Clinical and Microbiological Profile of Nosocomial Infections in the Pediatric Intensive Care Unit (PICU)

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This study was conducted in PICU of a teaching hospital to estimate the incidence of nosocomial infections, establish the clinical and bacteriological profile and identify probable exogenous source from the environment and personnel. 95 suspected cases of nosocomial infections were studied prospectively, identified as per the guidelines laid down by CDC. The rate of nosocomial infections was 27.3% with an incidence of 16.2 per 100 patient days. The incidence of urinary, respiratory and intravascular catheter related infections was 56.52%, 34.78%, 10.52% respectively. Klebsiella (33.33%) was the most common isolate with maximum sensitivity to amikacin. During the study, an outbreak of MRSA nosocomial infection was encountered and the source was traced to portable suction pump. The risk of nosocomial infection was directly related to the duration of stay in the PICU and duration of placement of indwelling catheters /tubes.

Key words: *Nosocomial, PICU.*

Nosocomial infections (NI) are those that are acquired in a hospital setting. The Centre for Disease Control and Prevention (CDC) defines ICU associated infections as those that occur after 48 hours of ICU admission or within 48 hours after transfer from an ICU(1). Each nosocomial infection adds 5-10 days to the affected patient's time in the hospital. Nosocomial infections have increased the morbidity and mortality of hospitalised patients and especially the ones admitted in an intensive care setup. In addition these infections lead to extra hospital stay and expenditure thus overburdening the already strained health economy. In studies conducted by various authors, the incidence of nosocomial infections ranged from 2.8% to 21.6%(2-7).

We conducted this study to estimate the incidence of nosocomial infections in the PICU of a teaching hospital, to identify the common sites of infections, to identify the common bacteria, their biotypes and antibiotic sensitivity patterns and to identify the probable exogenous source from the environment and personnel leading to such infections.

Subjects and Methods

This study was carried out in the PICU of a large teaching hospital of Mumbai over a one year period. Our hospital caters to patients from very low socio-economic status. It is a 1300 bedded hospital with 90 beds allotted to pediatric patients. The PICU is six bedded. Being a small PICU patient turnover is very rapid and only very critically sick children get admitted to this ICU.

Patients were suspected to have developed nosocomial infections after 48 hours of

admission to the PICU if they had (*i*) unexplained fever >38ºC, leukocytosis >10000/mm^3; (*ii*) new infiltrates on chest *X*-ray, persistent tracheal aspirates or secretions; (*iii*) turbid urine, suprapubic tenderness, dysuria, burning micturition; (*iv*) thrombophlebitis; or cloudy effluent containing more than 100 polymorphonuclear cells/mm^3, abdominal pain or tenderness or microorganisms in peritoneal dialysis fluid. Those having fever prior to admission to the PICU, or any other clinical features of infection secondarily acquired in the wards prior to transfer to the PICU were excluded.

Relative frequencies of known risk factors like age, anemia, malnutrition, severity of disease and duration of PICU stay were studied in patients who developed nosocomial infections. Each patient was evaluated for HIV status (after a pretest counseling with a well informed consent from the parents/ guardian) and other immunosuppressive drugs (steroids, anticancer drugs *etc.*) to find a correlation between nosocomial infections and immune status of the patients. Detailed clinical examination of all patients taken up for the study was done on a daily basis (Boston city method which has a sensitivity of 100%)(8). Routine laboratory investigations done included CBC, blood sugar, *X*-ray chest, RFT, LFT, and urine examination.

Specific site related investigations included the following:

- Blood culture at the time of admission to rule out an already existing infection and as and when patient developed clinical features suggestive of an infection.
- CVP or intravenous catheter tips were cultured in those with suspected thrombophlebitis along with simultaneous blood culture from a site different from the site of IV catheter after preparing the site with 70% alcohol and 1% betadine.
- Urine and tips of indwelling catheters were cultured simultaneously in patients with suspected urinary tract infections.
- Pleural fluid and ICD tips were also cultured.
- Tracheostomy tube (TT) tips along with TT aspirate.
- Gastric lavage,sputum samples or tips of endotracheal tubes (ET) or swabs taken from the tips of endotracheal suction catheter along with the tip of ETs were cultured.

