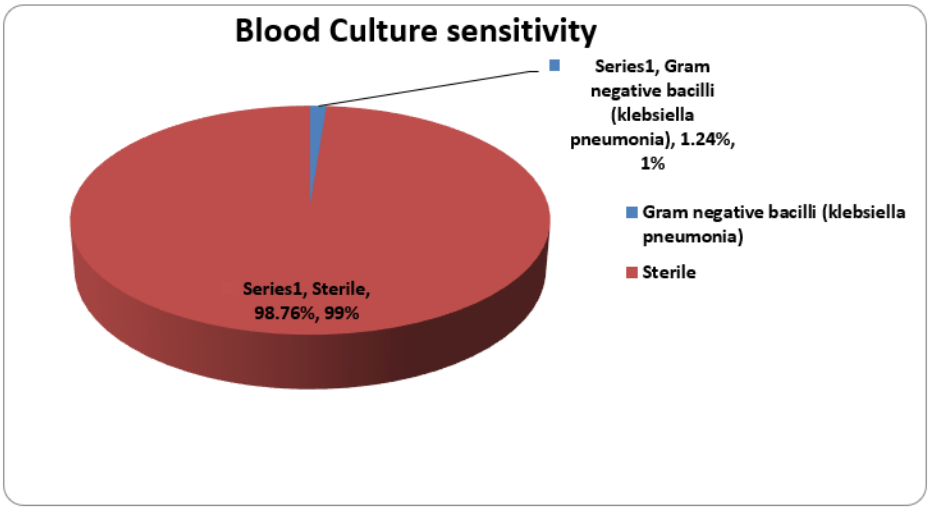
Distribution of patients according to Blood Culture sensitivity:

98.76 % of patients had a sterile culture and 1.24 % (n=1) showed the presence of gram negative bacilli.

Table 17: Distribution of patients according to Blood Culture sensitivity

Blood Culture sensitivity	No. of patients	Percentage
Gram negative bacilli (klebsiella pneumonia)	1	1.24
Sterile	80	98.76
Total	81	100.0

Figure 6: Distribution of patients according to Blood Culture sensitivity



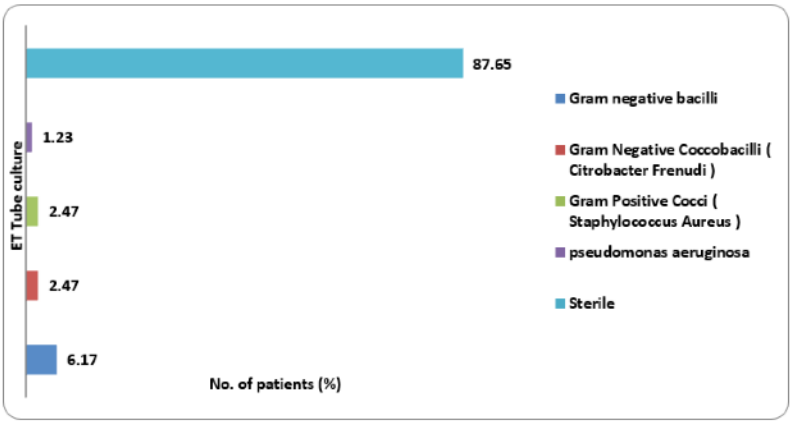
Distribution of patients according to ET Tube culture:

A majority of patients (87.65%) had a sterile culture from the endotracheal tube. 6.17 % of patients (n=5) had a ET tube culture showing the presence of gram negative bacilli. 2.47 % of patients had a ET culture, each showing the presence of Gram Negative Coccobacilli (*Citrobacter Frenudi*) and Gram Positive Cocci (*Staphylococcus Aureus*). 1.23 % of patients (n=1) had an ET culture with *Pseudomonas aeruginosa*.

Table 18: Distribution of patients according to ET Tube culture

ET Tube culture	No. of patients	Percentage
Gram negative bacilli	5	6.17
Gram Negative Coccobacilli (*Citrobacter Frenudi*)	2	2.47
Gram Positive Cocci (*Staphylococcus Aureus*)	2	2.47
Pseudomonas aeruginosa	1	1.23
Sterile	71	87.65
Total	81	100.0

Figure 7: Distribution of patients according to ET Tube culture.



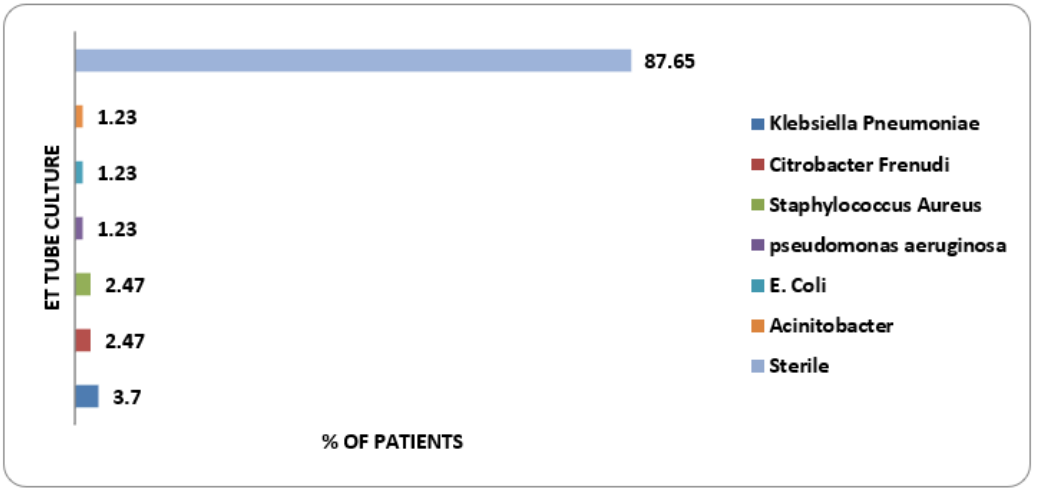
Distribution of patients according to ET Tube culture:

In our study, a majority of neonates (87.65 %, n=71) had a sterile ET Tube culture, while 3.70 % neonates (n=3) showed the presence of *Klebsiella pneumoniae* in ET Tube culture. *Citrobacter frenudi* and *Staphylococcus aureus* was detected in 2.47 % of cultures, each. *Pseudomonas aeruginosa, Escherichi coli* and *Acinitobacter* was seen in 1.23 % (n=1) of neonates, each.

Table 19: Distribution of patients according to ET Tube culture

ET Tube culture	No. of patients	Percentage
Klebsiella Pneumoniae	3	3.70
Citrobacter Frenudi	2	2.47
Staphylococcus Aureus	2	2.47
pseudomonas aeruginosa	1	1.23
E. Coli	1	1.23
Acinitobacter	1	1.23
Sterile	71	87.65
Total	81	100.0

Figure 8: Distribution of patients according to ET Tube culture



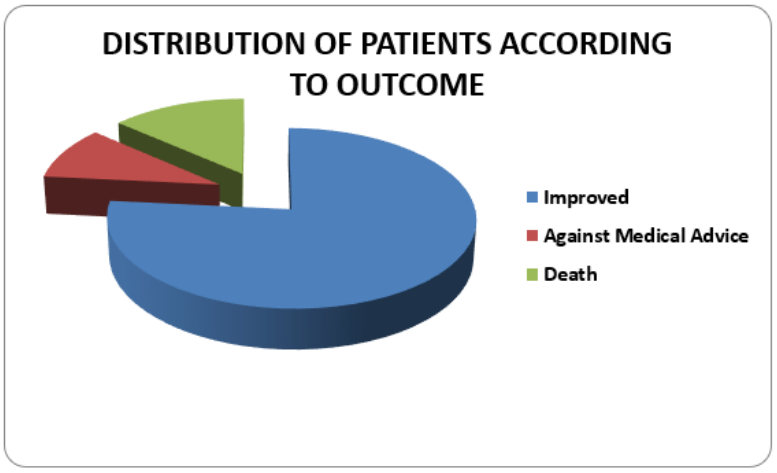
Distribution of patients according to Outcome:

76.54 % of the patients improved, while 9.88 % of patients had to be discharged against medical advice (n= 8). 13.58 % of patients (n= 11) had a fatal outcome.

