Original Research Article

Study of organisms causing healthcare associated infection in paediatric intensive care unit and their antibiotic susceptibility

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Abstract

Background: In Pediatric intensive care unit (PICUs), patients are often subjected to various invasive procedures, pumped with antibiotics. Therefore, the incidence of HAI related to mechanical ventilation, catheter insertion and some invasive procedures in PICUs are increasing. **Aim:** To determine the HAI rate in PICUs, causative organisms of HAIs and their antibiotic susceptibility profile. **Material and Methods:** A total of 200 children of age group 1month to 13 years admitted in PICUs who did not have any sign of infection at admission and remained hospitalised for at least 48 hrs were included. Investigations including microbiological culture and sensitivity were done on samples collected from the patient. **Results:** The incidence of HAI was 31.5%, excluding CONS (31/200) incidence of HAI was 15.5%. The most common causative microorganism was Klebsiella 6/39(15.4%) followed by, Pseudomonas aeruginosa (15.4%), E. coli 5/8 (62.5%), Coagulase negative Staphylococci [CONS] (51.3%). Common sites of HAI were mechanical ventilation (62%) and central line associated blood stream infection (15.8%). **Conclusion:** The incidence rate of HAI was 21.5% in our study and the common microorganisms isolated were E. coli, Klebsiella spp., Pseudomonas and MRSA. Common sites of HAI were mechanical ventilation (62%) and central line associated blood stream infection (15.8%).
Key Words: Paediatric intensive care unit, hospital acquired infection, Microbiological profile, resistance pattern

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INTRODUCTION

Healthcare associated infections (HAIs) in the Paediatric Intensive Care Units (PICUs) are a major clinico-managerial problem resulting in prolonged length of hospital stay, increased medical costs and increased morbidity and mortality.[1-6] Only a few studies, based on prospective, patient-based surveillance have estimated the burden of HAI in the paediatric age group.[7-10] In PICUs, patients are often subjected to various invasive procedures, pumped with antibiotics which alter their normal flora and at times inadvertently virulent organisms are transferred from one patient to another. Despite having a prominent role in the care of patients with infections, PICUs cause some complications and death, and increases the costs imposed on patients and society.[11] The overall incidence of nosocomial infections is 6.1% to 29.6% in pediatric ICUs. The incidence of HAI related to mechanical ventilation, catheter insertion and some invasive procedures are more than that in other hospital wards, which do not carry such procedures.[12] Prevention of HAIs is central to providing high quality and safe healthcare, even in settings with limited resources. Transmission of infectious agents between patients by health workers and irrational use of antibiotics are two important preventable factors involved in many HAIs. The present study was conducted to determine the HAI

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rate in Pediatric intensive care unit, causative organisms of HAIs and their antibiotic susceptibility profile.

MATERIAL AND METHODS

A hospital based prospective cohort study was conducted with 200 patients to analyze HAIs in PICU of a tertiary care center.

Study population

Patients admitted in PICU from 1 month to 13 years of age fulfilling the inclusion criteria were enrolled after due consent of parents. HAIs are diagnosed and categorised according to CDC guidelines.

Sample size

Considering a confidence level of 95% and confidence interval of 7the number of patients in our study to achieve statistical significance is 196. This was calculated by Survey System (http://www.surveysystem.com/sscalc.htm#one). The Survey System ignores the population size when it is "large" or unknown. Population size is only likely to be a factor when you work with a relatively small and known group of people (e.g., the members of an association). Hence, a sample size of 200 was considered adequate for our study.

Inclusion criteria

- Age group of 1month to 13 years.
- All patients in paediatric intensive care unit who did not have any sign of infection at admission and remained hospitalised for at least 48 hrs.

