NOSOCOMIAL PNEUMONIA AMONG VENTILATED CHILDREN IN PAEDIATRIC INTENSIVE CARE UNIT

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CERTIFICATE

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CONTENTS

INTRODUCTION

Nosocomial infections are those acquired during hospital stay and not present or incubating in the patient during admission. Nosocomial infections increase both morbidity and mortality in critically ill patients. Many of these infections are preventable. Data suggest that 35% of nosocomial bloodstream infections, 22% of pneumonias, 33% of urinary tract infections can be prevented if hospitals have an effective infection control programme.[1]

DEFINITION OF NOSOCOMIAL PNEUMONIA

(CDC DEFINITION)[2]

SIGNS AND SYMPTOMS

at least 3 of the following:

a) Fever (38.4^0C or 101.1^0F) or hypothermia (36.5^0C or 97.7^0F) with no other recognised cause

b) Leukopenia (≤4000 WBC/mm3) or leukocytosis (≥15,000 WBC/mm3)

c) New onset of purulent sputum or change in character of sputum or increased respiratory secretions or increased suctioning requirements

d) New onset or worsening cough or dyspnea, apnea, or tachypnea

e) Rales or bronchial breath sounds

f) Worsening gas exchange (eg, O_2 desaturations [<94%], increased oxygen requirements, or increased ventilator demand)

Chest radiographs with at least one of the following:

a) New or progressive and persistent infiltrate

b) Consolidation

c) Cavitation

d) Pneumatoceles, in infants <1 year old

LABORATORY CRITERIA

At least one of the following:

a) Positive growth in blood culture not related to another source of infection

b) Positive growth in culture of pleural fluid

c) Positive quantitative culture from minimally contaminated lower respiratory tract specimen (eg, Bronchoalveolar lavage (BAL) or protected specimen brushing)

d) >5% BAL-obtained cells contain intracellular bacteria on direct microscopic exam (eg, Gram stain)

e) Histopathologic exam shows at least one of the following evidences of pneumonia:

    1. Abscess formation or foci of consolidation with intense polymorphonuclear accumulation in bronchioles and alveoli.

    2. Positive quantitative culture of lung parenchyma

    3. Evidence of lung parenchyma invasion by fungal hyphae or pseudohyphae

The epidemiology and outcomes of ventilator-associated pneumonia are well described in adults, but few data exist for pediatric patients, particularly with respect to risk factors and outcomes such as attributable morbidity, mortality, and cost.

Nosocomial pneumonia (NP) forms the second most common nosocomial infection in pediatric intensive care unit (PICU). A study from United

States in 1999 showed that the most prevalent nosocomial infection was blood stream infection (41%), followed by pneumonia (23%), urinary tract infection (13%), skin and soft tissue (8%).[3]

The National Nosocomial Infection Surveillance (NNIS) program[4] sponsored by the Centers for Disease Control and Prevention collects information on nosocomial infections in several hundred hospitals of different sizes in United States (US).

Ventilator-associated pneumonia was the second most common cause of nosocomial infection in US, representing 20% of nosocomial infections in this population.

A study of 20 PICUs in 8 countries performed by the European Multicenter Study Group[5] found that the incidence of nosocomial infection was 23.6% and the most frequent nosocomial infection was pneumonia (53%).

The Pediatric Prevention Network of the National Association of Children's Hospitals and Related Institutions performed a cross-sectional observational study to determine the point prevalence of nosocomial infection, including bloodstream infections and ventilator-associated pneumonia on a single day in 35 PICUs in United States. In this study, the

overall prevalence of nosocomial infection was 12%. Bloodstream infection was the most common nosocomial infection (41.3%), and ventilator-associated pneumonia was the second most common (22.7%).

There are no such large scale studies from India. Many individual studies done show incidence between 27% to 35%[6,7,8]

In ICU patients, nearly 90% of nosocomial pneumonias occur during mechanical ventilation. In mechanically ventilated patients, the incidence increases with duration of ventilation. The risk of ventilator associated pneumonia (VAP) is highest early in the course of hospital stay, and is estimated to be 3% / day during first 5 days of ventilation, 2% / day during days 5 to 10 and 1% / day after this.[9]

Early onset VAP or NP is defined as occurring within first 4 days of hospitalization. This usually carries a better prognosis, and is more likely to be caused by antibiotic sensitive bacteria.

Late onset VAP or NP are those occurring 5 days or later of hospitalization. They are more likely to be caused by multidrug resistant organisms and associated with increased morbidity and mortaliity.

ETIOLOGY

NP is caused by a wide spectrum of bacterial pathogens. They may also be polymicrobial and are rarely due to viral and fungal pathogens in immunocompetent hosts[10,11]. Common pathogens include aerobic gram negative bacilli such as Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa and acinetobacter species. Infections due to gram positive cocci such as Staphylococcus especially Methicillin resistant Staphylococcus aurues are rapidly emerging. Significant growth of oropharyngeal commensols like viridans group of streptococci, coagulase negative staphylococci, niesseria species and corynebacterium species can produce infection in immunocompromised hosts and some immunocompetent hosts[12].

PATHOGENESIS

Colonisation of the buccal oropharyngeal mucosa and alteration of the endogenous microflora appear to be crucial antecedents to endotracheal colonisation and nosocomial pneumonia. Colonisation of upper airways is frequent in critically ill patients. It has been demonstrated that after 10 days in ICU, 86% of patients were colonized by gram negative bacilli and 70% with yeast[13]. Any patient who has been hospitalized likely to have altered endogenous pharyngeal microflora, associated with prolonged hospitalistion, serious underlying illness,

recent antimicrobial therapy and immunosuppression[14]. Once the buccal oropharyngeal mucosa is colonized, the risk of lower respiratory tract colonisation is greater resulting in pneumonia. A study that examined the relative predictive value of positive surveillance cultures of upper airways in high risk patients found that 45% of the patients became colonized with aerobic gram negative bacilli by the end of first week. Lower airway colonisation is followed by infection with same organisms and preceded VAP in 2/3 of episodes[15].

The presence of an endotracheal tube provides a direct route for colonized bacteria to enter the lower respiratory tract. Upper airway and oral secretions can pool above the cuff of an endotracheal tube and line the tube, forming a biofilm. Starting as early as 12 hours after intubation, the biofilm contains large amounts of bacteria that can be disseminated into the lungs by ventilator-induced breaths. [16,17,18] In addition, the biofilm may become dislodged by instillation of saline into the endotracheal tube, suctioning, coughing, or repositioning of the endotracheal tube[18]. Endotracheal tubes cause an abnormal interruption between the upper airway and the trachea, bypassing the structures in the upper airway and providing bacteria a direct route into the lower airway[16]. Because the upper airway is bypassed, a decrease occurs in the body's ability to filter and humidify air[18].

In addition, the cough reflex is often eliminated and/or decreased by the presence of an endotracheal tube[19], and mucociliary clearance can be impaired because of mucosal injury during intubation[20]. An endotracheal tube provides a place for bacteria to bind in the trachea, a situation that further increases production and secretion of mucus[20]. The impairment of these natural host defense mechanisms increases the likelihood of bacterial colonisation and subsequent aspiration of the colonized organisms.

The stomach-oral route may be a significant source of organisms colonizing the oropharynx[22]. Most patients receiving mechanical ventilation have a nasogastric or an orogastric tube in place for enteral feeding and administration of medications or for gastric decompression. The presence of a nasogastric or an orogastric tube interrupts the gastroesophageal sphincter, leading to increased gastrointestinal reflux and providing a route for bacteria to translocate to the oropharynx and colonize the upper airway. Enteral feedings increase both gastric pH and gastric volume, increasing the risk of both bacterial colonisation and aspiration[21]. However, tracheal colonisation precedes VAP in 93.5% cases versus gastric colonisation in only 13%.[2]

Less common routes include inhalation of contaminated aerosolized fluids or medication and hematogenous seeding (eg. Right sided bacterial endocarditis).

There is an increased adherence of microorganisms to the epithelial cells of oropharyhx in ill patients[24]. Patients with chronic tracheostomies also exhibit greater tracheal cell adherence. Poor nutrition aggravates this condition[25]. Once the organisms gain entry to the lower respiratory tract, the normal defenses usually are sufficient to prevent infection. However under certain conditions, the functions of alveolar macrophages are disturbed. For example, patients with ARDS or preexisting pneumonia, secretion of cytokines like interleukin-1 increases[26]. The recruited granulocytes likewise function abnormally. Pulmonary edema impairs bacterial clearance from lung[15,27].