Table 20: Distribution of patients according to Outcome

Outcome	No. of patients	Percentage
Improved	62	76.54
Discharged against Medical Advice	8	9.88
Death	11	13.58
Total	81	100.0

Figure 9: Distribution of patients according to Outcome



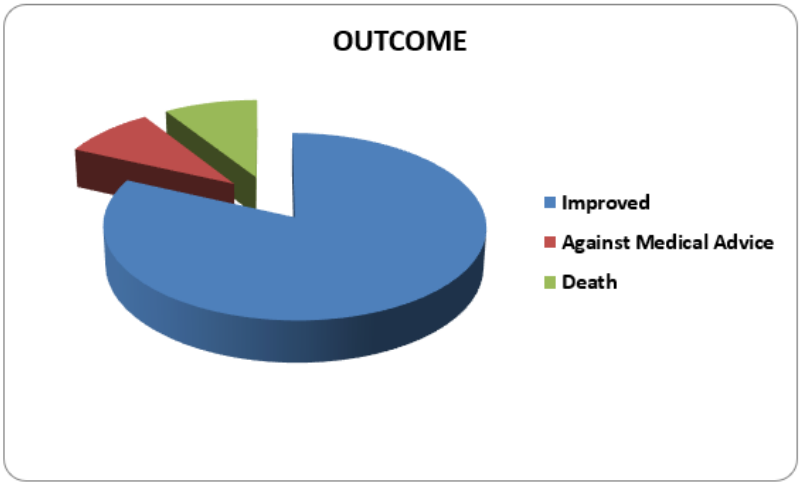
Distribution of patients according to Outcome in ventilator associated Pneumonia:

Of the patients who had VAP (n=11), 81.82 % improved with treatment, 9.09 % (n=1) were discharged against medical advice and there was mortality of 9.09 % (n=1).

Table 21: Distribution of patients according to Outcome in ventilator associated Pneumonia

Outcome (n=11)	No. of patients	Percentage
Improved	9	81.82
Discharged against Medical Advice	1	9.09
Death	1	9.09
Total	11	100.0

Figure 10: Distribution of patients according to Outcome in ventilator associated Pneumonia



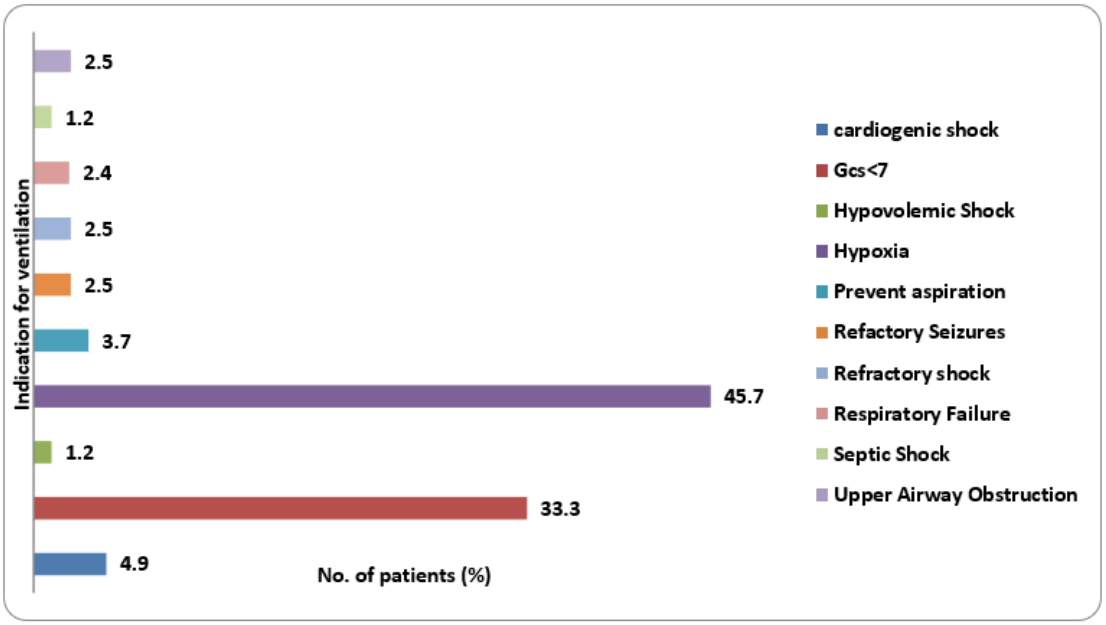
Indication for ventilation:

Hypoxia (45.7 %) was a major indication for ventilation followed by GCS<7 (33.3%)

Table 22: Indication for ventilation

Indication for ventilation	No. of patients	Percentage
cardiogenic shock	4	4.9
Gcs<7	27	33.3
Hypovolemic Shock	1	1.2
Hypoxia	37	45.7
Prevent aspiration	3	3.7
Refactory Seizures	2	2.5
Refractory shock	2	2.5
Respiratory Failure	2	2.4
Septic Shock	1	1.2
Upper Airway Obstruction	2	2.5
Total	81	100.0

Figure 11: Indication for ventilation



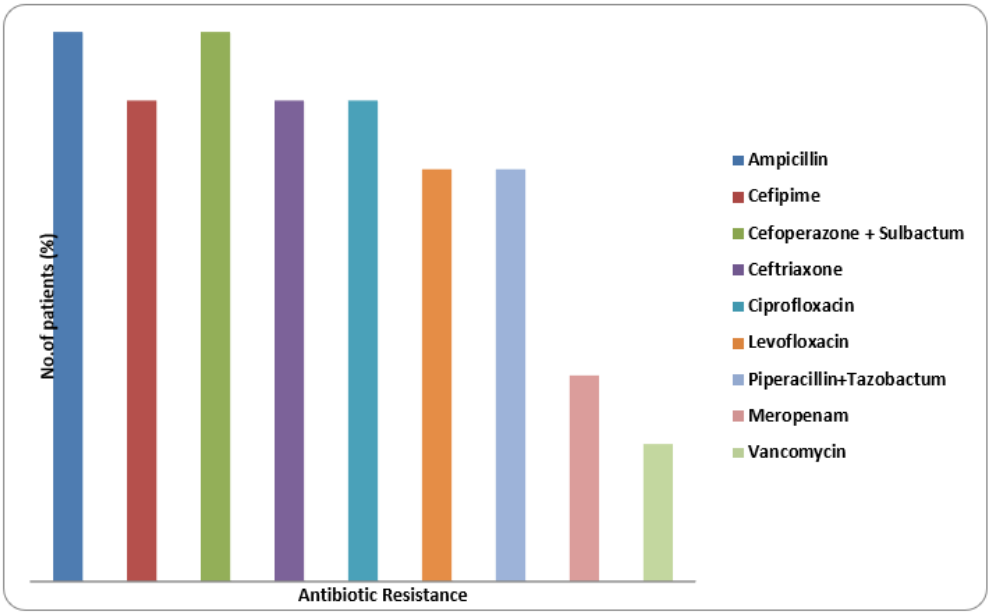
Antibiotic sensitivity pattern of isolates of ET Tube culture:

The isolates of ET Tube culture showed minimum resistance to Meropenam (30%) and Vancomycin (20%).

Table 23: Antibiotic sensitivity pattern of isolates of ET Tube culture

ET Tube culture	Resistant	
	No. of patients	Percentage
Ampicillin	8	80
Cefipime	7	70
Cefoperazone + Sulbactum	8	80
Ceftriaxone	7	70
Ciprofloxacin	7	70
Levofloxacin	6	60
Piperacillin+Tazobactum	6	60
Meropenam	3	30
Vancomycin	2	20

Figure 12: Antibiotic sensitivity pattern of isolates of ET Tube culture



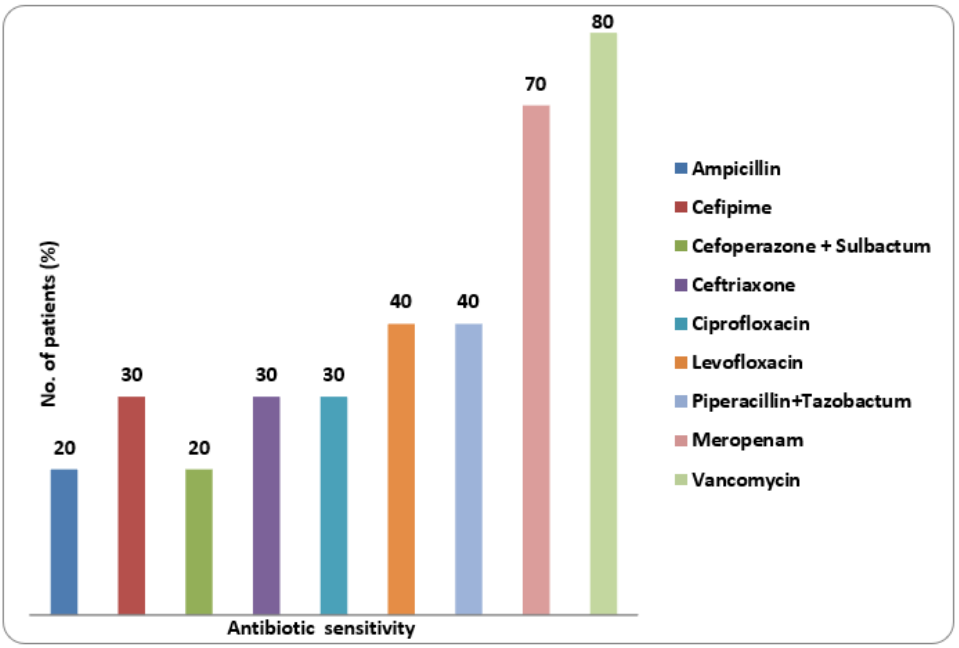
Antibiotic-sensitivity pattern of isolates of ET Tube culture:

The isolates of ET Tube culture showed minimum resistance to Meropenam (30%) and Vancomycin (20%).

