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Original Research Article

Clinico-microbiological profile of health-care associated infections in a paediatric intensive care unit of tertiary care hospital

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ABSTRACT

Background: The study was undertaken to determine the total burden of health-care associated infections, microbiological profile and their impact on length of stay and mortality in a PICU of a tertiary care Hospital by prospective surveillance.
Methods: All children ≥ one month and ≤ twelve years of age admitted in PICU for more than 48 hours from December 2009 to November 2010 were followed according to CDC/NHSN surveillance definitions of HCAI. Incidence rates, incidence densities and device utilization ratio were measured for different HCAI. Length of stay and mortality of HCAI were compared with non-HCAI patients. Antibiotic susceptibility pattern of isolated micro-organism was analyzed.
Results: Out of total 618 patients admitted in PICU during study period 324 fulfilled study criteria. In those 324 patients 58 patients developed 68 episodes of HCAI. The CIR and IDs’of HCAI were17.9/100 patients and 22.14/1,000 patient-days, respectively. Of the 68 episodes of HCAI, there were 36 VAP, 17 BSI, 8 UTI, 2 pneumonia, 2 LRI-LUNG and 1each of SSI-MED, SST-Skin and GI-IAB. The most common microorganism isolated was Acinetobacter spp. followed by Pseudomonas spp. HCAI increased the average length of PICU stay (20 days versus 5 days, P<0.01) and Hospital stay (28 days versus 12 days, P<0.01). Overall mortality was significantly higher in patients who developed HCAI than non-HCAI (50.9% versus 21.3%, P<0.01).
Conclusions: HCAI rates were higher than developed countries. VAP was the most common HCAI followed by BSI. HCAI increased the length of stay and mortality (P<0.01). Organisms isolated in HCAI were more resistant than non-HCAI isolates.

Keywords: BSI, Hospital-acquired infection, HCAI, Microbiological profile, VAP

INTRODUCTION

Health care-associated infections (HCAI) are an important cause of morbidity and mortality among critically ill patients of all age groups. Originally called nosocomial or hospital-acquired infections, the scope of HCAI have expanded as patients now receive medical care in a wide variety of healthcare settings. Many HCAI are preventable and thus should be a target for aggressive infection control programs.[1] The HCAI cause prolonged hospital stay, long-term disability, increased resistance of microorganisms to antimicrobials, massive additional financial burden for health systems, high costs for patients and their family, and unnecessary deaths.[1,2]

Pediatric intensive care units (PICU) in developing countries often admit more critically ill patients with younger age and low socioeconomic status.[3] Rates of HCAI among pediatric patients vary according to birth weight, age, severe underlying illness, loss of skin integrity, or the presence of multiple medical devices that breech normal defense mechanisms.[4,5]

Surveillance of HCAI helps in determining the infection rates, risk factors and in planning the preventive strategies to ensure quality health care.[6-8] The present study was undertaken to determine the total burden of HCAI, microbiological profile and their impact on length of stay and mortality in a PICU of a tertiary care Hospital by prospective surveillance.

METHODS

The study was conducted in PICU of tertiary care hospital, Chacha Nehru Bal Chikitsalaya, Geeta Colony, Delhi (Affiliated to Maulana Azad Medical College, Delhi) from December 2009 to November 2010. Study was approved by the ethical committee of research review board of the Hospital.

The study was conducted in 12 bedded NABH accredited PICU having 6 ventilators. One senior resident and one junior resident are posted round the clock. The patient nurse ratio of 2:1 is followed. There is an infection controlled surveillance system and an independent infection control nurse. The PICU is also under CCTV surveillance. Universal infection control precautions are strictly followed.

Prospective cohort study for all children ≥ one month and ≤ twelve years of age admitted in PICU for more than 48 hours were included in the study. These patients were followed according to Center for Disease Control/ National Healthcare Safety Network (CDC/NHSN) surveillance definitions of HCAI to diagnose HCAI episodes.[9] The Clinical Pulmonary Infection Score (CPIS) based Ventilator associated pneumonia (VAP) score sheet was used which scores various clinical and radiological signs from 0 to 2, with a total score greater than 6 indicating a high probability of VAP.[10,11] (Annexure-1).