Exclusion criteria

- Age less than 1month and more than 13 years
- Individual diagnosed with infection before 48 hr
- Patient who are discharged before 48 hrs
- HIV positive patients

Methodology

Approval from the Institutional Ethical Committee was obtained before commencing the study. Written and Informed Consent was obtained from all patients. The patients were informed regarding the purpose, procedures, risks and benefits of the study in their own vernacular language. A standard proforma for study participants were used for collection of data. Routine investigations such as complete hemogram, C-reactive protein, blood culture sensitivity, urine routine and microscopy, urine culture sensitivity, chest X-ray and tracheal aspirate culture sensitivity were carried out. Demography, admission diagnosis, referral place, daily clinical and laboratory data, risk factors for HAIs acquisition, and outcomes of HAIs including LOS and mortality data were collected. Case identification was based on the following criteria: (i) Clinical: based on the review of information in the patient's charts, (ii) Laboratory: based on results of blood cultures, bronchoalveolar lavage (BAL) cultures, and (iii) Supportive evidence: derived from diagnostic tests and results of X-rays. HAIs was suspected based on the CDC criteria. For example, ventilator associated pneumonia (VAP)was suspected in a mechanically ventilated child after 48 h of PICU stay if the child had fever, or increased respiratory tract secretions or increased requirement of ventilator support. The clinical team suspected and investigated for HAIs as per protocol. The team also considered urinary tract infection (UTI)/catheter associated urinary tract infection (CAUTI) as one of the HAIs. It is a UTI where an indwelling UC was in place for more than 2 calendar days and an indwelling UC was in place on the date of event or the day before. Central line- associated bloodstream infection (CLABSI): It is a laboratory-confirmed bloodstream infection where central line (CL) or umbilical catheter was in place for more than 2 calendar days and the line was also in place on the date of event or the day before. Ventilator associated pneumonia (VAP): it is a case of pneumonia where the patient is on mechanical ventilation (MV) for more than 2 calendar days, and the ventilator was in place on the date of event or the day before. It is identified by using a combination of imaging, clinical, and laboratory criteria. Bacteriologic cultures from different sites were collected on admission from blood, urine, sputum, bronchoalveolar lavage, and cerebrospinal fluid if needed. On suspicion, cultures were taken per suspected site(s) of infection. An episode was considered a second one if it occurred with another type of infection or with the same type of infection occurring more than 14 days after the start of the initial episode. Infection with a different organism within 14 days timeframe was included in the same episode. Standard microbiology methods were used for identification and antimicrobial susceptibility testing of bacterial isolates from all samples.

Statistical analysis

Quantitative data is presented with the help of Mean and Standard deviation. Comparison among the study groups is done with the help of unpaired t-test as per results of normality test. Qualitative data is presented with the help of frequency and percentage table. Association among the study groups is assessed with the help of Fisher test, student 't'-test and Chi-Square test. 'p' value less than 0.05 is taken as significant. Appropriate statistical software, including but not restricted to MS Excel, SPSS ver. 20 will be used for statistical analysis. Graphical representation will be done in MS Excel 2010.

RESULTS

The study sample consisted of 57% male children (114/200) and 43% female children (86/200). Majority of patients belonged to the age group of 1-3 years (32.7%), followed by the age group <1 year (24%) and 4-6 years being (20.5%). The mean age of the sample was 46.4 months ± 42.9 months (range was 1.5 months to 15 years). The mean ages of male and female patients in the study were almost equal, being 45.7 months and 47.3 months respectively (p=0.789). The mean PICU stay in number of days was 7.2±3 days (range 4 to 34 days). Mean number of days spent in PICU by male patients was 7.4±3.5 days as against 7±2.1 days by female patients. However, the difference was not significant (p=0.295). Majority patients (70%) spent 1-7 days in the PICU, followed by 27.5% who spent between 8-14 days in the PICU. The number of patients who required Foley's catheterization were 75/200 (37.5%), while 21/200 (10.5%) patients required mechanical ventilation. It was observed that 19/200 (9.5%) patients had a central line inserted. All 11 patients required all three interventions. However, prevalence of HAI according to number of patients was 51/200 (25.5%) patients, 75/200 (62.5%) patients were catheterized, 21/200(10.5%) patients were mechanically ventilated and 19/200 (9.5%) patients were required central line. Number of instances of hospital acquired infections (including multiple infections in the same patient there were 12 patients in present study who were with multiple episodes of HAI) in my study was 63/200 (31.5%) including CONS, excluding CONS HAI incidence was 31/200 (15.5%). Different categories of HAI in our study were 39/200 (19.5%) blood stream infections, 8/75 (10.7%) urinary infections in catheterized patients, 13/21 (62%) patients with mechanical ventilation had infections associated with mechanical ventilation and 3/19 (15.8%) patients with central line insertion had central line associated blood stream infection.