Table 24: Antibiotic-sensitivity pattern of isolates of ET Tube culture

ET Tube culture	Sensitive	
	No. of patients	Percentage
Ampicillin	2	20
Cefipime	3	30
Cefoperazone + Sulbactum	2	20
Ceftriaxone	3	30
Ciprofloxacin	3	30
Levofloxacin	4	40
Piperacillin+Tazobactum	4	40
Meropenam	7	70
Vancomycin	8	80

Figure 13: Antibiotic- sensitivity pattern of isolates of ET Tube culture



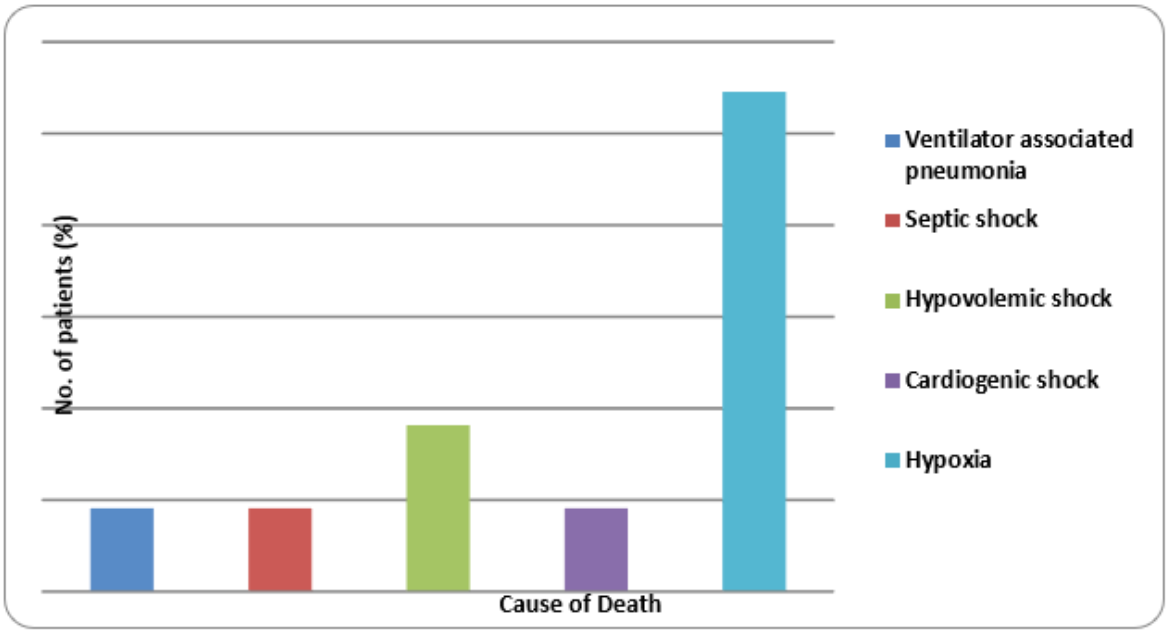
Distribution of patients according to Cause of Death:

The major cause of death was refractory shock (54.44%), followed by hypovalemic shock (18.18 %). 9.09 % of patients died due to VAP, septic shock and cardiogenic shock, each.

Table 25: Distribution of patients according to Cause of Death

Cause of Death	No. of patients	Percentage
Ventilator associated pneumonia	1	9.09
Septic shock	1	9.09
Hypovolemic shock	2	18.18
Cardiogenic shock	1	9.09
Refactory shock	6	54.55
Total	11	100.0

Figure 14: Distribution of patients according to Cause of Death



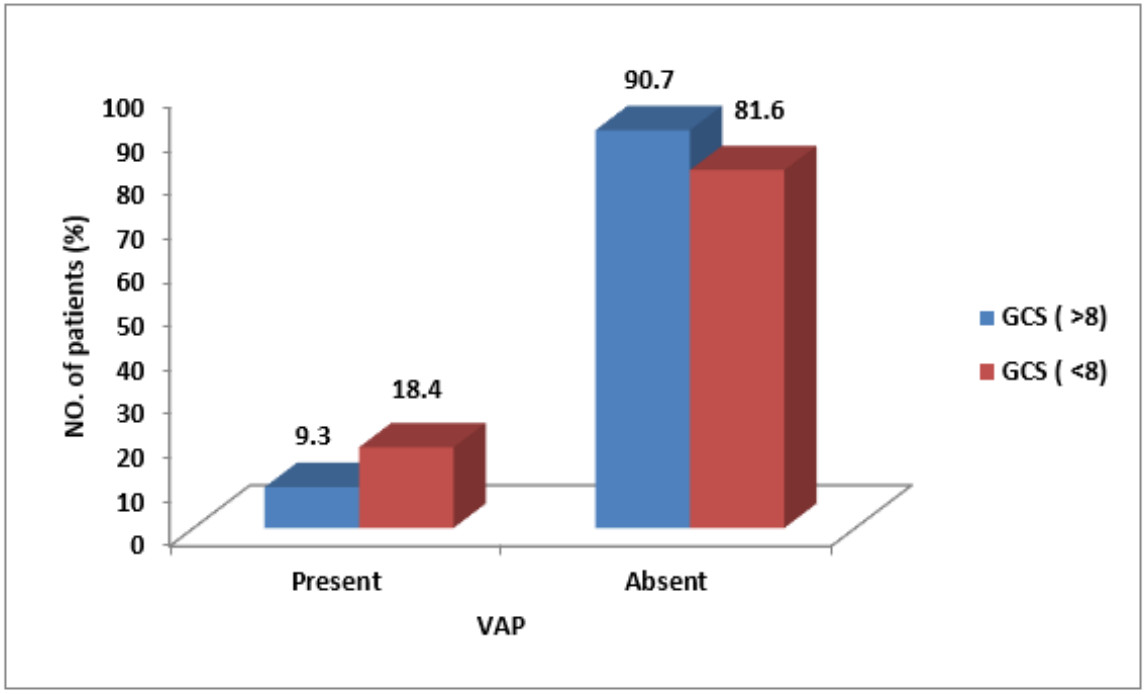
Grouping of patients according to Glasgow Coma Scale:

9.3% developed VAP in patients with GCS (>8) whereas 18.4% developed in patients with GCS (<8).

Table 26: Grouping of patients according to Glasgow Coma Scale

CNS	VAP		Total	Chi square est	P value
	Present	Absent			
GCS (>8)	4(9.3%)	39(90.7%)	43	X^2=1.429	P=0.2319
GCS (<8)	7(18.4%)	31(81.6%)	38		
Total	11	70	81		

Figure 15: Grouping of patients according to Glasgow Coma Scale



Descriptives of the study

The mean heart rate was 123.58/min ± 20.03/min, with the range being70 to 166/min. The respiratory rate was 38.51/min ± 8.73/min, with the range being 20to 66/min. The mean body temperature was 37.64 °C ± 0.811°C, with the range being 36 to40° C. The mean total count of the patients was 16593 ± 9950 with the range being 1320 to 55360. The mean duration of hospital stay was 4.40 days ± 1.96 days, with the range being 2 to 14 days.

Table 27: Descriptives of the study

Descriptives	Minimum	Maximum	Mean	Std. Deviation
HR(min)	70	166	123.58	20.032
RR(min)	20	66	38.51	8.735
Temperature(celsius)	36	40	37.64	.811
TC	1320	55360	16592.84	9949.593
Duration of Picu stay	2	14	4.40	1.966

DISCUSSION

DISCUSSION

This prospective cross-sectional study enrolled 81 patients admitted in PICU aged between 1 month to 12 years and kept on ventilator for > 48 hours.

Maximum number of patients (48.15 %) were in the age group 1 to 5 years. 27.1 % of patients were aged less than 1 year. 13.58% patients were in the age group of 5 to 10 years and 11.11 % of patients were more than 10 years of age. The mean age of the patients was 5.50 years ± 4.18 years (Table1 and Figure 1). In a study by Almuneef et al. [15] in Saudi Arabia, the mean age of the patients was 28.6 months. In a study by Balasubramanian and Tullu [21] in a PICU in Mumbai, India, the median age of the subjects (N = 232) was nine months.

The male sex is a host-related risk factor for VAP [7]. Male patients (66.67 %) were predominant in our study compared to female patients (33.33%). The male: female ratio was 2:1 (Table 2 and Figure 2). Balasubramanian and Tullu [21] also reported a male predominance in their study, with the male to female ratio being 1.3:1.

In case of paediatric and neonatal intensive care units, VAP is the second most common hospital-acquired infection. Overall, the occurrence of VAP is reported in 3 to 10% of ventilated pediatric ICU (PICU) patients in the U.S. [7] In the present study, the incidence of VAP was 11/81 (13.58%) in our hospital. Developed countries like U.S. and Europe and Germany individually have reported a VAP rate of 0.4-1.4/1000 MV days, 9.0/1000 MV days and 5.5/1000 MV days respectively [8,9,10]. On the other hand, in developing countries the overall VAP rate was 24.1/1000 ventilator days, which was considerably higher. Data from Asian countries suggested an incidence rate varying from 3.5- 46/1000 ventilator days in the

neonatal period (12). A study from Iran, Egypt and Saudi Arabia reported a VAP rate of 17.3 % and 31 % and 10.24 % respectively [13,14,15].