DIAGNOSIS

The diagnosis of nosocomial pneumonia is suspected if the patient has a radiographic infiltrate that is new or progressive, along with clinical findings suggesting infection, which include new onset fever, purulent sputum, leukocytosis and decline in oxygenation.

INVASIVE TECHNIQUES OF SAMPLING DISTAL AIRWAYS

Fibre optic bronchoscopy allows direct selective access to the distal airways for sampling. However, there are a number of problems associated with the use of bronchoscopy; the expertise and equipment required is not always available and sampling is often followed by a period of hypoxaemia.[28]

Two techniques are commonly used to obtain distal airway samples with the bronchoscope; Bronchoalveolar lavage (BAL) or protected specimen brushing (PSB).

BRONCHOALVEOLAR LAVAGE

BAL is performed by advancing the bronchoscope into a distal airway and instilling about 130–150 ml of sterile saline.[29] Selection of the area of the lung for sampling is guided by the pattern of consolidation on the chest radiograph.

As much of the saline as possible is aspirated and sent for quantitative culture. The most frequently used threshold for a positive culture is 10^4 colony forming units/ml.

PROTECTED SPECIMEN BRUSH

This technique was introduced in 1979 by Wiberley, et al in an attempt to reliably obtain lower respiratory tract specimens that are not contaminated with tracheal or tracheal tube organisms.[30] This technique

entails the advancement of a double lumen catheter system under direct vision into the desired distal airway. Once in position the brush is advanced expelling the carbowax plug at the distal end of the catheter. Brushings are taken and the brush is then retracted into the catheter and removed, thereby protecting the brush from contamination. The brush is suspended in 1 ml of saline and quantitative culture obtained. A threshold of 10^3 colony forming units/ml is used to signify a positive result.

NON-BRONCHOSCOPIC SAMPLING OF DISTAL AIRWAYS

BAL and PSB cannot both be performed without the aid of a bronchoscope. Non-bronchoscopic BAL is performed by blindly advancing a protected suction catheter through the tracheal tube until it becomes wedged in a distal airway. The inner cannula is then advanced past its protective sheath and 100 ml of saline introduced and aspirated. Non-bronchoscopic PSB is similarly performed by inserting a double lumen catheter through the tracheal tube until resistance is felt and then advancing the brush to obtain a specimen. The good concordance between microbiological data obtained by bronchoscopic and non-bronchoscopic techniques shows the diffuse nature of parenchymal infection in those with VAP.[31]

QUANTITATIVE CULTURES OF TRACHEAL ASPIRATES

Collection of material for microbiological analysis using this technique is quick, simple, and widely available. While there is some evidence to suggest that the use of this method has a high false positive rate in the diagnosis of VAP, other studies suggest that quantitative analysis of tracheal aspirates offers a reliable alternative to invasive techniques.[32,33,34]. A threshold of 10^5 colony forming units/ml is used to distinguish tracheal colonisation from true VAP.

Other tests include detection of elastin fibre,[36,37] endotoxin,[38] the triggering receptor expressed on myeloid cells (TREM-1)[35] in respiratory secretions and detection of neutrophil CD64 expression in blood.[39]

MANAGEMENT

Aggressive and prompt treatment is required when nosocomial pneumonia is suspected in a critically ill patient. The initial empirical antibiotic therapy should be able to treat the organisms that are prevalent in PICU. For early onset pneumonia, β lactums like pencillin and cephalosporin are recommended. Vancomycin is considered if methicillin resistant Staph. aureus (MRSA) is prevalent in the ICU.

In late onset pneumonia, monotherapy will lead to risk of multidrug resistant bacterial growth. The American thoracic society[40]

suggested a combination of at least two wide-spectrum antibiotics: 1) a β lactum (eg. ceftazidime, cefotaxime, imipenam or piperacillin) and 2) an aminoglycoside. Combined antibiotics like ticarcillin-clavunic acid or tazobactum-piperacillin also can be used instead of β lactums. Vancomycin is added if MRSA is prevalent. Antibiotics are changed after culture reports are available. Antibiotics are to be continued if nosocomial pneumonia is suspected by clinical and radiological evidence.

PREVENTION

Although VAP has multiple risk factors, many nursing interventions can reduce the incidence of this disease. Nurses are the first line of defense in preventing bacterial colonisation of the oropharynx and the gastrointestinal tract. Meticulous hand washing for 10 seconds should be performed before and after all contact with patients.[41] In addition, gloves should be worn when contact with oral or endotracheal secretions is possible. Strategically placing a sign on a patient's bed to remind health-care workers to wash their hands and wear gloves is an easy and cost-effective measure that can help minimize transmission of bacteria between patients. The use of protective gowns is not recommended as routine practice, but gowns should be used when antibiotic-resistant pathogens have been isolated and identified.[41]

Bacterial colonisation of the stomach can lead to aspiration and colonisation of the respiratory tract. Most patients receiving mechanical ventilation are given stress ulcer prophylaxis, often with medications that increase the gastric pH. A study[42] in the 1980s indicated that pathogens multiply in an alkaline gastric environment. In research[43] conducted in a pediatric intensive care unit, VAP rates did not differ between patients receiving ranitidine, omeprazole, or sucralfate for stress ulcer prophylaxis. Nowadays, as the use of proton pump inhibitors for stress ulcer prophylaxis has increased, few studies have been conducted to address whether the incidence of VAP is affected by proton pump inhibitors.

Mucus in the airways can become stagnant and serve as a medium for bacterial growth. Maintenance of aseptic technique when performing endotracheal suctioning is essential to prevent contamination of the airways. No difference has been found in the incidence of VAP with open versus closed suction systems.[44] When a closed system is used, the suction catheter should be rinsed free of secretions away from the patient.

Furthermore, saline lavage of endotracheal tubes before suctioning dislodges bacteria from the endotracheal tube into the lower airways, increasing the risk for VAP.[45] Saline lavage has long been considered a

means to liquefy secretions and prevent plugs of mucus in endotracheal tubes. However, in one study,[46] saline instillation did not thin secretions; rather it reduced the amount of oxygen that reached the lungs and increased blood pressure, heart rate, intracranial pressure, and the risk for VAP. Maintaining adequate hydration, ensuring proper humidification of the ventilatory circuit, and using nebulizer or mucolytic agents can help decrease the viscosity of secretions and eliminate the need for saline lavage.[45,46] Prophylactic use of systemic antibiotics does not decrease the incidence of VAP and when the agents are used inappropriately, antibiotic resistance can develop.[47]

Routine turning of patients a minimum of every 2 hours can increase pulmonary drainage and decrease the risk for VAP. Use of beds capable of continuous lateral rotation can decrease the incidence of pneumonia but do not decrease mortality or duration of mechanical ventilation.[48] These beds are costly and are not necessary for routine use in the prevention of VAP,[41] although the use of speciality beds may be cost-effective and therapeutic for patients with poor oxygenation or impaired wound healing.

Colonisation of the ventilator circuit can also play a role in the development of VAP. Daily changes of the ventilator circuit do not seem

to decrease the incidence of VAP.[49] The Centers for Disease Control and Prevention does not recommend changing the ventilator circuit more than once every 48 hours,[41] and research[50] has indicated that changing the ventilator circuit as infrequently as once a week does not increase the risk for VAP. It is recommended that the ventilator circuit be changed when visibly soiled.[41] Many investigators have compared the impact of heat and moisture exchangers on the incidence of VAP with the impact of heated humidifiers. The results were inconclusive as to which form of humidity is associated with a higher incidence of VAP.