Table 1: Distribution of hospital acquired infections

Source	n/N	%
Blood stream	39/200	19.5%
Foley's catheter	08/75	10.7%
Mechanical ventilation	13/21	62%
Central line	03/19	15.8%

Out of the 200 PICU patients, 130 were in the old PICU and 70 were admitted in the new PICU of the hospital. When data of hospital acquired infections was analyzed according to location of patient in the old or new PICU of our hospital, it was found that overall, even though the percentage of infections in each category was higher in the old PICU patients, there was no statistically significant difference in the rates of HAI's between the 2 PICUs in any of the categories.

Table 2: Distribution of organisms isolated according to their source

Microorganism isolated	Blood		Urine		Mechanical ventilation		Central line		Total	
	n	%	N	%	N	%	n	%	n	%
CONS	20	31.7	-	-	2	3.2	3	4.8	25	39.7
Klebsiella spp.	6	9.5	-	-	7	11.1	-	-	13	20.6
Pseudomonas (ESBL producing)	4	6.3	-	-	-	-	-	-	4	6.3
Pseudomonas aeruginosa	2	3.2	1	1.6	3	4.8	-	-	6	9.5
E. coli	1	1.6	5	7.9	-	-	-	-	6	9.5
Enterobacter spp.	2	3.2	-	-	-	-	-	-	2	3.2
Enterococcus spp.	-	-	2	3.2	-	-	-	-	2	3.2
Citrobacter spp.	1	1.6	-	-	1	1.6	-	-	2	3.2
MRSA	1	1.6	-	-	-	-	-	-	1	1.6
MSSA	1	1.6	-	-	-	-	-	-	1	1.6
Streptomonas (ESBL producing)	1	1.6	-	-	-	-	-	-	1	1.6
Total	**39**	**62**	**8**	**12.7**	**13**	**20.6**	**3**	**4.8**	**63**	**100**

The majority of blood stream isolates were CONS, in 20/39 patients (51.3%), followed by Klebsiella in 6/39 cases (15.4%) cases. Other organisms identified were ESBL producing Pseudonomas, Pseudomonas aeruginosa, E. Coli, MRSA, MSSA, Enterobacter, Citrobacter, and ESBL producing Streptomonas. Isolates obtained from urine cultures were predominantly those of E. Coli (5/8; 62.5%), followed by Enterococcus (2/8; 25%) and Pseudomonas (1/8; 12.5%). Those patients who required mechanical ventilation showed the following pattern of organisms in their cultures: majority were Klebsiella (7/13; 53.8%), followed by Pseudomonas (3/13; 23.1%) and CONS (2/13; 15.4%). Organisms isolated from central line associated infections were found to be only CONS (3/3; 100%). The results from this study show that Klebsiella were sensitive to Tigacyclin, Colistin, Imipenem, Amikacin, Piptaz, Gentamicin, Norfloxacin, Chloramphenicol, Oxacillin, Vancomycin, Linezolid, Ciprofloxacin, and Cotrimoxazole. CONS were sensitive to Oxacillin, vancomycin, Linezolid, ciprofloxacin, gentamicin among others. E. Coli were found to be sensitive to chloramphenicol, imipenem, gentamicin and amikacin. Pseudomonas were sensitive to gentamicin, amikacin, imipenem, ceftazidime + Tazo, carbecillin, ciprofloxacin, piptaz, chloramphenicol and norfloxacin. MSSA and MRSA were sensitive to gentamicin, vancomycin, linezolid and linezolid, vancomycin respectively. Enterococci were found to be sensitive to vancomycin, linezolid, ampicillin, and nitrofurantoin. Klebsiella were found to have resistance against ampicillin, cefexime, ceftazidime, and amoxicillin. CONS were resistant to cotrimoxazole, erythromycin, cefixin, cefoxitin, clindamycin. Resistance to norfloxacin and ampicillin was observed in E. Coli, while Pseudomonas were found to be resistant to cefotaxim, amoxicillin, Augmentin, and cefepime. MSSA was resistant to clindamycin and erythromycin, while MRSA was resistant to gentamicin and clindamycin.