In the Indian context, a study from north India, New Delhi and Mumbai reported a VAP rate of 17 to 30%, 11.9/1000 ventilator hours and 6.3/1000 ventilator days, respectively.[19,20,22]

A study by Apisarnthanarak et al. [23] on extremely preterm neonates in Missouri, USA, (n= 229) reported a VAP rate of 28.3%. Variations in study methodology and case mix can affect the reported incidence of VAP[25].

In our study, 12.35 % of patients had a clinical suspicion of pneumonia (Table 3 and Figure 3). In our study, 85.18% of patients showed a normal chest X-ray. 12.35 % of patients (n=10) showed a Chest X-ray suggestive of bilateral lung progressive infiltrate, while 2.4% of patients (n= 2) showed a Chest X-ray suggestive of bilateral lung progressive infiltrate with right side consolidation (Table 4 and Figure 4). Thus, in all, 12/81 (14.8 %) neonates had a chest x-ray suggestive of pneumonia.

Observation studies of hospital- acquired infections in NICU patients in the U.S. show that pneumonia constitutes 6.8 to 32.3% of nosocomial infections [7]. Overlap of signs and symptoms and radiographic findings with underlying respiratory conditions poses significant challenges to the diagnosis of VAP in neonates and may lead to overdiagnosis (Baltimore, 2003; Garland, 2010; Polin et al., 2012b). Chest X-ray suspicious of VAP may also point to the differentials of pulmonary edema, pulmonary infarction, atelectasis or acute respiratory distress syndrome [47].

Low level of consciousness is a host-related risk factor for VAP [7]. The Glasgow Coma Scale (GCS) is a neurological scale which aims to give a reliable and objective way of

recording the state of a person's consciousness for initial as well as subsequent assessment. Patients with scores of 3-8 are usually considered to be in a coma [78]. In our study, 53.08% patients had a GCS between 8 to 15, 12.34 % had a GCS between 5 to 8, while 34.57 % had a GCS less than 5 and among patients with GCS (>8) 9.3% developed VAP . A study in Serbia [79] on patients with severe traumatic brain injury reported that patients with late-onset VAP presented more frequently with coma on admission (GCS <9 71.1% vs. 42.3%; p = 0.004).

Blood stream infection is a risk factor for VAP [37]. In our study, 98.76 % of patients had a sterile blood culture and 1.24 % (n=1) showed the presence of gram negative bacilli (Table 6 and Figure 6). Balasubramanian and Tullu [21] reported that positive blood culture growth was a risk factor for VAP on multivariate analysis.

In order to choose appropriate antibiotic therapy for VAP, knowledge of organisms likely to be present is very essential. *Klebsiella pneumoniae* and *Staphylococcus aureus* are the causative organisms for early onset VAP whereas, *Pseudomonas aeruginosa, Enterobacter species* and *Acinitobacter* species are the causative organism for late onset VAP[52].

In our study, a majority of patients (87.65%) had a sterile culture from the endotracheal tube. 6.17 % of patients (n=5) had a E.T. tube culture showing the presence of gram negative bacilli. 2.47 % of patients had a E.T. culture, each showing the presence of Gram Negative Coccobacilli (*Citrobacter Frenudi*) and Gram Positive Cocci (*Staphylococcus Aureus*). 1.23 % of patients (n=1) had an E.T. culture with *Pseudomonas aeruginosa*.

In our study, a majority of patients (87.65 % , n=71) had a sterile E.T. Tube culture, while 3.70 % patients (n=3) showed the presence of *Klebsiella pneumoniae* in E.T. Tube

culture. *Citrobacter frenudi* and *Staphylococcus aureus* was detected in 2.47 % of cultures, each. *Pseudomonas aeruginosa, Escherichia coli* and *Acinitobacter* was seen in 1.23 % (n=1) of neonates, each.

A Chinese study by Zhu et al. [42] reported 76.9 % gram negative bacilli, followed by gram positive coccus (17.9%) in the culture of VAP patients. Another Chinese study reported that the main pathogens were gram negative bacterium (82.1%, 23/28) [43]. In a study by Petdachai [12], endotracheal tube culture was take from 49.4% patients and haemoculture from 20 % patients; Pseudomonas aeruginosa, Klebsiella pneumoniae and Acinetobacter spp were the predominant organisms. Polymicrobial infection was found in 12.9 % of patients from endotracheal aspirate culture. A Serbian study by Jovanovic et al. [79] reported that both early and late onset VAP harboured the same pathogen -*Acinetobacter* species.

VAP infections have an adverse effect on patient outcomes. The all-cause mortality associated with VAP has been reported to range from 20% to 50%, but it is difficult to precisely associate mortality directly related to VAP; a recent meta-analysis based on randomised VAP prevention studies estimated the attributable mortality at 13%[1]. Ventilator-associated pneumonia (adjusted odds ratio: 3.4; 95% CI: 1.2-12.3) was an independent predictor of mortality in extremely preterm neonates[23].

In our study, of the 81 patients, 76.54 % of the patients improved, while 9.88 % of patients were discharged against medical advice (n= 8). 13.58 % of patients (n= 11) had a fatal outcome.

In our study, of the patients who had VAP (n=11), 81.82 % improved with treatment, 9.09 % (n=1) were discharged against medical advice and there was mortality of 9.09 %

(n=1) (Table 10 and Figure 10). Thus the mortality in our study, attributable to VAP was 1/81 (1.23%).

A Thai study reported the in-hospital mortality rate in the VAP group to be 17.6 % and non-VAP groups to be 15.3% (p=0.73)[24]. Balasubramanian and Tullu [21] reported a mortality rate of VAP to be 42.8% in a hospital in Mumbai which was similar to that of subjects without VAP. Similarly, Almuneef et al.[15] also observed that there was no significant difference between VAP and non-VAP patients regarding mortality rate in a PICU in Saudi Arabia. A Chinese study reported that the mortality rate of the VAP group was 13.5% (7/52) vs. 12.1% in controls (P>0.05)[43].

In our study, the major indication for ventilation was hypoxia (45.7 %), followed by GCS < 7 (33.3%). 4.9 % (n=4) of neonates had to be ventilated for cardiogenic shock and 3.7 % to prevent aspiration. Other minor indications for ventilation were hypovolemic shock (1.2 %), refractory seizures (2.5 %), refractory shock (2.5 %), respiratory failure (2.4%), septic shock (1.2%) and airway obstruction (2.5%).

As several researches have shown that appropriate antimicrobial treatment of patients with VAP significantly improves outcome. Early identification of infected patients and accurate selection of antimicrobial agents are important clinical goals [46]. In our study, the isolates of E.T. Tube culture showed maximum resistance to Ampicillin and combination of Cefoperazone and Sulbactum (80 % each), followed by 70 % resistance each, to Cefipime, Ceftriaxone and Ciprofloxacin. The isolates showed a resistance of 60 % to the antibiotics Levofloxacin and combination of Piperacillin and Tazobactum. The isolates showed minimum resistance to Meropenem (30 %) and Vancomycin (20%).

VAP is the most frequent reason for starting empirical antibiotics in PICU patients [27]. In our study, the isolates of E.T. Tube culture showed minimum sensitivity to Ampicillin and combination of Cefoperazone and Sulbactum (20 % each), followed by 30 % sensitivity each, to Cefipime, Ceftriaxone and Ciprofloxacin. The isolates showed a sensitivity of 40 % to the antibiotics Levofloxacin and combination of Piperacillin and Tazobactum. The isolates showed maximum sensitivity to Meropenem (70 %) and Vancomycin (80%). Thus, Meropenem and Vancomycin were found to be the most appropriate antibiotics for VAP in our hospital PICU.

In our study, of a total of 11 deaths, 54.55 % were due to refractory shock, 18.18 % were due to hypovolemic shock and 9.09 % each (n=1) due to VAP, septic shock and cardiogenic shock.

In our study, the mean heart rate of patients was 123.58/min ± 20.03/min, with the range being70 to 166/min. The mean respiratory rate was 38.51/min ± 8.73/min, with the range being 20 to 66/min. The mean body temperature was 37.64 °C ± 0.811°C, with the range being 36 to40° C. The mean total count of the patients was 16593/ mm^3 ± 9950/ mm^3 with the range being 1320/ mm^3 to 55360/ mm^3 (Table 15). Fever and leukocytosis are highly non-specific predictors of VAP and can occur due to any condition that causes release of cytokines[47].

In paediatric populations, the published data are univariate and unmatched for seriousness of illness but indicate that paediatric patients with VAP may have excess mortality and length of PICU and NICU stay. Conversely, length of stay in NICU is a risk factor for VAP (OR=23.45) [38].

In our study, the mean duration of hospital stay was 4.40 days ± 1.96 days, with the range being 2 to 14 days. However, the length of hospital stay in VAP and non-VAP patients was not determined separately.