In addition to strategies to prevent colonisation, strategies to prevent aspiration can also be used to decrease the risk for VAP. Because the presence of an endotracheal tube predisposes patients to VAP, patients should be assessed on a daily basis for potential weaning and extubation from mechanical ventilation. Several methods of assessing readiness for extubation exist. These include T-piece trials, weaning intermittent mandatory ventilation, and pressure-support ventilation.[51]

Positioning patients in a semi-recumbent position with the head of the bed elevated 30° to 45° prevents reflux and aspiration of bacteria from the stomach into the airways. Simply elevating the head of the bed 30° can decrease VAP by 34%.[52] Impaired gastric emptying can lead to

over distention, or increased gastric residual volume, of the stomach and the potential for regurgitation and aspiration. Minimising the use of narcotic agents can help prevent aspiration of gastric and/or oral contents.[19]

Decreasing use of narcotic and/or sedative agents in the intensive care unit must be done cautiously, because pain can limit deep breathing and impair oxygenation. Daily interruptions of continuous sedative infusions can shorten the duration of mechanical ventilation by more than 2 days and length of stay in the intensive care unit by 3.5 days.[53] Monitoring gastric residual volumes and administering agents to increase gastric motility have been suggested as ways to prevent gastric overdistention.[19] Although the effectiveness of these interventions in reducing VAP has not been tested in clinical trials, it is reasonable to avoid gastric over distention in an attempt to prevent aspiration.

Because secretions tend to pool above the cuffs of endotracheal tubes, the oropharynx should be thoroughly suctioned to prevent aspiration of the pooled secretions before an endotracheal tube is replaced. Use of tubes with ports for continuous subglottic suctioning can decrease the incidence of VAP by 50%.[54]

Studies are also being conducted with endotracheal tubes coated with silver nitrate. It is hypothesized that silver nitrate interferes with the ability of bacteria to line the endotracheal tube and form a biofilm. Further studies are needed to determine the cost-effectiveness of these coated tubes in preventing VAP.

REVIEW OF LITERATURE

Compared to the exhaustive data on adult nosocomial infections and nosocomial pneumonia(NP), there are very few studies on pediatric NP especially from developing countries.

Patra P.K, et al [6] from Chandigarh did a prospective study in PICU of a multispeciality hospital. 72 children were included in the study. CDC criteria was used and infection was defined by a semiquantitative count of more than 10^5 cfu/mL of endotracheal aspirate.

The incidence of NP in their study was 30.5%. .Acinetobacter anitratus was the most predominant isolate in 12 (54.5%), followed by Pseudomonas aeroginousa in 5 (22.7%), Klebsiella in 3 (13.6%) and E.coli in 1 (4.5%). Staphylococcus aureus (MRSA) was seen in one patient only. Ventilated patients who developed NP were compared with those who did not, with respect to age, sex, PRISM scores, nutritional status, duration and frequency of intubation (reintubation) and duration of mechanical ventilation, nasogastric feeding, sedation and use of H_2 blockers to identify risk factors for NP. Univariate analysis revealed that patients with NP had a significantly higher duration of mechanical ventilation and higher proportion and frequency of reintubation. On subjecting the significant variables to multiple logistic regression,

reintubation was the only independent risk factor for development of NP. The percentage mortality in the group with NP and no NP was 31.8% and 16% respectively. However this difference was not statistically significant. All the deaths in the group with NP were secondary to Gram negative infections with Pseudomonas contributing to 4 (57.1%) deaths followed by Klebsiella, E. coli and Acinetobacter in one patient each.

Tullu MS, et al [7] from Mumbai did a prospective study for 6 months in PICU to determine the incidence, risk factors, mortality and organisms causing nosocomial pneumonia in intubated patients. In the study, 69 patients (49 males : 20 females) had an ET tube inserted. NP developed in 19 out of 59 patients with mechanical ventilation (MV) (32.20%; 8.92/100 days of MV; 3.65/100 patient-days). NP developed in 19 out of the 69 patients with ET intubation (27.54%; 7.96/100 days of ET intubation). All these 19 patients had undergone mechanical ventilation. The organisms commonly isolated were E. coli (34.4%), Klebsiella (30.2%), Pseudomonas (11.5%), Proteus (11.5%), and Acinetobacter (5.2%). Other organisms isolated included 2 isolates each of Enterobacter and Citrobacter, and 1 isolate each of coagulase negative Staphylococci, Non-lactose fermentors and Salmonella. Age, sex, altered sensorium and immunocompromised status (including 3 HIV positive cases) did not increase the incidence of NP. MV for more than 48 hours

and a PICU stay of more than 3 days significantly increased the incidence of NP. Mortality in patients with NP was 47.37% and those without NP were 45%. The difference was not statistically significant.

Alexis M Elward, et al [55] from Washington did a prospective cohort study in the year 2000 to determine the rates, risk factors, and outcomes of ventilator-associated pneumonia in pediatric intensive care unit (PICU) patients. There were 34 episodes of ventilator-associated pneumonia in 30 patients of 911 admissions (3.3%) and 595 (5.1%) mechanically ventilated patients. The mean ventilator-associated pneumonia rate was 11.6/1000 ventilator days. The most common organisms isolated was Pseudomonas aeruginosa (29.4%). The other isolates were Klebsiella pneumoniae (14.7%), Staphylococcus aureus (11.8%), yeast (8.8%), Haemophilus influenza (8.8%), Streptococcus pneumoniae (5.9%). Multiple factors were analysed for risk factors. Ventilator-associated pneumonia was associated with the following procedures: reintubation, tracheostomy, transfusion, transport out of the PICU, the presence of a central line, multiple central venous catheters, bronchoscopy, thoracentesis, and burn debridement. The following medications were associated with ventilator-associated pneumonia: Total Parenteral Nutrition, steroids, and histamine type 2 receptor blockers.

Patients with VAP had higher mean PRISM score and longer PICU and hospital stay.

Only transfusion, reintubation, and transport out of the PICU remained significant in the forward stepwise logistic regression model. Patients with VAP had higher mortality rate (20% vs 7%) which approached statistical significance.

A similar study was done by the same author in 1999 in Washington[56]. 322 intubated patients were included in study. There were 18 episodes of VAP in 13 pts. The VAP rate was 10.39/1000 ventilator days. Increased VAP rates were associated with seizures , transplant , burns, congenital immmunodeficiency , respiratory arrest, cardiopulmonary arrest , transfusion, sepsis .Patients with VAP had higher admission Pediatric Risk of Mortality (PRISM) scores .Patients with VAP had longer hospital length of stay (LOS) , longer PICU LOS & were more likely to die.

A prospective surveillance study was done by **Almuneef M, et al**[57] from Riyadh, Saudi Arabia to describe the rate, risk factors, and outcome of ventilator-associated pneumonia in pediatric patients. 361 eligible patients were enrolled. 37 developed VAP. The mean VAP rate was 8.87 per 1,000 ventilation-days. Among VAP patients, Pseudomonas

aeruginosa was the most common organism, followed by Staphylococcus aureus. Other gram-negative organisms were also encountered. There was no significant difference between VAP and non-VAP patients regarding mortality rate. Witnessed aspiration, reintubation, prior antibiotic therapy, continuous enteral feeding, and bronchoscopy were associated with VAP. On multiple logistic regression analysis, only prior antibiotic therapy, continuous enteral feeding, and bronchoscopy were independent predictors of VAP.

Emad H. Ibrahim, et al [58] from Washington did a prospective cohort study identify the occurrence of ventilator-associated pneumonia in a community hospital, and to determine the risk factors for VAP and the influence of VAP on patient outcomes in a nonteaching institution. Eight hundred eighty patients received mechanical ventilation and comprised the study cohort. One hundred thirty-two patients (15.0%) who received mechanical ventilation acquired VAP during their ICU stay. Patients with VAP were also statistically more likely to require reintubation, tracheostomy, multiple central venous lines, and to receive treatment with histamine type-2 receptor antagonists or sucralfate . Similarly, the durations of central vein catheterisation and mechanical ventilation were statistically longer among patients with VAP, Pseudomonas aeruginosa was the most common Gram-negative bacterial

pathogen isolated from the respiratory tract among infected patients with VAP for both survivors and nonsurvivors. Staphylococcus aureus was the most common Gram-positive bacterial pathogen associated with VAP. The mortality rate of patients developing VAP (45.5%) was significantly greater than the mortality rate of patients without VAP (32.2%). Patients developing VAP had significantly longer lengths of stay in the ICU (23.9 days vs 5.9 days) and in the hospital (38.6 days vs 15.2 days), compared to patients without VAP.

Many studies have been published which analysed individual risk factors for development of VAP.