After removal under full aseptic precautions, the tip of each catheter was cut using a sterile blade and the tip was sent to microbiology laboratory in a sterile tube for bacterial culture. Standard CDC criteria 1988 were used to differentiate colonization from infection(9). The same criteria were also used to define nosocomial respiratory, urinary and catheter related infections.

Catheter associated infection (CAI) was defined as a semiquantitative culture yielding 15 cfu or more in the presence of positive blood culture. Bacteriological culture and antibiotic sensitivity was done using standard microbiological methods.

Environmental sampling was done on a monthly basis from floor and walls of the PICU, bed and linen, disinfectants, hand swabs of personnel - doctors, nurses, patient's relative and aayabais, gowns and masks, stethoscopes, air sampling, cots, taps and basins, IV fluids, AMBU bags, ventilator tubings, cradles, suction pumps and oxygen catheters.

For each type of catheter related infection, different risk factors were studied *e.g.*, type and duration of the catheter in situ, duration and indication of mechanical ventilation, *etc*.

Statistical significance was calculated by the Chi square method and standard error of proportion. The probable 'p' value was obtained using standard Chi square charts.

In one of the months during our study, we had an outbreak of MRSA nosocomial septicemia. Isolates were sent to Maulana Azad Medical College, New Delhi for phage typing. The phage typing of isolates from the patients and inanimate objects was then compared and an attempt was made to trace back the source of this outbreak.

Results

In this one year period, a total of 347 patients were admitted to the PICU. Of these, 27.3% (95/347) had clinically suspected nosocomial infection. The incidence of nosocomial infections per 100 patient days was found to be 16.2.

Maximum patients (n = 31) were less than 1 month old (32.63%) followed by patients between one month to one year (n = 23). The mean age of patients in the study group was 3.83 years. Male : female ratio was 3 : 2. All patients belonged to low socio-economic status and had a mean hemoglobin of 8.8 g/dL.

Out of 42 malnourished patients, 64.2% developed nosocomial infection while 52.8% of normally nourished developed NI ($P < 0.05$). Maximum patients who developed NI were in grade IV malnutrition of IAP classification (n = 19). Out of 51 patients with some sort of altered immune status, (HIV positive - 12, prolonged steroids - 3, grade IV PEM - 36) 64.7% developed NI which was

TABLE I–*Microbiological Growth from Samples Analysed from Different Sites of Infection.*

Sample	Growth obtained / Total No. sent	Percentage
Blood cultures	16/95	16.8
Peripheral lines	37/95	38.9
CVP line	4/8	50
Urine	13/31	31.9
Foley's catheter	16/23	69.6
ET/TT aspirate	7/21	33.3
Pleural fluid	1/2	50
Endotracheal tube	7/9	77.8
Tracheostomy tube	10/12	83.3
Intercostal drain tube	2/2	100
Peritoneal fluid	3/4	75
PD catheter tip	4/4	100
Total	120/298	40.3

TABLE II–*List of Organisms Isolated from Nosocomial Infections According to Sites of Infections.*

Organism	IVC	UTI	RTI	PD Fluid	Total
Klebsiella	11	15	11	3	40
E. coli	4	10	7	2	20
Pseudomonas	10	2	4	–	19
Staph. aureus	12	–	1	–	13
CONS	10	–	2	–	12
Acinetobacter spp.	3	–	2	2	7
Candida albicans	2	2	–	–	4
Non pigmented Serratia sp.	1	–	–	–	1

statistically significant (P <0.05). 82.10% of patients developed nosocomial infections after 96 hours of stay in the PICU, thus proving that longer the stay in the PICU higher is the risk of NI (P <0.05).

We used PRISM-I as the severity of illness index. Of the 95 patients with nosocomial infections, 55 patients (57.5%) had PRISM-I more than 10 (mean 18.7) *i.e*., they were critically sick. Remaining 40 patients had PRISM-I less than 10 (mean 6.6). Major problems included respiratory failure (12), shock (8), bronchiolitis (5), snake bite (2), tetanus (5), renal failure (6), congenital heart disease (5), rheumatic heart disease (4), very severe pneumonia (6), aspiration pneumonia(3), poisoning (3), LGBS (5), spinal muscular atrophy (3), arrhythmia (3), DKA(4), pyogenic meningitis (3), TBM (4), Hepatic encephalopathy (2), and empyema (3).