In a large European Multicentre trial (n=14675), the investigators observed that infected patients had a longer mean length of stay in the PICU (26.1 ± 17.3 versus 10.6 ± 6 days; P < 0.001) as compared to uninfected patients. However, the mortality and length of stay associated specifically with VAP were not reported. A study in 2017 in a Thai NICU by Thatrimontrichai et al. [24] reported that as compared with the non-VAP group, the median difference in the VAP group resulted in a significantly longer period of NICU stay (18 days, P=0.001), total length of hospital stay (16 days, P=0.002) and higher hospital costs ($5113, P=0.001). In a prospective cohort study (n = 361) in Saudi Arabia, Almuneef et al. [15] reported that PICU lengths of stay with (n= 37) and without (n = 324) VAP were more for patients with VAP (33.70 ± 30.28 days versus 14.66 ± 17.34 days; p = 0.001). Balasubramanian and Tullu [21] reported that VAP patients had a significantly longer duration of mechanical ventilation (22.5 vs. 5 median days; P < 0.001), longer PICU stay (23.25 vs. 6.5 median days; P < 0.001) and longer hospital stay (43.75 vs. 13.25 median days; P < 0.001). Two studies in 2010 and 2012 estimated that VAP prolongs length of hospitalisation by 11.5 to 13.1 days compared to similar patients without VAP [29,28]. In a Chinese study, hospital stay in the VAP group was 19.9+/-5.9 vs. 16.7+/-7.2 days in controls (P<0.01) [43]. Petdachai [12] reported that infants with VAP had a longer duration on ventilator (14.2 days vs 5.9 days; p<0.001) and longer hospital stay (28.2 days vs 13.8 days; <0.001).

Extremely preterm neonates with VAP also had extended NICU length of stay (median: 138 vs 82 days).[23] A study in Amsterdam reported that PICU stay and mechanical ventilation lasted longer in children with co-infections than children with negative cultures (9.1 vs 7.7 days, p = 0.04 and 8.1vs 6.5 days, p = 0.02) [26].

CONCLUSION

CONCLUSION

- In this prospective cross-sectional study 81 patients admitted in PICU aged between 1 month to 12 years and kept on ventilator for > 48 hours were enrolled during the study period of 1.5 years.
- The incidence of VAP was 11/81 (13.58%) in our hospital. Of the 81 enrolled patients, 77 % of the patients improved, while 10 % of patients were discharged against medical advice (n= 8). 13 % of patients (n= 11) had a fatal outcome.
- Of the patients who had VAP (n=11), 82 % improved with treatment, 9 % (n=1) were discharged against medical advice and there was mortality of 9 % (n=1). Thus the mortality in our study, attributable to VAP was 1/81 (1.23%).
- In our study, the isolates of E.T. Tube culture showed minimum sensitivity to Ampicillin and combination of Cefoperazone and Sulbactum (20 % each), followed by 30 % sensitivity each, to Cefipime, Ceftriaxone and Ciprofloxacin. The isolates showed maximum sensitivity to Meropenem (70 %) and Vancomycin (80%).
- Meropenem and Vancomycin were found to be the most appropriate antibiotics for the management of VAP in our hospital PICU.
- VAP percentage was less in our hospital compared to other centre studies which can be attributed to quality improvement initiatives including VAP bundle.

Limitation of the Study: The limitation of our study is small sample size.

SUMMARY

SUMMARY

This prospective cross-sectional study enrolled 81 patients admitted in PICU aged between 1 month to 12 years and kept on ventilator for > 48 hours during the study period of 1.5 years. We made the following observations based on our study:

- The incidence of VAP was 11/81 (13.58%) in our hospital.
- Maximum number of patients (48.15 %) were in the age group 1 to 5 years. 27.1 % of patients were aged less than 1 year. 13.58% patients were in the age group of 5 to 10 years and 11.11 % of patients were more than 10 years of age. The mean age of the patients was 5.50 years ± 4.18 years.
- Male patients (66.67 %) were predominant in our study compared to female patients (33.33%). The male: female ratio was 2:1.
- 12.35 % of patients (n=10) had a clinical suspicion of pneumonia.
- In our study, 85.18% of patients showed a normal chest X-ray. 12.35 % of patients (n=10) showed a Chest X-ray suggestive of bilateral lung progressive infiltrate, while 2.4% of patients (n= 2) showed a Chest X-ray suggestive of bilateral lung progressive infiltrate with right side consolidation. Thus, in all 12/81 (14.8 %) patients had a chest x-ray suggestive of pneumonia.
- 53.08 % of patients had a Glasgow Coma Scale (GCS) score between 8 to 15, 12.34 % had a GCS between 5 to 8, while 34.57 % had a GCS less than 5.
- In our study, 98.76 % of patients had a sterile blood culture and 1.24 % (n=1) showed the presence of gram-negative bacilli.

- A majority of patients (87.65 %, n=71) had a sterile E.T. Tube culture, while 3.70 % neonates (n=3) showed the presence of *Klebsiella pneumoniae* in E.T. Tube culture. *Citrobacter frenudi* and *Staphylococcus aureus* was detected in 2.47 % of cultures, each. *Pseudomonas aeruginosa, Escherichia coli* and *Acinitobacter* was seen in 1.23 % (n=1) of neonates, each.

- Of the 81 enrolled patients, 76.54 % of the patients improved, while 9.88 % of patients were discharged against medical advice (n= 8). 13.58 % of patients (n= 11) had a fatal outcome.

- Of the patients who had VAP (n=11), 81.82 % improved with treatment, 9.09 % (n=1) were discharged against medical advice and there was mortality of 9.09 % (n=1). Thus, the mortality in our study, attributable to VAP was 1/81 (1.23%).

- The isolates of E.T. Tube culture showed maximum resistance to Ampicillin and combination of Cefoperazone and Sulbactum (80 % each), followed by 70 % resistance each, to Cefipime, Ceftriaxone and Ciprofloxacin. The isolates showed a resistance of 60 % to the antibiotics Levofloxacin and combination of Piperacillin and Tazobactum. The isolates showed minimum resistance to Meropenem (30 %) and Vancomycin (20%).

- In our study, the isolates of E.T. Tube culture showed minimum sensitivity to Ampicillin and combination of Cefoperazone and Sulbactum (20 % each), followed by 30 % sensitivity each, to Cefipime, Ceftriaxone and Ciprofloxacin. The isolates showed a sensitivity of 40 % to the antibiotics Levofloxacin and combination of Piperacillin and Tazobactum. The isolates showed maximum sensitivity to Meropenem (70 %) and Vancomycin (80%).

- Meropenem and Vancomycin were found to be the most appropriate antibiotics for the management of VAP in our hospital PICU.
- In our study, of a total of 11 deaths, 54.55 % were due to refractory shock, 18.18 % were due to hypovolemic shock and 9.09 % each (n=1) due to VAP, septic shock and cardiogenic shock.
- The mean heart rate of patients was 123.58/min ± 20.03/min, with the range being70 to 166/min.
- The mean respiratory rate was 38.51/min ± 8.73/min, with the range being 20 to 66/min.
- The mean body temperature was 37.64 °C ± 0.811°C, with the range being 36 to 40° C.
- The mean total count of the patients was 16593/ mm^3 ± 9950 / mm^3 with the range being 1320/mm^3 to 55360 /mm^3.
- The mean duration of hospital stay was 4.40 days ± 1.96 days, with the range being 2 to 14 days.