Yildizdas D, et al [43] from Turkey evaluated the effects of sucralfate, ranitidine, and omeprazole use on incidence of ventilator-associated pneumonia (VAP) and mortality in ventilated pediatric critical care patients. Seventy patients (44%) developed VAP. VAP rate was 42% (16 of 38) in the sucralfate group, 48% (20 of 42) in the ranitidine group, 45% (17 of 38) in the omeprazole group, and 41% (17 of 42) in the nontreated group. Overall mortality rate was 22% (35 of 160); it was 21% (8 of 38) in the sucralfate group, 23% (10 of 42) in the ranitidine group, 21% (8 of 38) in the omeprazole group, and 21% (9 of 42) in the nontreated group. There was no difference in the incidence of VAP and

mortality in mechanically ventilated PICU patients treated with ranitidine, omeprazole, or sucralfate, or nontreated subjects. Nine patients (5.6%) had macroscopic bleeding. There was no statistically significant difference in macroscopic bleeding between groups.

Torres, et al [59] from Spain did a case control study to confirm that reintubation can be a risk factor of nosocomial pneumonia in mechanically ventilated patients. Forty consecutive patients needing reintubation were selected as cases. Each case was paired with a matched control for the previous duration of mechanical ventilation (+/- 2 d). Nineteen (47%) of the cases developed pneumonia after reintubation compared with 4 (10%) of the controls. After adjusting for age, sex, and presence of prior bronchoscopy, the conditional logistic regression analysis demonstrated that reintubation was the only significant factor related to the development of pneumonia. Sixteen (73%) of the 22 patients lying semi recumbent during the interval between extubation and reintubation developed nosocomial pneumonia versus three (16%) of the 18 in supine position. These results indicate that semirecumbency during the period between extubation and reintubation may play a role in nosocomial pneumonia development in patients who need reintubation. Total intensive care unit stay and crude mortality were also higher in reintubated patients when compared with controls.

Jordi Valles, et al [60] did a randomised, controlled, blinded study to determine whether continuous subglottic aspiration prevents nosocomial pneumonia in mechanically ventilated patients. 76 patients were randomly allocated to receive continuous aspiration of subglottic secretions, and 77 control patients were allocated to receive usual care. The incidence rate of ventilator-associated pneumonia was 19.9 episodes/1000 ventilator days in the patients receiving continuous aspiration of subglottic secretions and 39.6 episodes/1000 ventilator days in the control patients .This difference was due to a significant reduction in the number of gram-positive cocci and Haemophilus influenzae organisms in the patients receiving continuous aspiration. However, no differences were observed in the number of Pseudomonas aeruginosa or Enterobacteriaceae organisms. Episodes of ventilator-associated pneumonia occurred later in patients receiving continuous aspiration (12.0 ±7.1 days) than in the control patients (5.9 ±2.1 days) (P = 0.003). The microorganisms isolated from protected specimen brush or bronchoalveolar lavage cultures in patients with ventilator-associated pneumonia were same as previously isolated from cultures of subglottic secretions in 85% of cases. No significant differences in outcome were found.

Mitra B Draculovic, et al [61] studied whether the incidence of nosocomial pneumonia can be reduced by semi recumbent body position in intensive-care patients. 86 intubated and mechanically ventilated patients were randomly assigned to semi recumbent (n=39) or supine (n=47) body position. The frequency of clinically suspected nosocomial pneumonia was lower in the semi recumbent group than in the supine group (3 of 39 [8%] *vs* 16 of 47 [34%]). This was also true for microbiologically confirmed pneumonia (semi recumbent 2/39 [5%] *vs* supine 11/47 [23%]). Supine body position and enteral nutrition were independent risk factors for nosocomial pneumonia and the frequency was highest for patients receiving enteral nutrition in the supine body position (14/28, 50%). Mechanical ventilation for 7 days or more and a Glasgow coma scale score of less than 9 were additional risk factors.

Bonten MJ, et al [62] analysed the role of enteral feeding in VAP in a randomised controlled trial in Netherlands. They studied the influence of intermittent enteral feeding [IEF] (18 h/d) and continuous enteral feeding [CEF] (24 h/d) on gastric and oropharyngeal colonisation. Sixty patients were randomised to receive either IEF or CEF, and continuous intragastric pH monitoring was performed in 50 patients. Median intragastric pH levels were similar before enteral feeding was instituted (pH 2.5 for CEF and pH 2.4 for IEF), and median pH values increased

slightly after institution of nutrition (not significant). In patients receiving IEF, median pH decreased from 3.5 to 2.2 ($p = 0.0002$) when enteral feeding was discontinued. However, despite this, 80% of the patients in both study groups were colonized in the stomach after 7 days in study. In addition, colonisation rates of the oropharynx and trachea, the incidence of VAP, and mortality were similar in both study groups. They concluded that almost all patients receiving enteral feeding are colonized in the stomach with gram-negative bacteria which subsequently leads to VAP.

Marin H. Kollef, et al [63] from Washington did a prospective cohort study to determine whether patient transport out of the ICU is associated with an increased risk of developing ventilator-associated pneumonia. A total of 273 (52.4%) mechanically ventilated patients required at least one transport out of the ICU while 248 (47.6%) patients did not undergo transport. Sixty-six (24.2%) of the transported patients developed ventilator-associated pneumonia compared with 11 (4.4%) patients in the group not undergoing transport (relative risk=5.5; 95% confidence interval [CI]=2.9 to 10.1; $p<0.001$). Multiple logistic regression analysis demonstrated that a preceding episode of transport out of the ICU was independently associated with the development of ventilator-associated pneumonia (adjusted odds ratio=3.8; 95% CI=2.6 to 5.5; $p<0.001$). Other variables independently associated with the

development of ventilator-associated pneumonia included reintubation, presence of a tracheostomy, administration of aerosols, and male gender.

To evaluate the attributable morbidity and mortality of ventilator-associated pneumonia (VAP) in intensive care unit (ICU) patients, **Daren K Heyland, et al** [64] from Canada conducted a prospective, matched cohort study. To determine the excess ICU stay and mortality attributable to VAP, they matched patients with VAP to patients who did not develop clinically suspected pneumonia. One hundred and seventy-seven patients developed VAP. As compared with matched patients who did not develop VAP, patients with VAP stayed in the ICU for 4.3 days (95% confidence interval [CI]: 1.5 to 7.0 d) longer and had a trend toward an increase in risk of death (absolute risk increase: 5.8%; 95% CI: −2.4 to 14.0 d; relative risk (RR) increase: 32.3%; 95% CI: −20.6 to 85.1%). They concluded that VAP prolongs ICU length of stay and may increase the risk of death in critically ill patients.

Many studies were done to identify the best method for collection of respiratory tract secretions and analysis. Although lung biopsy is the best method, bronchoscopy is the best feasible option. However this is an invasive procedure. Many studies are done to identify the best non invasive method.

The accuracy of quantitative culture and microscopic examination of lower respiratory tract secretions for the diagnosis of VAP was validated by **Chastre, et al** [65,66] who compared the results of quantitatively cultured lower respiratory tract secretions with those of culture and histopathologic examination of simultaneously obtained lung tissue. In the first study, quantitative culture of secretions obtained by protected specimen brush (PSB) was compared with histopathologic examination and quantitative culture of lung tissue. Of six patients with pneumonia confirmed by histologic criteria, all had at least one microorganism obtained at a concentration of $\geq 10^4$ CFU/g of lung tissue. Compared with the results of histologic examination and quantitative culture of lung tissue, quantitative culture of secretions obtained by PSB using a diagnostic threshold of $\geq 10^3$ Cfu/mL had a sensitivity of 100%, specificity of 60%, positive predictive value of 43%, and negative predictive value of 100%.

In the second study, the results of protected specimen brush (PSB), bronchoalveolar lavage (BAL) were compared with simultaneously obtained lung tissue . Patients were included in the study only if they had never had pneumonia or had acquired it during the terminal phase of their illness. Bronchoscopy was performed within 1 hour after death, while mechanical ventilation was continued and PSB and BAL samples were

taken. Immediately after bronchoscopy, a left thoracotomy was performed, and lung tissue specimens were taken from the areas of lung where the bronchoscopic samples had been obtained. All but two patients had been receiving antibiotics before death, but antibiotic therapy had not been changed for ≥3 days. All lung segments judged to have moderate to severe pneumonia by histologic criteria yielded $\geq 10^4$ cfu/g of tissue. PSB cultures ($\geq 10^3$ cfu/mL) had a sensitivity of 82% and specificity of 89%. BAL cultures ($\geq 10^4$ cfu/mL) had a sensitivity of 91% but a specificity of 78%.