When the development of an HCAI was suspected, appropriate samples for the diagnosis of a site-specific HCAI were collected aseptically processed and interpreted, following standard procedures guidelines. For diagnosing VAP tracheal aspirate samples were cultured semi-quantitatively and colony count of more ≥ 10^5 cfu/ml was taken as significant. The data for calculation of patient-days, device-days, crude infection rate (CIR) and incidence density (ID) of HCAI were calculated using CDC/NHSN protocols.[12-14] Crude excess mortality (CEM) was determined as the difference between the crude overall case-fatality rate of patients with HCAI and the crude case-fatality rate non-HCAI patients (Annexure-2).

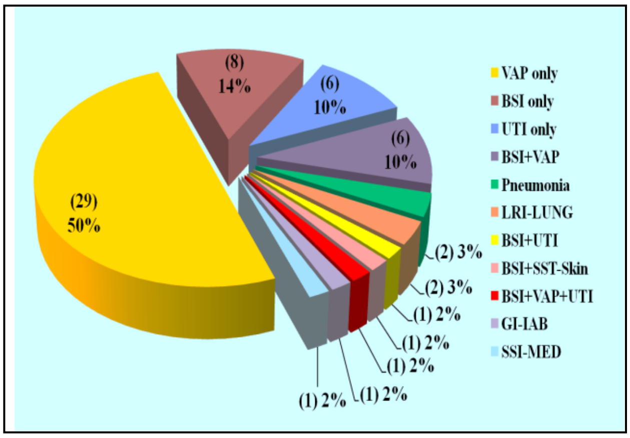
Bacterial isolates were identified by conventional biochemical tests. Antimicrobial susceptibility testing was performed using the disc diffusion technique by Clinical and Laboratory Standards Institute guidelines. Bacterial isolates of same species, obtained from a patient, were considered different when their antibiograms differed by two or more different classes of antibiotics.

Clinical details of the patients were entered in predesigned Proforma (as per guidelines of NHSN).[9] Compilations of data was done in Microsoft Excel 2007 sheet. The Open Epi software was used for statistical analysis.[15] Data analysed using descriptive statistics. Categorical variables were evaluated using the Chi Square or Fisher's exact test, as appropriate. Continuous variables were evaluated using non-parametric test (Mann-Whitney test). P-value of <0.05 was considered significant.

RESULTS

A total of 618 admissions to PICU occurred during the study period of one year, 324 patients fulfilled the inclusion criteria. Out of those 324 patients 58 patients developed 68 episodes of HCAI. Of these, 190 (59%) were male and 134 (41%) were female. The mean age at presentation was 28 months. The mean length of stay of the 324 study patients was 8.63 days. Eleven patients (4%) either left against medical advice or referred out. Out of these, 3 were HCAI and 8 non-HCAI. These 11 patients were excluded for mortality assessment. Out of rest 313 patients, 83 patients died during their stay in PICU (Table 1).

Patients with HCAI had significantly higher PRISM III score (5±3.22) than non-HCAI (3.42±3.75) (P <0.01). The mortality was significantly higher (P< 0.01) in patients with HCAI (50.90%) than non- HCAI patients (21.32%) (Table 1).



BSI- Blood stream infection; GI-IAB - Gastrointestinal system infection-Intra Abdominal; not specified elsewhere; HCAI- Health care-associated infection, LRI-Lung - Lower respiratory tract infections other than Pneumonia-Other infections of the lower respiratory tract; SSI-MED - Surgical Site Infection-Mediastinitis; SST-Skin - Skin and Soft Tissue Infection-Skin; VAP- Ventilator-associated pneumonia; UTI - urinary tract infection.

Figure 1: Distribution of HCAI patients according to HCAI episodes.

Overall, 68 episodes of HCAI occurred in 58 patients. (Table 2) Crude infection rate for HCAI was 17.9 per 100 patients. All patients admitted in PICU accounted for 3066 patient-days. The incidence density (ID) of all HCAI was 22.17/1,000 patient-days. Most common HCAI observed in our study group was VAP (53%), followed by Health care-associated blood stream infection (HCA-BSI) in 25% (Figure 1).

Of 58 patients with HCAI, 49 patients developed single episode of HCAI and 9 patients developed multiple episode of HCAI. Mortality rate of patients with multiple episodes (75%) was higher than with single episode HCAI (46.8%) (P-value = 0.27). Device utilization ratios for HCAI patients were more than those without HCAI group for central venous catheter, ventilator, and urinary catheters (P<0.01) (Table 3).