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BIBLIOGRAPHY

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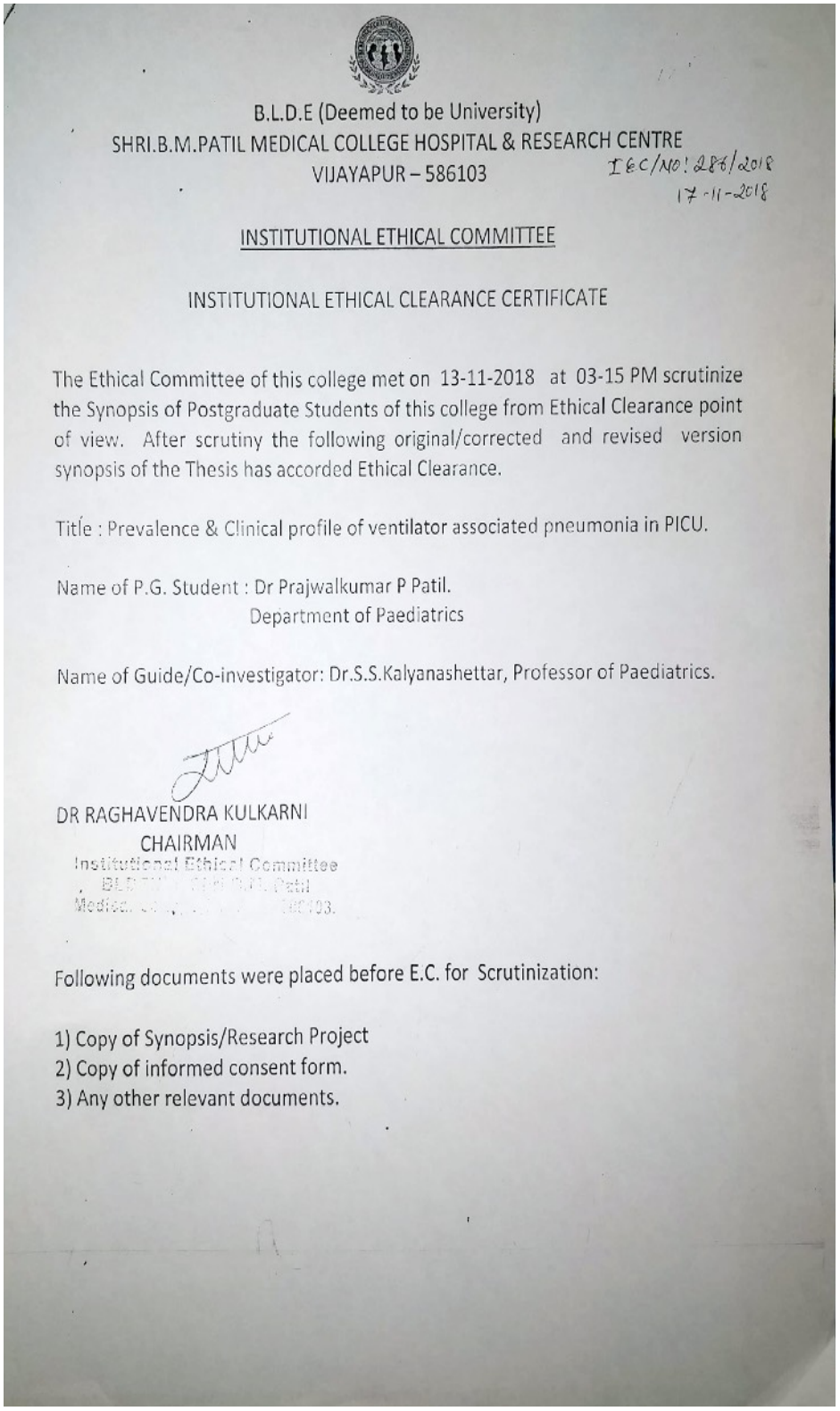
ANNEXURES

ANNEXURE I

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE



B.L.D.E (Deemed to be University)
SHRI.B.M.PATIL MEDICAL COLLEGE HOSPITAL & RESEARCH CENTRE
VIJAYAPUR – 586103

IEC/NO! 286/2018
17-11-2018

INSTITUTIONAL ETHICAL COMMITTEE

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this college met on 13-11-2018 at 03-15 PM scrutinize the Synopsis of Postgraduate Students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected and revised version synopsis of the Thesis has accorded Ethical Clearance.

Title : Prevalence & Clinical profile of ventilator associated pneumonia in PICU.

Name of P.G. Student : Dr Prajwalkumar P Patil.
Department of Paediatrics

Name of Guide/Co-investigator: Dr.S.S.Kalyanashettar, Professor of Paediatrics.

DR RAGHAVENDRA KULKARNI
CHAIRMAN
Institutional Ethical Committee
B.L.D.E. (Deemed to be University)
Shri. B.M. Patil
Medical College Hospital & Research Centre
Vijayapur-586103.

Following documents were placed before E.C. for Scrutinization:

1) Copy of Synopsis/Research Project
2) Copy of informed consent form.
3) Any other relevant documents.

ANNEXURE II

B.L.D.E.(DU), SHRI B. M. PATIL MEDICAL COLLEGE HOSPITAL AND RESEARCH CENTRE, VIJAYAPURA.

Department of Paediatrics;

"PREVALENCE AND CLINICAL PROFILE OF VENTILATOR ASSOCIATED PNEUMONIA IN PICU"

S.NO

PROFORMA

NAME :

AGE :

SEX :

CHIEF COMPLAINT :

PAST HISTORY : SIGNIFICANT / NOT SIGNIFICANT , IF SIGNIFICANT SPECIFY

BIRTH HISTORY : SIGNIFICANT / NOT SIGNIFICANT , IF SIGNIFICANT SPECIFY

VITALS :

HR

RR

BP

TEMPERATURE

SYSTEMIC EXAMINATION:

CARDIOVASCULAR SYSTEM:

RESPIRATORY SYSTEM:

PER ABDOMEN:

CENTRAL NERVOUS SYSTEM:

DIAGNOSIS:

INDICATION FOR MECHANICAL VENTILATION:

INVESTIGATIONS:

TOTAL COUNT:

DIFFERENTIAL COUNT:

BLOOD CULTURE AND SENSITIVITY:

CHEST X-RAY:

ENDOTRACHEAL TUBE CULTURE:

DURATION OF STAY IN PICU:

SIGNATURE OF THE CANDIDATE

ANNEXURE III.

CONSENT FORM

BLDE(DU), Shri B.M. PATIL Medical College, Hospital & Research Centre,

Vijayapura, Karnataka -586103.

TITLE OF THE PROJECT: "PREVALENCE AND CLINICAL PROFILE OF VENTILATOR ASSOCIATED PNEUMONIA IN PICU"

GUIDE : DR.S.S. KALYANSHETTAR, MD

PROFESSOR and HEAD

DEPARTMENT OF PEDIATRICS

PG STUDENT : DR. PRAJWALKUMAR P. PATIL

PROCEDURE:

I understand that after having obtained a detailed clinical history, thorough clinical examination and relevant investigations, a final work up of the procedure and its outcome is planned.

RISK AND DISCOMFORTS:

I understand that I may experience some pain and discomforts during the examination or during my treatment. This is mainly the result of my condition and the procedures of this study are not expected to exaggerate these feelings which are associated with the usual course of treatment.

BENEFITS:

I understand that my participation in the study will have no direct benefit to me other than the potential benefit of the treatment.

CONFIDENTIALITY:

I understand that the medical information produced by this study will become a part of hospital records and will be subject to the confidentiality. Information of sensitive personal nature will not be part of the medical record, but will be stored in the investigations research file. If the data are used for publication in the medical literature or for teaching purpose, no name will be used and other identifiers such as photographs will be used only with special written permission. I understand that I may see the photograph before giving the permission.

REQUEST FOR MORE INFORMATION:

I understand that I may ask more questions about the study at any time; Dr. Prajwalkumar P Patil, at the department of paediatrics is available to answer my questions or concerns. I understand that I will be informed of any significant new findings discovered during the course of the study, which might influence my continued participation. A copy of this consent form will be given to me to keep for careful reading.

REFUSAL FOR WITHDRAWAL OF PARTICIPATION:

I understand that my participation is voluntary and that I may refuse to participate or may withdraw consent and discontinue participation in the study at any time without prejudice. I

also understand that Dr. Prajwalkumar P Patil may terminate my participation in the study after he/she has explained the reasons for doing so.

INJURY STATEMENT:

I understand that in the unlikely event of injury to my child resulting directly from child's participation in this study, if such injury were reported promptly, the appropriate treatment would be available to the child. But no further compensation would be provided by the hospital. I understand that by my agreements to participate in this study and not waiving any of my legal rights.

I have explained to _____the purpose of the research, the procedures required and the possible risks to the best of my ability.

DR. PRAJWALKUMAR P. PATIL

Date

(Investigator)

PARENTS / GUARDIAN CONSENT STATEMENT:

We confirm that Dr. Prajwalkumar P. Patil is doing a study on "PREVALENCE AND CLINICAL PROFILE OF VENTILATOR ASSOCIATED PNEUMONIA IN PICU" under the guidance of Dr S.S. KALYANSHETTAR. Dr. Prajwalkumar P Patil has explained to us the purpose of research and the study procedure. We are willing to allow our child to get treated in Shri B.M. Patil Medical College Hospital, Vijayapura. We have been explained about the study, benefits and possible discomforts in detail in our native language and we understand the same. We are aware that child will get best treatment, and no compensation like financial benefits will be given if our child's condition deteriorates and any un happens, and we will not sue anyone regarding this. Therefore, we agree to give our full consent for child's participation as a subject in this research project.