Christian Brun-Buisson, et al [67] from France did a prospective observational study of 68 first episodes of suspected pneumonia in which specimens were obtained blindly (endotracheal aspirate [EA] and blinded protected telescoping catheter [PTC]) and via bronchoscopy (directed PTC bronchoscopy and BAL). Their adequacy was assessed using quantitative BAL fluid culture as the diagnostic standard. Their conclusions were as follows: Qualitative EA cultures have a high sensitivity but a high proportion (> 80%) of false-positive results when compared to BAL. Using simple semiquantitative cultures and a threshold corresponding to approximately 10^4cfu/mL markedly improved the diagnostic accuracy of EAsq relative to BAL and increased its specificity to 82%, while its sensitivity decreased to 77%. Protected samplings

(blinded PTC and directed PTC) were associated with a similar sensitivity (77%) and an excellent specificity (97%) as compared with the nonprotected techniques, especially nonquantitative EA. They proposed that blinded samplings with quantitative (or possibly semiquantitative) culture may be an alternative tool for the routine management of suspected VAP, especially where and when bronchoscopy is not readily available.

Rajasekhar T, et al [68] from Hyderabad studied the role of quantitative cultures of non-bronchoscopic samples such as blinded bronchial sampling (BBS) and endotracheal aspirates (ETA) in the management of ventilator associated pneumonia. The diagnostic thresholds for ETA and BBS were taken as 10^5 cfu/mL and 10^4 cfu/mL respectively. In a total of 15 patients suspected of VAP, 73.3% (11/15) cases tested positive for VAP. Quantitative culture results were positive for pathogenic organisms for VAP in which the colony counts were more than the diagnostic thresholds for ETA/BBS. 12 out of those 15 cases were subjected to both ETA and BBS quantitative cultures due to sample quality issues. In 10 out of 12 cases (83.3%) the ETA and BBS quantitative culture results were in total agreement detecting the same organism. The predominant organisms in the early-onset VAP group were Acinetobacter baumanii and Klebsiella spp. In the late onset group

Pseudomonas aeruginosa was the most predominant. Reintubation and prior use of broad-spectrum antibiotics were found to be the two most significant risk factors associated with the development of VAP based on statistical analysis of risk factors. Other risk factors studied were hospital stay >2 days, surgery, nasogastric tube, tracheostomy, stress ulcer prophyaxis and IV sedation. None of those were found significant.

Mauricio Ruiz, et al [69] from Spain studied the impact of noninvasive and invasive diagnostic approaches on outcome in a prospective, open, and randomised study in three intensive care units (ICUs) of a 1,000-bed tertiary care university hospital. Patients with suspected VAP were randomly assigned to noninvasive (Group 1) versus invasive (Group 2) investigation (tracheobronchial aspirates versus bronchoscopically retrieved protected specimen brush and bronchoalveolar lavage). Samples were cultured quantitatively, and BAL fluid was examined for intracellular organisms (ICO) additionally. Initial empiric antimicrobial treatment was administered following the guidelines of the American Thoracic Society and adjusted according to culture results (and ICO counts in Group 2). Outcome variables included length of ICU stay and mechanical ventilation as well as mortality. Overall, 76 patients (39 noninvasive, 37 invasive) were investigated. VAP was microbiologically confirmed in 23 of 39 (59%) and 23 of 37 (62%)

(p = 0.78). There were no differences with regard to the frequencies of community-acquired and potentially drug-resistant microorganisms. Antimicrobial treatment was changed in seven patients (18%) of Group 1 and 10 patients (27%) of Group 2 because of etiologic findings (including five of 17 with ICO = 2% (p = not significant). Crude 30 day mortality was 31 of 76 (41%), and 18 of 39 (46%) in Group 1 and 14 of 37 (38%) in Group 2 (p = 0.46). Adjusted mortality was 16% versus 11% (p = 0.53), and mortality of microbiologically confirmed pneumonia 10 of 23 (44%) in both groups. Lengths of ICU stay and mechanical ventilation as well as mortality were not significantly influenced by diagnostic techniques. They concluded that noninvasive microbial investigation is to be used as the principal approach to microbial investigation in suspected VAP.

STUDY JUSTIFICATION

About 50% of patients admitted in Pediatric Intensive Care Unit (PICU) of Institute of Child Health (ICH) require ventilatory support. Many patients develop nosocomial pneumonia. The causative agents and risk factors vary in each PICU. Nosocomial pneumonia increases morbidity and mortality in critically ill children. This increases the duration of stay, need for prolonged antibiotic administration and increased utilisation of hospital resources.

Many studies on nosocomial pneumonia had been done in western countries. There has been limited data from developing countries especially India. There are no prior studies from our institute on nosocomial pneumonia. Hence it was decided to study the incidence, etiological agents, risk factors and outcome of nosocomial pneumonia in our PICU. The results of the study will be helpful in identifying potential risk factors and implementing preventive measures. The data on etiological agents will help in formulating antibiotic policy for nosocomial pneumonia. This can reduce irrational use of antibiotics and subsequently prevent colonisation of multidrug resistant organisms.

AIM OF THE STUDY

To study the

- incidence,
- etiological agents,
- risk factors and
- outcome

of nosocomial pneumonia among ventilated children between 1 month and 12 years of age in pediatric intensive care unit.

METHODOLOGY

STUDY DESIGN: - Cohort study

STUDY PERIOD: - Oct 2007 to Aug 2008

STUDY PLACE: - Pediatric Intensive Care Unit, Institute of Child Health and Hospital for Children.

STUDY SUBJECTS:-

Inclusion criteria: All children between 1 month and 12 years of age intubated and ventilated in PICU during the study period.

Exclusion criteria:- 1) Children with preexisting pneumonia,

2) Children intubated for airway protection but not ventilated.

GROUP 1

Children with nosocomial pneumonia

Case definition for nosocomial pneumonia among ventilated children.

Pneumonia developing after 48 hours of endotracheal intubation and ventilation with,

a) Fever (38.4^0C or 101.1^0F) with no other recognised cause

b) Leukopenia (≤4000 WBC/mm3) or leukocytosis (≥15,000 WBC/mm3)

c) New onset of purulent sputum or change in character of sputum or increased respiratory secretions or increased suctioning requirements.

d) Rales or bronchial breath sounds and

Chest radiographs with at least one of the following:

a) New infiltrate

b) Consolidation

c) Cavitation

d) Pneumatoceles, in infants <1 year old and

Semiquantitative culture of endotracheal aspirate positive for microorganisms (>10^5 colony forming units (cfu) / mL).

GROUP 2

Ventilated children who never developed pneumonia

MANOEUVRE

All patients fulfilling the inclusion criteria were enrolled in the study. Their demographic details like name, age, sex, address were collected. Data regarding their current illness and indication for PICU admission were noted. Parents were enquired about any premorbid conditions like chronic respiratory illness, cardiac diseases (congenital and acquired), neurological illness (cerebral palsy, neurodegenerative diseases).

Indications for intubation were collected and classified into respiratory, cardiovascular and neurological conditions.

Patients were followed up for occurrence of pneumonia. During follow up, duration of coma (Glasgow coma scale $\leq$ 8), duration of nasogastric feeding, duration of administration of H_2 blockers were noted.

The number of times a patient is reintubated was noted. Reintubations following accidental extubation, extubations following endotracheal tube block or displacement or reintubation following a planned extubation were recorded.

Any patient developing pneumonia after 48 hours of intubation were considered as group 1.

Pneumonia was diagnosed by the criteria mentioned above. Blood was drawn for complete blood count and blood culture. Endotracheal aspirate (ETA) was collected from such cases.

Prior to endotracheal aspirate collection, the patient was preoxygenated with 100% oxygen. The heart rate and oxygen saturation were continuously monitored with a pulse oxymeter. The procedure was abandoned if saturation drops below 92%.

Under strict aseptic precautions, the suction catheter was inserted beyond carina and secrections were collected in a sterile mucus trap. The secretions within mucus trap were sent to microbiology lab immediately for analysis.

In the laboratory 0.001 mL of sample was directly inoculated on the chocolate agar and Mc Conkey's agar. Following overnight incubation at 37ºC, the media were examined for any growth. Infection was defined by a semi quantitative count of more than 100 cfu/ 0.001 mL, equivalent to 10^5 cfu/mL of ETA.The sensitivity pattern was studied by

Disc Diffusion method. Isolation of microorganism with a cfu of <100/0.001 mL was defined as colonisation.