A total of 298 samples were analyzed. Samples sent were blood cultures, peripheral lines, CVP lines, urine, Foley's catheters, ET/TT aspirates, Pleural fluid, ET/TT ICD, PD fluid and PD catheter tips. One hundred and twenty samples (40.26%) showed growth as shown in *Table I.* Klebsiella was the most common pathogen (33.3%) followed by *E. coli* in 16.7% (*Table II*). Amongst the catheter related infections, UTI was most common infection (56.52%) followed by RTI (34.78%) and IV catheter related infections (10.52%). Three patients had both pneumonia as well as probable catheter associated bacteremia (PCAB) while none of the patients had combination of pneumonia and UTI or pneumonia, UTI and IV catheter associated bacteremia. One patient had UTI as well as catheter associated infection (CAI).

Exogenous source from the environment: Out of 160 samples, we isolated 60 organisms (29.83%). CONS was the most common organism (n = 28) followed by *S. aureus* (n = 10), *Acinetobacter* (n = 6), *Klebsiella* (n = 4), *Pseudomonas* (n = 4), and *Enterococci* (n = 2).

Mortality: Of the 95 patients, 29 (30.5%) expired. Of these, 82.4% had a PICU stay of more than 7 days. In UTI the mortality was 52.1% while in LRTI and blood stream infections the mortality was 40% each. Of the 29 patients who expired, seven had *Klebsiella*, *Pseudomonas* (7), MRSA (4), *Staph. aureus* (5), CONS (4), *E. coli* (1), and *Candida* (1).

Of the 95 catheter tips, 43.1% showed IV catheter related infection and only 10.5% (n = 10) showed definite catheter related bacteremia. Average duration of intravenous (IV) cannula being *in situ* was 3.2 days. Type of catheter whether peripheral or central was not found to be significant in influencing the incidence of NI in our study. Maximum colonization (32.63%) as well as definite bacteremia (60%) took place after the catheter was left *in situ* for more than 72 hours, the result being statistically significant (P = 0.031). *Staphylococcus aureus*, coagulase negative *staphylococci, Klebsiella* and *Pseudomonas* were the dominant isolates.

Nosocomial pneumonias: Out of 30 suspected cases of nosocomial pneumonia 23 had some form of respiratory invasive device (endo-tracheal tube/tracheostomy tube/intercostal drain tube). 80.9% of the ET/TT showed growth, 7 isolates corresponded to the growth on TT/ET aspirates. Thus, these 7 patients had proven nosocomial pneumonia, an incidence of 33.3%.

Out of 21 patients with ET/TT, 15 patients were on a ventilator. Average days of intubation was 3.7 days with an average duration of change of ET being 5 days. Of these 15 mechanically ventilated patients,

TABLE III –*AST Pattern of E. coli and Klebsiella.*

Antibiotic	*E. coli* (n = 20)				*Klebsiella* (n = 40)			
	S		R		S		R	
	n	%	n	%	n	%	n	%
Amoxyclav	6	30	14	70	16	40	24	60
Cefotaxime	4	20	16	80	13	32.5	27	67.5
Certiaxone	5	25	15	75	12	30	28	70
Chloramphenicol	0	20	2	80	3	7.5	37	92.5
Amikacin	11	55	9	45	15	37.5	25	62.5
Ciprofloxacin	0	0	20	100	13	32.5	27	67.5

S - Sensitive; R - Resistant.

6 developed pneumonia *i.e.*, 40% as opposed to 1 in non ventilated patients (P = 0.045). It was also seen that maximum patients (83%) developed Ventilator Associated Pneumonia (VAP) after being ventilated for more than 96 hours (P <0.01). Average duration of mechanical ventilation was 8.4 days. Of the 10 patients ventilated for a respiratory cause, 50% developed VAP as opposed to only 20% in patients ventilated for non-respiratory cause. (GBS, polio, tetanus, *etc.*) (P = 0.031). Incidence of nosocomial pneumonia in non-ventilated patients but with ET/TT *in situ* was 16.7%. *Klebsiella* species was the predominant isolate sensitive to amikacin.