_____ _____

(**Parents / Guardian**) **Date**

_____ _____

(**Witness to signature**) **Date**

ANNEXURE IV

MASTER CHART

KEY TO MASTER CHART:

- **AMA - AGAINST MEDICAL ADVICE**
- **B/A - BILATERAL AIR ENTRY PRESENT**
- **C/O - CONSCIOUS AND ORIENTED**
- **D - DEATH**
- **F - FEMALE**
- **GN - GRAM NEGATIVE**
- **GP - GRAM POSITIVE**
- **I - IMPROVED**
- **N - NORMAL**
- **NI - NO INFILTRATES**
- **PA - PSEUDOMONAS AERUGINOSA**
- **S - STERILE**

ANNEXURE V

MASTER CHART

S NO	IP NO	NAME	AGE(yrs)	SEX	CHIEF COMPLAINTS	HEART RATE (BPM)	RESPIRATORY RATE(CPM)	BLOOD PRESSURE(mmHg)	TEMPERATURE (CELSIUS)	CVS	RS	PER ABDOMEN	CNS	DIAGNOSIS	INDICATION FOR VENTILA	TOTAL COUNT	NEUTROPHIL/LYMPHOCYT	BLOOD CULTURE/SENSITI	CHEST X-RAY	ET TUBE CULTURE	DURATION OF PICU STAY	OUTCOME
1	14103	Irrayya	2	M	Cough, Fever, Breathlessness	120	36	100/60	37	N	BA+, B/L (	N	C, O	Bronchitis	ent aspira	8600	55/38.8	S		S	5	I
2	37716	Atharav	8	M	Fever, Convulsions	124	32	100/70	37	N	BA+	N	UnC, Non O	ephalitis with Status Ep	Hypoxia	12230	93.5/3.8	S	NI	S	5	I
3	25993	Dannamma	13	F	Fever, Convulsions	114	36	120/90	39	N	BA+	N	C, Non O	Meningitis	Hypoxia	17860	85.7/9.4	S	gressive in	GN	14	D
4	40912	Roopali	12	F	Fever, Edema,Rashes	110	50	100/60	37	N	BA+	N	C, Non O	Rickettsial Encephalitis	Hypoxia	14000	71.4/26.8	S	NI	S	10	I
5	42974	Anu	4	F	Intake of Organophosphorous compound	126	34	90/60	38	N	BA+	N	C, O	nophosphorous Poisc	Hypoxia	11210	90/7.5	S	NI	S	5	I
6	43984	Mallu	<1	M	Fever, Hurried breathing	136	48	86/48	37	N	BA+, B/L \	N	C, O	Bronchitis	Hypoxia	55360	54/38	S	NI	S	9	I
7	42973	Anjali	4	F	Intake of Organophosphorous compound	108	34	100/64	37	N	BA+	N	C, Non O	nophosphorous Poisc	Hypoxia	9490	81/14.9	S	NI	S	7	I
8	26311	Subhas	<1	M	Refusal of feed, Vomiting, Loose stools	156	52	88/64	39	N	BA+	N	/Activity/Tone : F	Cholestasis , Sepsis	eptic Shoc	12290	54/38	S	NI	S	3	AMA
9	26716	Siddarth	<1	M	Convulsions	138	46	90/54	38	N	BA+	N	UnC, Non O	Status Epilepticus	Gcs<7	14340	66/31	S	NI	S	3	I
10	26642	Honamma	14	F	Convulsions, vomiting	100	30	100/56	39	N	BA+, B/L (	N	UnC, Non O	Status Epilepticus	Gcs<7	3900	65/31	S	gressive in	GP	2	I
11	27023	Altamesh	<1	M	Refusal of feed, Vomiting, Loose stools	146	60	70/40	40	N	BA+, B/L (	N	/Activity/Tone :	Rhine Transferase defic	Hypoxia	13240	46/39	S	gressive in	GN bacilli	4	I
12	27591	Roopa	<1	F	Fever,Vomiting,Loose stools	136	46	80/40	38	N	BA+	N	C, Non O	oentritis with Severe D	Hypoxia	19920	56/42	S	NI	S	3	D
13	27394	Tejashwini	<2	F		130	38	110/70	37	N	BA+	N	C, Non O	Tubular Acidosis with	Hypoxia	26990	60/36	S	NI	S	4	D
14	28159	Shreenidhi	1	M	Fever,Vomiting,Loose stools	142	40	70/42	38	N	BA+	N	C, Non O	oentritis with Severe D	Hypoxia	25200	67/28	S	NI	S	3	I
15	28428	Sunil	2	M	Fever,Vomiting,Loose stools	128	38	78/48	37	N	BA+	N	C, Non O	oentritis with Severe D	Hypoxia	16180	66/30	S	NI	S	4	I
16	27029	Irranna	<1	M	Fever, loose stools , vomiting	160	50	76/44	39	N	BA+, B/L (	N	C, Non O	te gastrentritis with Se	Hypoxia	18910	35/61	S	gressive in	GN bacilli	6	I
17	29420	Karthik	9	M	Snake bite @1pm	108	20	140/90	37	N	BA+	N	UnC, Non O	genic Snake Envenom	Gcs<7	12220	66/30	S	NI	S	3	I
18	29424	Kushi	<1	M	Fever,lethargy, vomiting	160	46	76/44	37	N	BA+	N	C, Non O	osis with Refactory Sh	Hypoxia	19420	57/37	S	NI	S	5	I
19	29932	Aditya	<1	M	Fever, Edema,Rashes, Convulsions	146	40	88/48	38	N	BA+	N	Drowsy, Non O	Rickettsial Encephalitis	Gcs<7	21550	62/32	S	NI	S	3	I
20	30331	yamanagoud	10	M	Intake of Organophosphorous compound	110	30	98/52	37	N	BA+	N	C, Non O	nophosphorous Poisc	Hypoxia	16920	92/33	S	NI	S	3	I
21	32797	Prem	5	M	Fever, Edema,Rashes, Vomiting	120	36	98/54	38	N	BA+	N	Drowsy, Non O	Rickettsial Fever	Hypoxia	18080	60/20	S	NI	S	3	I
22	31595	Bhagyashree	8	F	Hit by Car at 1pm	110	30	100/56	39	N	BA+	N	Drowsy, Non O	Subdural Hemorrage	Gcs<7	22050	90/6	S	gressive in	GP	5	I
23	30949	Sohil	3	M	Intake of Organophosphorous compound	118	24	90/60	37	N	BA+	N	UnC, Non O	nophosphorous Poisc	Gcs<7	7660	24/76	S	NI	S	3	D
24	33924	Laxmi	2	M	Fever, Cough, Hurried breathing	110	46	90/50	37	N	BA+, B/L \	N	C, O	Bronchitis	Hypoxia	18940	26/72	S	NI	S	3	I
25	34245	Nandini	2	M		130	40	84/48	38	N	BA+	N	Drowsy, Non O	Septic shock	Hypoxia	25110	56/39	S	NI	S	3	D
26	36704	Yallamma	9	M	Fever, loose stools , vomiting	128	38	78/38	38	N	BA+	N	C, Non O	oentritis with Severe D	Hypoxia	12710	63/32	S	NI	S	4	I
27	36031	Prithviraj	2	M	Convulsions	130	36	96/56	37	N	BA+	N	UnC, Non O	Status Epilepticus	ctory Seiz	6290	68/23	S	NI	S	5	I
28	35224	Soujanya	7	F	Fever, loose stools , vomiting	120	30	90/60	39	N	BA+	N	C, Non O	oentritis with Severe D	Hypoxia	4670	81/10	S	NI	S	4	I
29	37224	Md Zaid	<1	M	Fever, loose stools , vomiting	160	46	80/44	39	N	BA+	N	C, Non O	oentritis with Severe D	Hypoxia	16330	89/8	S	NI	S	8	D
30	36837	/O Draupath	<1	M	Refusal of feed, Vomiting, Lethargy	166	66	72/40	39	N	BA+	N	UnC, Non O	Septic shock	Gcs<7	16040	60/31	S	NI	S	3	D
31	34669	Prashant	<2	M	Fever, loose stools , vomiting	130	44	84/52	39	N	BA+, B/L (	N	C, Non O	oentritis with Severe D	Hypoxia	16630	79/18	S	ate with Ri	GN bacilli	5	I
32	37355	Arjun	1	M	Refusal of feed, Vomiting, Lethargy	144	40	80/44	39	N	BA+, B/L (	N	UnC, Non O	Septic shock	Hypoxia	11410	45/51	S	gressive in	GN bacilli	5	I
33	2670	Madushree	2	M		136	46	86/48	37	N	BA+	N	C, Non O	Viral Myocarditis	diogenic sh	20610	62/34	S	NI	S	3	I
34	605	Sameer	<2	M	Intake of Organophosphorous compound	136	28	90/50	37	N	BA+	N	UnC, Non O	nophosphorous Poisc	Gcs<7	26640	51/40	S	NI	S	4	I