The patients were followed up till 48 hrs of extubation or death.

Ventilated children who improve without pneumonia on follow up were considered as group 2.

The duration of ventilation, the duration of intubation (patients on T-piece ventilation) and duration of stay in PICU were recorded. The outcome was measured as death or recovery.

Statistical analysis

Data were collected in the proforma (Annexure 1). The categorical values were analysed using 'chi-square test' and relative risk was calculated. For continuous variables, mean of each variable in both groups were calculated and analysed using 'student t test'. The variables found to be significant in both groups were subjected to multiple logistic regression analysis to adjust for confounding effect and to identify the independent risk factors. P value < 0.05 was considered as significant.

OBSERVATIONS

A total of 96 children, who fulfilled the inclusion criteria were included in the study. 35 of them developed nosocomial pneumonia (Group 1) and 61 children did not develop pneumonia (Group 2).

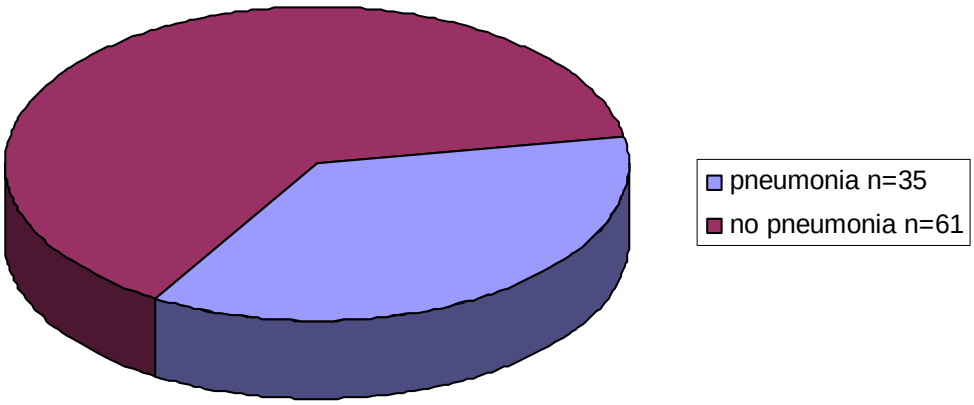

Fig 1. Incidence of nosocomial pneumonia among ventilated children.

Out of 96 children studied, 35 (36.4%) developed nosocomial pneumonia. The incidence of nosocomial pneumonia among ventilated children in the study population was 36.4%.

Among 35 children in group 1, 16 (45.7%) were less than 1 year, 15 (42.9%) were between 1 and 5 years and 4 (11.4%) were between 6 and 12 years. Among 61 children in group 2, 41 (67.2%) were less than 1

year, 9 (14.8%) were between 1 and 5 years and 11 (18%) were between 6 and 12 years.

Table 1. Etiological organisms isolated in endotracheal aspirate

ORGANISM	n = 35	%
Klebsiella	22	62.9%
Staphylococcus aureus	5	14.3%
E coli	3	8.6%
Pseudomonas	3	8.6%
Streptococci pneumoniae	2	5.7%

The most common organism isolated was Klebsiella (22 cases; 62.9%). Other isolates were Staphylococcus aureus (5 cases; 14.3%), E coli (3 cases; 8.6%), Pseudomonas (3 cases; 8.6%) and Streptococci pneumoniae (2 cases; 5.7%). Gram negative organisms were predominant among the isolates (80.1%).

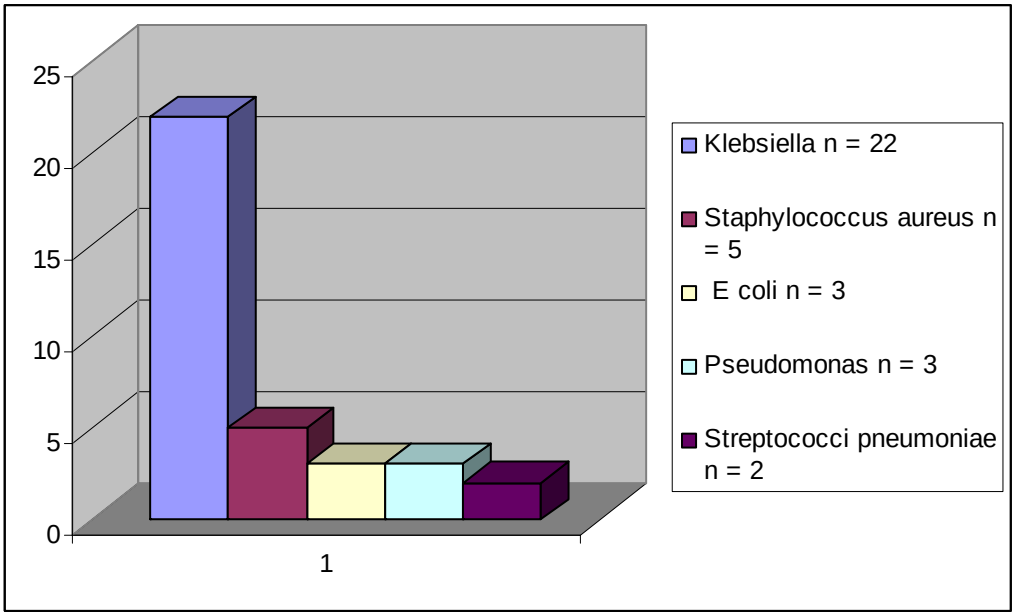

Fig 2. Etiological organisms isolated in endotracheal aspirate.

Table 2: Risk factors for nosocomial pneumonia among ventilated children (univariate analysis)

Risk factors	Pneumonia n (%)	No pneumonia n (%)	RR (95% CI)	P value
Sex M	19(54.2)	18 (29.5)	1.9 (1.1-3.1)	0.01
F	16 (45.7)	43 (70.4)		
Preexisting illnesses				
Resp Y	4 (11.4)	6 (9.8)	1.1 (0.3–3.8)	0.80
N	31 (88.5)	55 (90.2)		
Cardiac Y	2 (5.7)	2 (3.3)	1.7 (0.2–11.8)	0.56
N	33 (94.3)	59 (96.7)		
Y	4 (11.4)	8 (13.1)		

CNS N	31 (88.6)	53 (86.9)	0.8 (0.2–2.6)	0.81
Indication for intubation Y Resp N	8 (22.9) 27 (77.1)	18 (29.5) 43 (70.5)	0.7 (0.3–1.5)	0.48
Y Cardiac N	8 (22.9) 27 (77.1)	15 (24.6) 46 (75.4)	0.9 (0.4–1.9)	0.84
Y CNS N	19 (54.3) 16 (45.7)	28 (45.9) 33 (54.1)	1.1 (0.7 – 1.7)	0.42
Y Bloodstream infection N	14 (40) 21 (60)	22 (36) 39 (64)	1.1 (0.6 – 1.8)	0.70

$P < 0.05$ by chi-square test

Among children who developed NP 19, (54.2%) were male and 16 (45.7%) were female. In children who did not develop pneumonia, 18 (29.5%) were male and 43 (70.4%) were female. Males had 1.9 times more risk to develop NP than females. [RR (95% CI) = 1.9 (1.1 – 3.1) P = 0.01].

Pre existing respiratory, cardiac and neurological illnesses were not found to be significantly associated with NP. The current indication for intubation was studied in both groups and found to be not significant.

Concurrent bloodstream infection was present in 14 children (40%) in pneumonia group and in 22 children (36%) in no pneumonia group showed evidence of bloodstream infection. There difference observed among both groups was not significant.

Table 3

Risk factors	Pneumonia Mean ± SD	No pneumonia Mean ± SD	P value
Age in months	27.94 ± 25.0	26.61 ± 33.3	0.83
Reintubation (no. of times)	1.46 ± 1.12	0.41 ± 0.78	0.00
NG feeds (no. of days)	8.63 ± 3.62	4.20 ± 4.36	0.00
H2 blockers (no. of days)	5.09 ± 6.09	4.13 ± 3.53	0.95
Low GCS (no. of days)	7.83 ± 4.81	5.48 ± 5.62	0.04
Duration of intubation (no. of days)	13.0 ± 4.79	7.15 ± 5.08	0.00
Duration of ventilation (no. of days)	12.20 ± 5.09	6.79 ± 4.92	0.00

P <0.05 by student t test

The mean age in children developing pneumonia was 27.94 ± 25 months and those not developing pneumonia was 26.61 ± 33.3 months. There was no significant difference between two groups in terms of age.