Table 3: Sensitivity and resistance patterns of isolates from blood

CONS (n=25)		Klebsiella spp. (n=13)		Pseudomonas (ESBL producing) (n=4)	
Sensitivity	Resistance	Sensitivity	Resistance	Sensitivity	Resistance
Oxacillin	Cotrimoxazole	Tigacyclin	Ampicillin	Gentamicin	Cefotaxim
Vancomycin	Cefixime	Colistin	Cefixime	Amikacin	Amoxycillin
Linezolid	Cefoxitim	Imipenem	Ceftazidime	Imipenem	Augmentin
Ciprofloxacin	Carbacellin	Amikacin	Amoxycillin	Ceftazidime+ Tazobactam	Cefipime
Gentamicin		Piptaz		Piptaz	Cotrimoxazole
Amikacin		Gentamicin		Chloram phenicol	
Clindamicin		Norfloxacin		Norfloxacin	
Erythromycin		Chloram phenicol			
Imipenem		Oxacillin			
Chloram phenicol		Vancomycin			
		Linezolid			
		Ciprofloxacin			
		Co-trimoxazole			

P. aeruginosa (n=6)		E. coli (n=6)		Enterobacter spp. (n=2)	
Sensitivity	Resistance	Sensitivity	Resistance	Sensitivity	Resistance
Gentamicin	Amoxycillin	Chloramphenicol	Norfloxacin	Cotrimoxazole	Ampicillin
Piptaz	Cefipime	Imipenem	Ampicillin	Cloxacillin	Norfloxacillin
Amikacin	Cefoxitin	Gentamicin		Imipenem	Gentamicin
Imipenem	Cefixime	Amikacin		Colistin	Amoxycillin
	Cephalexin				Amikacin
	Ceftazidime				Chloramphenicol
	Cotrimoxazole				

Enterococcus spp. (n=2)		Citrobacter spp. (n=2)		MRSA (n=1)	
Sensitivity	Resistance	Sensitivity	Resistance	Sensitivity	Resistance
Vancomycin	Amikacin	Colistin	Cotrimoxazole	Linezolid	Gentamicin
Linezolid	Nalidixic acid		Gentamicin	Vancomycin	Clindamicin
Ampicillin	Clindamycin		Ampicillin		
Nitrofurantoin			Tazobactum		

When logistic regression was used to determine the factors associated with HAI, it was found that none of the factors such as age and sex of the patient, length of PICU stay, requirement of catheterization, mechanical ventilation or central line insertion were significantly associated with presence of HAI.

Table 4: Logistic regression analysis for factors contributing to HAI

Factors	OR	95% CI	p value
Age (months)	0.89	0.98 – 1.0	0.08
Gender	0.99	0.46 – 1.7	0.74
Length of PICU stay (days)	0.94	0.84 – 1.0	0.27
Requirement of mechanical ventilation	1.43	0.36 – 5.5	0.61
Requirement of Foley's catheterization	0.97	0.46 – 2.0	0.94
Requirement of central line insertion	0.84	0.23 – 3.1	0.80