Nosocomial Urinary Tract Infections: Of the 31 suspected cases of UTI, 23 had an indwelling urinary catheter with an average duration of catheterization being 5.8 days. 81.2% of the patients with Foley's catheter had the same growth on the catheter tip as urine. Only 18.8% of Foley's catheters were merely colonized without bacteriuria. Maximum patients developed UTI after the indwelling catheter was left in situ for more than 5 days. *Klebsiella* species (51.7%) was the predominant isolate in these infections.

We had four patients on peritoneal dialysis of which three developed peritonitis (75%) with same organism from PD catheter tip as well as PD fluid. We had two patients on ICD one of which showed same growth on ICD tip and pleural fluid.

Antibiotic sensitivity patterns

We attempted to correlate the organisms isolated with the antibiotic sensitivity pattern so as to formulate antibiotic protocols.

Both *Klebsiella* and *E. coli* were most sensitive to amikacin (*Table III*). It was found that *S. aureus* was most sensitive to vancomycin (100%) and amoxyclav (76%) whereas CONS was found to be sensitive to amoxyclav (75%). *Pseudomonas* had maximum sensitivity to ticarcillin (52.6%) followed by amikacin and ciprofloxacin (47.3% each).

Outbreak of Nosocomial MRSA infection

In one of the months during our study, 10 patients developed septicemia with 4 of them having methicillin resistant *Staph. aureus* (MRSA) and the same antibiotic susceptibility pattern thus giving rise to an outbreak of MRSA septicemia. An environmental surveliance was immediately instituted after

Key Messages

- Nosocomial infections are an important preventable cause of increased morbidity and mortality in hospitalized patients.
- Nosocomial infections increase with the use of invasive device and with increased duration of hospitalization.

informing the hospital infection control committee. MRSA was isolated from the air settle plates, suction pump (portable), wash basin and ventilator surfaces, however the phage typing sent to Maulana Azad Medical College, Delhi showed the correlation only with the isolates from the portable suction pump and air settle plates. Thus the source of the outbreak of nosocomial infection was traced to the portable suction pump. PICU was shut down for fumigation and reopened after the post fumigation swabs showed no growth.

Discussion

Nosocomial infections are a significant problem in the delivery of intensive care services. The incidence of nosocomial infections varies in different PICUs. In our study the incidence was higher because of a different clinical profile of our patients and a different PICU setting. Our patients belonged to a lower socio-economic status. Males out numbered the females as shown by Freeman (10) and Ganguly(11). Cell mediated immunity is greatly suppressed in mal-nourished children which predisposes these children to NI. Malnourished children had a higher incidence of NI which corroborated with the study by Isaack, *et al.*(12). Children with HIV, prolonged steroid treatment have significantly reduced immunity which is a major risk factor for acquisition of nosocomial infections.This factor was corroborated by Donowitz, *et al.*(13).

Most of the patients developed NI after 96 hours of stay in PICU. This could be explained by the fact that longer the stay, greater is the contact of the patient with the health care personnel, often in a crisis situation, greater exposure to environmental microorganisms and more frequent are the invasive procedures. This observation was in accordance with the study done by Delagado, *et al.*(14) and Singh, *et al.*(15) who had shown the mean duration of stay to be longer in patients with NI (9.8 *vs* 1.8 days).

Percentage of microbial isolation is different in various studies. In a study by Singh, *et al.*(15), percentage of isolates was 60.6 (as compared to 40.3% in our study). Etiological agents depend upon the prevailing local flora in the ICU. *Klebsiella* as the most common organism was also isolated in a study by Yinnon, *et al.*(16) and Drews, *et al.*(17).

Presence of an indwelling catheter is an important risk factor for nosocomial infections. Our study did not show any significant difference in the incidence of catheter related infections due to the use of central or peripheral catheters which was in contrast to the study of Darbyshire, *et al.*(18), Narendaran, *et al.*(19) and Archibald, *et al.*(20). Duration of catheterization was found to be an important risk factor for vascular access infections as shown by Tacconelli, *et al.*(21).