Reintubation occurred more frequently in pneumonia group (mean 1.46 ± 1.12 times) when compared to no pneumonia group

(mean 0.41 ± 0.78 times). This difference was statistically significant (P = 0.00).

Nasogastric tube feeding was given for a mean duration of 8.63 ± 3.62 days in pneumonia group and 4.20 ± 4.36 days in no pneumonia group. This difference was statistically significant and hence prolonged duration of nasogastric feeding was associated with developing pneumonia in ventilated children.

The mean duration of administration of H2 blockers was 5.09 ± 6.09 days and 4.13 ± 3.53 days among pneumonia and no pneumonia groups respectively. This difference was not statistically significant.

Children who developed pneumonia had Glasgow Coma Scale (GCS) ≤ 8 for 7.83 ± 4.81 days whereas those who did not develop pneumonia for 5.48± 5.62 days. There was statistically significant difference among both groups (P = 0.04) suggesting that GCS ≤ 8 is associated with developing pneumonia.

The mean duration of ventilation and intubation was 12.2 ± 5.09 days and 13 ± 4.79 days respectively in pneumonia group and 6.79 ± 4.92 days and 7.15 ± 5.08 days respectively in no pneumonia group which was

statistically significant (P = 0.00). Patients with NP had longer duration of ventilation and intubation.

Table 4: Multivariate analysis of significant risk factors

Risk factors	OR (95% CI)	P value
Sex	2.27 (0.69 – 7.42)	0.17
NG feeding	1.12 (0.83 –1.53)	0.43
Low GCS	1.06 (0.87 – 1.31)	0.53
Reintubation	0.31 (0.15 – 0.66)	0.02
Duration of intubation	0.73 (0.35 – 1.51)	0.39
Duration of ventilation	0.96 (0.49 – 1.87)	0.91

The following risk factors were significantly associated with NP by univariate analysis: male sex, long duration of nasogastric feeding, prolonged duration of low GCS, increased frequency of reintubation, longer duration of intubation and ventilation. These factors were subjected to multivariate analysis. On multiple logistic regression analysis only reintubation was found to be significant risk factor for developing NP in ventilated patients.

Outcome in patients with nosocomial pneumonia

Table 5: Comparison of mortality among children with and without nosocomial pneumonia.

	Pneumonia n (%)	No pneumonia n (%)	RR (95% CI)	P value
Death	20 (57.1)	19 (31.1)	1.8 (1.1 – 2.9)	0.01

57.1% of children who developed NP died. But only 31.1% of children without NP died. This difference was statistically significant. [RR (95% CI) = 1.8 (1.1 – 2.9) P = 0.01). The risk for death was 1.8 times higher for children who developed nosocomial pneumonia.

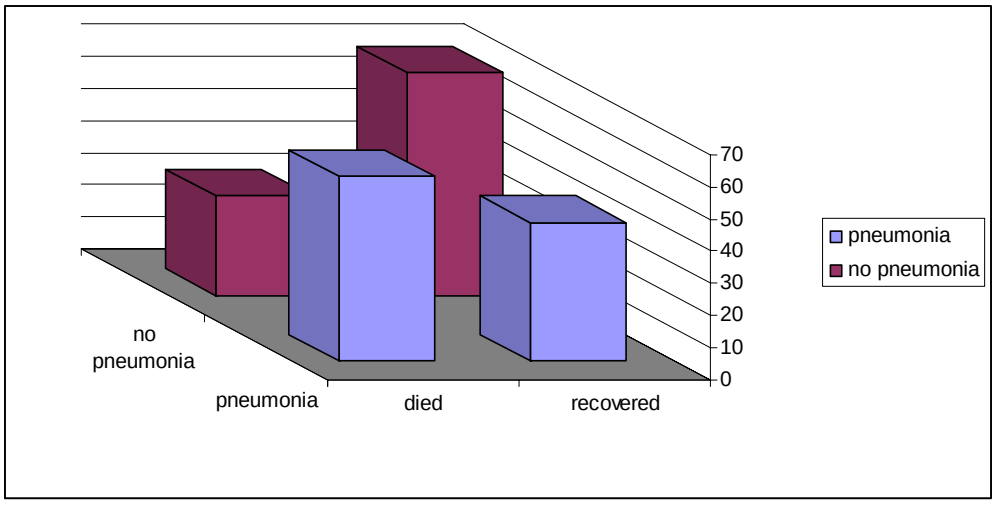

Fig 3. Comparison of outcome among two groups

Table 6: Comparison of duration of stay in PICU among the two groups

	Pneumonia	**No pneumonia**	**P value**
Duration of stay in PICU (mean ± SD) days	15.2 ± 5.5	9.6 ± 6.0	0.00

Children who developed NP stayed in PICU for a mean of 15.2 ± 5.5 days whereas those who did not develop NP stayed for a mean of 9.6 ± 6 days. Thus children with NP stayed a significantly (P = 0.00) longer duration in our PICU.

Table 7: Early VS late onset pneumonia

	n = 35	**%**
Early onset pneumonia	19	54.3%
Late onset pneumonia	16	45.7%

Out of 35 children who developed pneumonia, 19 children (54.3%) had early onset pneumonia (≤ 4 days) and 16 children (45.7%) had late onset pneumonia (≥ 5 days).

Table 8: Etiological organisms in early and late onset pneumonia

ORGANISM	EARLY ONSET PNEUMONIA n (%)	LATE ONSET PNEUMONIA n (%)
Klebsiella	13 (68.4)	9 (56.2)
Staphylococcus aureus	2 (10.5)	3 (18.2)
E coli	3 (15.7)	0 (0)
Pseudomonas	0 (0)	3 (18.7)
Streptococci pneumoniae	1 (5.2)	1 (6.2)
Total	19	16

Klebsiella was the predominant organism isolated in both early onset (13 cases) and late onset pneumonia (9 cases). E coli was isolated only in early onset pneumonia. Similarly pseudomonas was isolated only in late onset pneumonia. The predominance of gram negative organisms was encountered in both groups.

Table 9: Comparison of mortality among early and late onset pneumonia

	Early onset pneumonia n (%)	Late onset pneumonia n (%)	RR (95% CI)	P value
Died	8 (42.1)	12 (75.0)	0.5 (0.3 – 1.0)	0.05

42.1% of children with early onset pneumonia died when compared to 75% of children with late onset pneumonia. This difference was however not statistically significant (P = 0.05).

DISCUSSION

The incidence of nosocomial pneumonia among ventilated children in this study population was 36.4%. This may not reflect the true incidence in the PICU as children with preexisting pneumonia were excluded in this study.

Other Indian studies also had reported a similar higher incidence. Patra PK,et al[6] from Chandigargh had quoted an incidence of 30.5%. Tullu MS,et al[7] from Mumbai had reported an incidence of 27.54%. However studies from western countries reported a very lower incidence.

In their study by Elward AM, et al[55] from Washington, the incidence was just 5.1%. Almuneef, et al[57] from Riyadh, Saudi Arabia found out an incidence of 10.2% in their PICU.

Among the etiological organisms isolated, gram negative organisms were predominant. Klebsiella was the most predominant isolate in endotracheal aspirates, followed by Staphylococcus aureus, E coli. Pseudomonas and Streptococci pneumoniae. The microbiological flora associated with nosocomial pneumonia reflects the common organisms present in gut, oropharynx and environment. The colonisation of oropharynx by gram negative organisms from gut and then causing nosocomial pneumonia had been explained by Kervez AJ, et al[13] and Atherton ST, et al[22].

In the study by Tullu MS, et al[7], gram negative enterobacter organisms were predominant viz E coli in 34.4% and Klebsiella in 30.2%. Acinetobacter was the predominant isolate in the study by Patra PK, et al[6]. This was not isolated in our study population. This may be also due to the difference in organisms prevalent in each ICU.

Pseudomonas is mostly a nosocomial pathogen and this was isolated only in late onset pneumonia in this study. This correlates with the hypothesis that late onset pneumonia is usually acquired by nosocomial pathogens and early onset pneumonia by community acquired pathogens. In this study, Pseudomonas was isolated only in late onset pneumonia, concurring with the hypothesis. In contrary, Ibrahim, et al[58] in their study reported that this distinction did not hold true in an ICU setting and organisms in both groups were similar.