35	915	Ashwini	13	F	Intake of Organophosphorous compound	100	20	86/48	38	N	BA+	N	UnC, Non O	inophosphorous Poisc	Gcs<7	14500	48/38	S	NI	S	3	I
36	3749	Swetha	13	F	Fall from height	80	30	130/90	37	N	BA+	N	UnC, Non O	ost Traumatic Meningit	Gcs<7	23470	92/4	S	NI	S	7	I
37	14818	Prajwal	<1	M	Convulsions	150	48	80/50	37	N	BA+	N	UnC, Non O	Seizure Disorder	Gcs<7	19790	51/42	S	NI	S	3	AMA
38	15075	Harshita	1	F	Fever, loose stools , vomiting	130	36	78/44	39	N	BA+	N	C, Non O	oentritis with Severe D	Hypoxia	3140	19/50	S	NI	S	3	I
39	15026	Darshan	2	M	Noisy breathing , hurried bresthing	110	46	90/50	37	N	BA+	N	UnC, Non O	: Stenosis with Seizure	Gcs<7	12840	83/15	S	NI	S	3	I
40	19189	Shivanand	2	M	Fever, Edema,Rashes, Vomiting	108	36	88/50	38	N	BA+	N	C, Non O	Rickettsial Encephalitis	Hypoxia	26330	91/5	S	NI	S	4	I
41	2887	Boramma	<1	F	Ingestion of Organophosphorous compound	130	20	80/42	37	N	BA+	N	UnC, Non O	inophosphorous Poisc	Gcs<7	21260	60/36	S	NI	S	2	I
42	19396	Chiranjeevi	3	M	Ingestion of Paracetamol syrup	110	40	90/46	37	N	BA+	N	UnC, Non O	Paracetamol Poisoning	Gcs<7	9320	39/53	S	NI	S	3	I
43	19777	B/O Saila	3	M	Fever, rash,convulsion	114	36	86/46	38	N	BA+	N	UnC, Non O	HSV Encephalitis	Gcs<7	12290	55/39	S	NI	S	4	I
44	19190	Kausar	3	F	Convulsions, vomiting	126	32	84/48	37	N	BA+	N	UnC, Non O	ire Disorder with Ence	Gcs<7	25600	88/7	S	NI	S	8	AMA
45	4429	Mallikarjun	1	M	Road Traffic Accident	124	36	80/46	37	N	BA+	N	UnC, Non O	Accident with Left Fer	Gcs<7	8010	75/19	S	NI	S	2	D
46	4503	Riyan	4	M	Fever, Swelling of Neck	130	40	78/42	38	N	BA+	N	C, Non O	Diptheric Myocarditis	liogenic sh	20290	79/13	S	NI	S	3	D
47	6097	Susmita	<2	F	Fever, loose stools , vomiting	136	40	84/44	38	N	BA+	N	C, Non O	oentritis with Severe D	Hypoxia	16310	72/24	S	NI	S	4	I
48	8263	Prajwal	5	M	Convulsions	110	30	110/64	37	N	BA+	N	UnC, Non O	Status Epilepticus	Gcs<7	9810	68/24	S	NI	S	3	I
49	8779	Shamshodin	6	M	Fever, Swelling of Neck	104	35	86/54	38	N	BA+	N	C, Non O	Diptheria	irway Obs	4710	77/20	S	NI	S	3	AMA
50	9149	Bhimbai	2	F	Fever, Vomiting,Convulsions	76	34	86/56	38	N	BA+	N	Drowsy, Non O	Meningitis	Gcs<7	52610	66/30	S	NI	S	8	I
51	10929	Shahida	2	F	Hurried breathing	110	38	92/56	38	N	BA+	N	C, Irritable	oreign Body Aspiratio	Hypoxia	20090	59/35	S	NI	S	7	I
52	11330	Pratik	<2	M	Fever, Vomiting,Convulsions	80	40	120/64	38	N	BA+	N	Drowsy, Non O	viral meningitis	Gcs<7	8710	77/20	S	NI	S	4	I
53	12047	Rohnak	<1	M	Convulsions	160	36	94/52	37	N	BA+	N	UnC, Non O	C/C/O Seizure Disorde	Hypoxia	26150	53/43	S	NI	S	3	AMA
54	12422	Vaibhav	<2	M	Noisy breathing , hurried breathing	130	56	90/54	37	N	BA+	N	Drowsy, Non O	Croup	Hypoxia	4580	81/15	S	NI	S	3	D
55	12746	Ganesh	8	M	Fever,anuria	110	40	140/90	37	N	BA+	N	C, Non O	CKD	Hypoxia	30580	85/10	S	NI	S	6	I
56	13269	safiya	4	F	h/o fall	114	30	110/80	37	N	BA+	N	UnC, Non O	Extradural Hemorrhage	Gcs<7	8820	76/19	S	NI	S	3	I
57	39146	Parashuram	<1	M	Fever,vomiting,refusal of feed	150	50	70/50	39	N	BA+, B/L (	N	Drowsy, Non O	Septic shock	ractory sh	1320	48/37	osiell	ate with R	S	3	AMA
58	38374	sinchana	<1	F	h/o foreign body ingestion	140	58	90/56	37	N	BA+	N	C, Irritable	oreign Body Aspiratio	Hypoxia	5290	49/31	S	NI	S	3	I
59	19632	Kabir	<1	M	Lethargy,refusal of feeds,vomiting	140	46	90/60	38	N	BA+	N	C, Non O	e anemia with septic s	ractory sh	28800	46/50	S	NI	S	2	D
60	16994	Sahil	<2	M	fever,loose stools,vomiting,lethargy	130	46	86/52	38	N	BA+	N	C, Non O	gastroenteritis with a	Hypoxia	2630	22/55	S	NI	S	2	I
61	40232	Divyashree	2	F	Fever,convulsion	132	40	90/66	37	N	BA+	N	UnC, Non O	ite Encephalitis syndro	Gcs<7	10070	49/27	S	NI	S	5	I
62	40218	Huarain	<1	M	fever,loose stools,vomiting,lethargy	130	39	88/54	38	N	BA+	N	C, Non O	oentritis with Severe D	Hypoxia	14110	26/69	S	NI	S	5	I
63	40626	Basavaraj	3	M	Fever,rash,convulsion,edema	120	30	90/50	39	N	BA+, B/L (	N	UnC, Non O	Rickettsial Encephalitis	Gcs<7	23600	69/24	S	gressive in	GN bacilli	7	I
64	41764	Suramadevi	3	F	Hurried breathing	110	45	90/60	38	N	BA+	N	C, Non O	Status asthmaticus	piratory Fa	8520	89/8	S	NI	S	3	I
65	42485	Amoghsidda	2	M	Fever,rash,edema	110	35	86/48	38	N	BA+	N	C, Non O	Rickettsial fever	Hypoxia	34070	87/9	S	NI	S	4	I
66	42914	Savita	14	F	Convulsions	110	30	100/54	37	N	BA+	N	UnC, Non O	Status epilepticus	Gcs<7	14110	88/9	S	NI	S	4	I
67	43078	Vaishnavi	<1	F	H/O hit by car	160	44	110/50	37	N	BA+	N	UnC, Non O	with traumatic brain in	Gcs<7	43560	61/35	S	NI	S	5	AMA
68	494	Suchit	<1	M	Fever,lower limb weakness	130	30	90/60	37	N	BA+	N	C, O	ADEM	atory depr	6240	61/37	S	gressive in	PA	5	I
69	3432	Chinmaya	1	F	H/O drowning	110	40	84/48	38	N	BA+	N	C, Non O	Dry Drowning	Hypoxia	6510	46/51	S	NI	S	4	I
70	3543	Vishwa	<1	M	Vomiting	130	42	84/52	37	N	BA+	N	C, O	IHPS	ent aspira	16310	34/55	S	NI	S	5	I
71	3907	Akshay	6	M	Convulsions	110	30	96/68	37	N	BA+	N	UnC, Non O	Status epilepticus	ictory Seiz	12810	79/14	S	NI	S	4	I
72	5839	Nagappa	9	M	H/O snake bite	90	32	90/60	36	N	BA+	N	UnC, Non O	genic Snake Envenom	Gcs<7	23190	86/10	S	NI	S	4	AMA
73	6525	Anushree	<1	F	Fever,hurried breathing	150	48	80/40	37	N	BA+	N	C, Non O	rdiomyopathy with m	liogenic sh	23280	38/56	S	NI	S	4	I
74	12342	Suraksha	13	M	Fever, Swelling of Neck	110	30	86/48	39	N	BA+	N	C, Irritable	ubmandibular Cellulit	irway Obs	8800	71/15	S	NI	S	5	I
75	12613	Vinod	11	M	Fever, Vomiting,Convulsions	70	34	120/80	39	N	BA+	N	UnC, Non O	Viral Meningitis	Gcs<7	23790	88/8	S	gressive in	GN	5	I
76	15984	Vidyashree	9	F	Vomiting, Fever, Hurried Breathing	100	40	100/56	38	N	BA+	N	C, O	Diabetic Ketoacidosis	Hypoxia	20450	88/6	S	NI	S	4	I
77	15950	Lava	3	M	H/o unknown bite	120	38	130/84	37	N	BA+	N	C, Non O	Scorpian Sting	diogenic sh	12090	73/24	S	NI	S	4	I
78	15153	Shivakumar	3	M	Vomiting, Fever, Hurried Breathing	110	36	96/50	38	N	BA+	N	C, O	Diabetic Ketoacidosis	Hypoxia	8550	64/30	S	NI	S	5	I
79	14275	B/O Radha	<1	F	Vomiting, Blood in stool	140	40	90/52	37	N	BA+	N	Activity/Tone : C	prung Disease with Se	Hypoxia	22110	60/35	S	NI	S	5	I
80	284770	Sanket	12	M	Fever, rash,Vomiting	110	25	80/40	38	N	BA+	N	C, Non O	Severe Dengue	volemic S	13000	50/35	S	NI	S	6	I
81	14103	Irrayya	3	M	Cough, Fever, Breathlessness	120	36	100/60	37	N	BA+, B/L (	N	C, O	Rt sided pneumon	ent aspira	8600	55/38.8	S	NI	S	5	I