DISCUSSION

Despite the recent advances in pediatric intensive care, HAIs still cause considerable morbidity and mortality. HAIs are highest in intensive care units and surgical wards, and lowest in medical units.13 Active surveillance of HAIs plays a substantial role in infection control in the PICU, which may contribute to improving patient care. Although there are many data on the epidemiology of HAIs in PICU from industrialized countries, data from developing countries are limited. Majority of the patients in our study (70%) had PICU stay of 1-7 days while 55 (27.5%) and 4 (2%) patients had PICU stay of 8-14 days and 15-21 days respectively. The mean length of PICU Stay of patients was 7.34±3.04 days. This is comparable to the studies of Sodhi J *et al*,[14] Folgori L *et al*,15 and Moustafa AA *et al*.[16] In our study, 75 (38%) patients required urinary catheter while 125 (62%) patients did not require urinary catheter. 21 (10.5%) patients were on mechanical ventilation while 179 (88.5%) patients did not require mechanical ventilation. Folgori L *et al*[15] reported 120 (80.5%) of 149 LRTIs were mechanically ventilated (100 [67.1%] of these 149 for >48 hours). Among 85 urinary tract infections, 38 were in children who had a urinary catheter (28 [32.9%] of the 85 for >48 hours). It was observed in our study that 19 (9.5%) patients required central line while 181 (89.5%) patients did not require central line. Folgori L *et al*[15] noted similar observation in their study. They reported 195 (79.9%) were involved children with a central venous catheter in situ when diagnosed (179 [73.4%] of these 244 for >48 hours). There were 63 episodes of HAI in our study. The incidence of HAI was 31.5%, excluding CONS 31/200 incidence rate is 15.5%. This is concordant to the studies of Sodhi J *et al*,[14] Folgori L *et al*[15] and Moustafa AA *et al*.[16] Sodhi J *et al*[14] reported a total of 119 children admitted in the PICU of whom 20 (16.8%) eligible children who developed HAI. Folgori L *et al*[15] reported cumulative incidence of HAI was 3.6/100 ICU admissions whereas the rate of infections was 3.6/1,000 ICU-days. No significant trends in HAI incidence and rate were identified. 478 (88.8%) of the 538 HAIs were diagnosed in patients with an invasive device in situ. Moustafa AA *et al*[16] reported incidence of HAIs was 12.8/100 PICU admissions and 15.6/1000 PICU-days. Mathot F *et al*,[17] McGrath EJ *et al*,[18] Banerjee SN *et al*[19] and Rutledge-Taylor K *et al*[20] reported incidence of HAIs as between 7% and 12% in pediatric and between 15% and 20% in neonatal ICUs. In the present study, 39/200 (19.5%) episodes of HAIs were bloodstream infection. In blood stream infection CONS are positive in 20 patients and as CONS has no significant role in HAI, excluding CONS with blood stream infection comes down to 19/200 (9.5%) while 13 (32.6%) and 8 (17.4%) episodes were mechanical ventilation infection and urinary tract infection respectively. 3 (6.5%) episodes were Central line-associated bloodstream infection (CLABSI). These findings were consistent with the studies of Atıcı S *et al*,[21] Folgori L *et al*[15] and Mathot F *et al*.[17] Atıcı S *et al*[21] reported three most commonly detected HAI types were bloodstream infection (BSI) (35.7%), pneumonia (21.4%), and urinary tract infection (UTI) (20.6%). BSI was the most common HAI type every year. Pneumonia was the second-most common HAI type in 2013 and 2014, and UTI was the second-most common HAI type in 2011 and 2012. Folgori L *et al*[15] reported Bloodstream infections (BSIs) were the leading pattern accounting for 244 episodes (45.4%), followed by lower respiratory tract infections (LRTIs) with 149 (27.8%) and urinary tract infections with 85 (15.8%). Mathot F *et al*[17] have reported bloodstream infections as the leading cause of HAIs in the PICU. The most common causative microorganism in our study was Klebsiella 13 (32.5%) followed by, P. aeruginosa (15.4%), E. coli (13%), Coagulase negative Staphylococci [CONS] (11%), Pseudomonas: ESBL producing (8.8%), Enterobacter (4.4%), Citrobacter (4.4%), Enterococcus (4.4%), Methicillin-sensitive Staphylococcus aureus [MSSA] (2.2%), Methicillin-resistant Staphylococcus aureus [MRSA] (2.2%) and Streptomonas: ESBL producing (2.2%). This is in concordance to the studies of Atıcı S *et al*,[21] Folgori L *et al*,[15] and Moustafa AA *et al*.[17] Atıcı S *et al*[21] reported that Klebsiella species accounted for 19.4% of all isolates and were the most common cause of HAIs, followed by E. coli (13.8%) and A. baumanii (12%). Candida species were found to be the fourth-most common agent causing HAIs. They were isolated from 11.5% of the infected patients. Candida albicans and non-albicans Candida strains accounted for 7.8% and 3.7% of HAIs, respectively. Folgori L *et al*[15] reported total of 573 microorganisms were isolated. Of these 573 microorganisms, 317 (55%) were Gram-negative bacteria, 184 (32%) were Gram-positive bacteria, and 40 (7%) were fungi. The most frequently isolated pathogens were Enterobacteriaceae (30.9%), followed by P. aeruginosa (19.2%) and Staph. aureus (11.0%). The percentage of MDR isolates was 44%. Moustafa AA *et al*[17] found of the isolated 25 microorganisms, 18 (72%) isolates were Gram-negative bacteria (GNB) and seven (28%) isolates were Gram-positive bacteria. The most frequently isolated pathogens were Klebsiella spp. (14 isolates, 56%), followed by Acinetobacter spp. and Staphylococci spp. (three isolates, 12%each). Diphtheroids spp., Streptococcus viridans group, and Stenotrophomonas spp. accounted for 8, 8, and 4%, respectively. Klebsiella spp. caused 44.4% of VAP, 83% of CLABSI, and 100% of CAUTI. The National Nosocomial Infection Surveillance