Risk factors for nosocomial pneumonia in ventilated children.

The mean age group was found to be similar in both pneumonia and no pneumonia groups. Age was studied as a risk factor by many authors but none found it as a risk factor[6,7,55]. Similarly age was not found to be a significant risk factor for nosocomial pneumonia in ventilated children in this study also.

Males had 1.9 times increased risk than females for developing nosocomial pneumonia in this study. In this study, sex was a significant risk factor in univariate analysis but not in multivariate analysis. This might be probably due to unequal distribution of sex among both groups.

Kollef, et al[63] from Washington found that male gender is a significant risk factor in his study. But in studies by many others[6,7,55], this was not a significant risk factor.

Previous respiratory and cardiac illnesses may lead to lower respiratory infections due to parenchymal changes or pulmonary congestion. Neurological illnesses may predispose to recurrent aspirations. But previous significant illnesses were not significantly associated with pneumonia in this study. In the study by Tullu MS, et al[7], even immunodeficiency including HIV infection, was not associated with pneumonia.

Also the various indications for intubation were not influencing the development of pneumonia.

Co existing septicemia was noted only in 40% of children with pneumonia and 36% of children without pneumonia.

Thus the absence of association of previous illnesses and co existing sepsis with development of pneumonia, suggest that the pathophysiology of nosocomial pneumonia is predominantly aspiration of gastric and pharyngeal secretions.

Reintubation was identified as the only significant independent risk factor for nosocomial pneumonia in multiple logistic regression analysis. During every attempt of intubation, there is a risk of aspiration of subglottic and oropharyngeal secretions. This predisposes to colonisation and subsequently infection of respiratory tract.

A similar conclusion was made by Patra PK, et al[6] from their study in Chandigarh. Reintubation and prolonged duration of ventilation was found to be significant risk factors in univariate analysis. Only reintubation was a significant risk factor in logistic regression analysis.

Torres, et al[59] had analysed separately the role of reintubation in nosocomial pneumonia. They found that reintubation was a significant risk factor after adjusting for age, sex and prio bronchoscopy. Studies by Ibrahim, et al[58], Kollef, et al[63] and Rajasekhar, et al[68] had come up with similar results.

Prolonged duration of nasogastric feeding was found to be a significant risk factor for nosocomial pneumonia in the present study. This may be probably due to increased chances of aspiration of gastric contents during enteral feeding. Bonten MJ, et al[62] had found that there is slight increase in intragastric pH during enteral feeding and this leads to colonisation of stomach with gram negative bacteria. Almuneef, et al[57] had found that continuous enteral feeding was an independent risk factor for developing nosocomial pneumonia. Hence enteral feeds can also increase the risk of nosocomial pneumonia.

H_2 blockers increase the gastric pH and this was thought to promote colonisation of stomach with organisms. On aspiration, this may predispose to pneumonia. It has been observed in this study that H_2 blockers administration was not a significant risk factor for nosocomial pneumonia in ventilated children. Yildizdas, et al[43] in their study found no difference in the incidence and mortality in patients developing ventilator associated pneumonia being treated with ranitidine, omeprazole, or sucralfate, and nontreated patients. Patra PK, et al[6] also found that H_2 blockers were not increasing the risk of nosocomial pneumonia in intubated children. But a study by Ibrahim, et al[58] found a statistically significant association of H_2 blockers with ventilator associated pneumonia. But the study subjects were adults whereas other

two authors studied in pediatric population. Hence H_2 blockers were not a significant risk factor for nosocomial pneumonia especially in pediatric population.

Altered mental status with Glasgow Coma Scale (GCS) ≤ 8 was found to be a significant risk factor in this study. Draculovic, et al[61] in their study found that GCS < 9 as a risk factor for nosocomial pneumonia. GCS ≤ 8 is a critically low GCS below which airway reflexes are impaired.

George DL, et al[70] had suggested that an altered mental status or depressed level of consciousness with impaired airway reflexes predisposes the patient to aspiration of gastric or oropharyngeal secretions leading to pneumonia.

Longer the duration of intubation and ventilation, higher the risk of nosocomial pneumonia. This risk factor was significantly associated with pneumonia in studies by Patra PK, et al[6], Elward AM, et al[55] and Tullu MS, et al[7].

On univariate analysis, risk factors viz. male sex, frequent reintubations, longer duration of nasogastric feeding, prolonged duration of low GCS, longer duration of intubation and ventilation were found to

be significant. When adjusting for confounding effects of factors over each other, only reintubation was found to be significant. Patra PK, et al[6] study also found that duration of ventilation and reintubation were significant risk factors. But reintubation was the only independent risk factor. The study by Elward AM, et al[55] analysed multiple risk factors but reintubation, transfusion and transport out of PICU were independent risk factors. The duration of ventilation was not an independent risk factor in many studies. This may be because aspiration could be the prime cause for development of pneumonia and it is commonly seen during reintubations.

The patients with nosocomial pneumonia were higher risk of death and longer duration of stay in PICU than those who survived. Children with pneumonia were 1.8 times more likely to die than those who did not had nosocomial pneumonia following intubation. Heyland DK, et al[64] found that absolute risk of death increased by 5.8% in patients developing ventilator associated pneumonia.

Among those who survived, the stay in PICU was significantly longer than who survived without pneumonia. This increases the burden on health care system by increasing health expenditure.

SUMMARY

The incidence of nosocomial pneumonia in this study was 36.4%. There was a predominance of gram negative organisms in endotracheal aspirates in our study. Klebsiella was the organism isolated in 62.9% cases. Pseudomonas was isolated only in late onset pneumonia cases.

Age was not a significant risk factor for pneumonia in ventilated children. Males had 1.9 times higher risk of developing nosocomial pneumonia among ventilated children. Comorbid illnesses did not increase the risk of nosocomial pneumonia. Bloodstream infections did not influence the occurrence of pneumonia in ventilated children. Nasogastric feeding and GCS $\leq$ 8 were also risk factors for nosocomial pneumonia as they had the similar risk of aspiration. H_2 blockers were not a significant risk factor for nosocomial pneumonia. Patients who developed pneumonia had a significantly longer duration of intubation and ventilation. Reintubation emerged as an independent risk factor for nosocomial pneumonia among ventilated patients.

Mortality was higher in children who developed pneumonia and this difference was statistically significant. There was no significant difference in mortality in early and late onset pneumonia. The duration of stay in PICU was significantly longer in children developing nosocomial pneumonia following ventilation.

CONCLUSION

- The incidence of nosocomial pneumonia among ventilated children was 36.4% in the study population.
- Gram negative bacteria especially Klebsiella was the predominant organism.
- Reintubation was the most significant independent risk factor for developing nosocomial pneumonia in ventilated children.
- Mortality was more than 50% in children with nosocomial pneumonia.
- Reduction in the frequency of reintubation can reduce the incidence of nosocomial pneumonia in intubated children.
- Adequate sedation and analgesia can prevent accidental extubations and thereby reducing the need for reintubation.

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ANNEXURE

DATA ENTRY FORM

Name

Age

Sex

Address

Date and time of admission in hospital

Date and time of admission in PICU

Date and time of endotracheal intubation

Diagnosis

Preexisting illness

- Respiratory illness yes/no
- Heart disease yes/no
- Neurological illnesses yes/no

Indication for intubation

- Respiratory yes/no
- Cardiac yes/no
- CNS yes/no

On follow up

DAYS OF FOLLOW UP

Day of intubation					
Reintubation					
NG feeding					
GCS ≤ 8					
H2 blockers					
Day of extubation					
Died on/ transferred out of PICU					

Blood stream infections yes/no

Pneumonia yes/no

In patients developing pneumonia

Day of onset of pneumonia

Endotracheal aspirate Semiquantitative culture

Antibiotic sensitivity

Outcome

Death

Recovery

Duration of assisted ventilation

Duration of endotracheal intubation

Duration of stay in PICU

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Certificate

The dissertation committee for 2007, Institute of Child health and Hospital for Children, Madras Medical College, Chennai comprising of the following members has granted permission to MD postgraduate Dr.R.Arunkumar to proceed with his study titled **"A study of nosocomial pneumonia among ventilated children in PICU – incidence, etiologic agents, risk factors and outcome"** after carefully scrutinizing his study proposal with special reference to ethical standards, methodology and relevance. His study proposal was approved on 27.9.2007

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