Pneumonias developing after intubation (with or without ventilation) or tracheostomy

is well known despite meticulous care of the same. Ventilated patients developed nosocomial infections more common than the non ventilated patients and especially if ventilation was instituted for a respiratory cause. The incidence of Ventilator Associated Pneumonia (VAP) increased with the duration of ventilation as also shown by Tullu, *et al.*(22) and Langer, *et al.*(23). During suction procedures and mechanical ventilation the infectious particles lodged within the tracheal tubes can get dislodged into distal airways causing VAP. All patients who developed nosocomial pneumonia had ET/TT colonized. Thus, the risk of nosocomial pneumonia increases if ET/TT is colonized. Prior respiratory disorders may put the patients at a higher risk as there is a greater chance of airway colonization by gram negative bacilli in these patients and compounding factors like impairment of mucosal clearance and loss of mucosal integrity also exists. Our study corroborated this fact as proven by Salata, *et al.*(24) and Schaberg, *et al.*(25).

Micro-organisms can enter the bladder either during the procedure of catheterization or migration between the external catheter surface and the urethral epithelium(26). Infection was more when the catheter was left in situ for more than 5 days as also shown by Kunin and McCormack, *et al.*(27).

Mortality in patients in ICU strongly co-relate with nosocomial infections. 68.7% of the 29 patients who expired were critically ill with shock, hemodynamic instability etc. Thus, the underlying condition rather than NI could have been responsible for these deaths. Tullu, *et al.*(22) reports this morality to be 20% while CDC(6) gives the mortality figures as 13%. The increased mortality in our study was probably due to the fact that very critically sick children got admitted to the PICU with an increased duration of hospitalization and associated malnutrition, anemia and low socio economic status further added to the critical illness. The mortality was found to be higher in patients who had a longer PICU stay, a fact corroborated by Bruno Cavanillas, *et al*(.28).

The aerosols produced during suctioning by the contaminated suction pump tubing could probably explain the presence of MRSA in the air which was responsible for the outbreak of MRSA sepsis in PICU.

Thus our study helped us to have an insight into the incidence of nosocomial infections and we were able to institute various interventional strategies to decrease the occurrence of these infections. The challenges for the future are to minimize infection in the PICU while limiting the emergence of antibiotic resistant organisms with optimal cost effective care. There is an urgent need for clinical studies like ours to evaluate strategies for the prevention and management of such infections in critically ill patients.

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Safety Profile of Ciprofloxacin used for Neonatal Septicemia

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We conducted a case matched control study to observe the adverse effects of ciprofloxacin used in neonatal septicemia We enrolled 30 neonates with multidrug-resistant septicemia who were treated with intravenous ciprofloxacin for 14 days. Thirty matched neonates with septicemia treated with other antibiotics were enrolled as controls There was no difference in the mean serum electrolytes, hepatic, renal and hematologic parameters of the two groups. Serial ultrasonographic measurements of the cartilage of the knee after 1 and 6 months showed no difference in the two groups. The femoral cartilage showed an increase of 78.8% in the mean longitudinal area after 6 months in the study group. In the control group, the femoral cartilage showed a 78.4% increase after 6 months. Similarly, the tibial cartilage showed no difference in the percentage increase in size of the study and control group at the end of 6 months. When controlled for birth weight and gestation, cartilage size was not affected by ciprofloxacin.

Key words: *Arthropathy, Ciprofloxacin, Newborn.*

Ciprofloxacin is an antibacterial agent with a broad spectrum of activity, effective against various pathogens like *Pseudomonas aeruginosa* and *Klebsiella pneumoniae.* Notwithstanding its immense potential as a "life saving" drug, its use is restricted in neonates and children due to its adverse effects, especially on the joints and growing cartilage(1).

Septicemia is one of the commonest causes of mortality in the Neonatal Intensive Care Units (NICU) in India(2) and multidrug resistant *Klebsiella pneumoniae* is the commonest offending bacterial agent.