System survey (NNISS) of PICU patients in study done by Wisplinghoff H *et al*22 identified coagulase negative Staphylococcus spp. as the predominant organism associated with CLABSI, accounting for 37.8% of reported cases. GNB accounted for 19 and 21% of CLABSIs reported to CDC and the Surveillance and Control of Pathogens of Epidemiological Importance database in a study done by Wolf J *et al*[23] respectively. The sensitivity and resistance pattern of the isolates in our study is shown in Table 3. Similar observations were noted in the studies of Atıcı S *et al*,[21] Folgori L *et al*[15] and Moustafa AA *et al*.[16] Atıcı S*et al*[21] study reported that methicillin resistance was detected in 78% of coagulase-negative Staphylococcus. Nineteen (45%) Klebsiella spp. isolates and seven (54%) E. coli isolates produced ESBLs. Vancomycin and ampicillin resistance were detected in 38% and 75% of Enterococcus spp. strains, respectively. Carbapenem susceptibility was detected in 63% and 31% in P. aeruginosa and A. baumanii isolates, respectively. Folgori L *et al*[15] reported 79 (45%) of the 175 Enterobacteriaceae were positive for extended-spectrum beta-lactamase. Culture-confirmed carbapenem resistance was reported in 3 (2%) of the 175 Enterobacteriaceae, 46 (42%) of 110 P. aeruginosa, and 6 of 10 A. baumannii. Among Gram-positives, 35 (56%) of 63 S. aureus were methicillin-resistant whereas no vancomycin-resistant Enterococcus spp. were isolated. 76 coagulase-negative staphylococci were isolated, of which 47 (62%) were classified as MDR. A study by Moustafa AA *et al*[16] showed that all the isolates were multidrug resistant. All Klebsiella spp. Isolates were extended-spectrum β-lactamase producers. Two isolates of S. aureus were methicillin resistant and one isolate of coagulase- negative Staphylococcus was also methicillin resistant. Acinetobacter spp. isolates were sensitive only to quinolones. The Stenotrophomonas spp. isolate was sensitive only to ceftazidime, levofloxacin, and trimethoprim/sulphamethexazole. In the present study, logistic regression analysis was used to evaluate predictors of Hospital Acquired Infections (HAI). The logistic regression analysis showed that none of the factors such as length of PICU stay, requirement of mechanical ventilation, urinary catheterization, insertion of central line, or age and sex were associated with presence of HAI. However, this is in contrast with observations by Folgori L *et al*,[15] Moustafa AA *et al*1[6] and Hatachi T *et al*[24] who noted significant associations between HAI and length of PICU stay and requirement of mechanical ventilation in their studies.

CONCLUSION

The incidence rate of HAI was 21.5% in our study and the common microorganisms isolated were Klebsiella spp., Pseudomonas, E. coli and MRSA. Common sites of HAI were mechanical ventilation (62%) and central line associated blood stream infection (15.8%).

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