Site-specific infections

VAP

Of the 324 study patients, 112 (34.56%) were mechanically ventilated for ≥48 hours, VAP developed in 36 patients. Total ventilator-days were 1134 (Table 3). The crude infection rate of VAP was 32.14/100 patients and incidence density was 31.7/1,000 ventilator-days. The mean duration of ventilation (DOV) of 36 patients who developed VAP was higher [17±26.8 days (range: 2-64; median: 14.5)] when compared with the 76 patients without VAP [7±10.8 days (range: 2-26; median: 4)].

The device utilization of patient who developed VAP was also higher than those who had not developed VAP (0.59 versus 0.22). Out of the 36 episodes of VAP, three (8.33%) were diagnosed on the basis of clinical and radiological criteria's alone, whereas 33 (91.66%) fulfilled microbiological criteria in addition. The attributed mortality of VAP was 46.4%. (Table 4) Acinetobacter spp. (16 cases) were the most common organism isolated followed by *Pseudomonas spp.* (7 cases) (Table 5).

Table 1: Clinical profile and outcome of the children with and without HCAI.

		HCAI (n = 58)	Non-HCAI (n = 266)	P- value	Odds ratio	Confidence interval (95%)
Gender (M/F)		39/19	151/115	0.14	1.56	0.85, 2.84
Age						
<1 year		39 (67%)	130 (48.9%)	0.01	2.14	1.18, 3.90
1-5 years		15 (26%)	89 (33.45%)	0.22	0.67	0.35, 1.28
> 5 years		4 (7%)	47 (17.66%)	0.05	0.34	0.11, 0.99
Mean±SD		18±28.40	30±38.13	0.032		
Initial presentation of patients						
Respiratory		22	85	0.38	1.3	0.72, 2.34
Sepsis		19	63	0.14	1.52	0.85, 2.9
Neurological		7	40	0.56	0.77	0.32, 1.83
Renal		4	14	0.81	1.33	0.42, 4.2
Surgical		2	8	0.99	1.15	0.24, 5.57
Cardiovascular		1	9	0.87	0.50	0.06, 4.03
Others		3	47	0.018	0.25	0.08, 0.84
PRISM score						
PRISM III Score		5±3.22	3.42±3.75	<0.01		
Length of stay						
PICU	Median	20	5	<0.01		
	Mean±SD	24±27.3	7±8.5			
Hospital	Median	28	12	<0.01		
	Mean±SD	31 ±14.26	14 ±7.39			
Patients days		1254	1812			
Outcome*						
LAMA/referred		3	8			
Mortality		28	55			
Mortality rate*		(28/55) 50.90%	(55/258) 21.32%	0.01	3.828	2.086,7.022

HCAI - Health care-associated infection; SD - Standard deviation; LAMA - Left against medical advice; *LAMA/Referred cases excluded for mortality calculations.

Table 2: Distribution of HCAI episodes.

Health care-associated infection as per CDC/NHSN[9] surveillance definition		Episodes	%
VAP	Ventilator associated pneumonia	36	52.94%
BSI	Blood stream infection	17	25%
UTI	Urinary tract infection	8	11.76%
Pneumonia	Pneumonia	2	2.94%
LRI-LUNG	Lower respiratory tract infections other than pneumonia - other infections of the lower respiratory tract	2	2.94%
SST-Skin	Skin and soft tissue infection - skin	1	1.47%
GI-IAB	Gastrointestinal system infection - intra abdominal, not specified elsewhere	1	1.47%
SSI-MED	Surgical site infection-mediastinitis	1	1.47%
Total episodes		**68**	

CDC-Centers for disease control and prevention; NHSN- National healthcare safety network.

Table 3: Device utilization in study population.

	HCAI			Non HCAI			Total device days
	Device use	Median	DUR	Device use	Median	DUR	
CVC days	503	12.5	0.40	234	7	0.13	737
UC days	574	12	0.46	350	6	0.19	924
Ventilator days	740	12	0.59	394	4	0.22	1134

CVC- Central venous catheter; DUR-Device utilization ratio; UC- Urinary catheter; HCAI- Health care-associated infection

Table 4: Features of the various site specific infections.

Variables	VAP	HCA-BSI	CA- UTI
Cases	36	17	8
Episodes	36	17	8
Crude infection rate	32.14/100 patients with ventilators ≥48 hours	5.24/100 patients	9.3/100 patients with UC ≥48hrs
Incidence density	31.74/1000 ventilator days	5.5/1000 patient days	8.65/1000 UC days
Outcome			
LAMA/referred	1	1	-
Patients with > 1 episode of HCAI	7		2
Attributed mortality#	13	5	1
Attributed mortality rate#	46.4% (13/28)	71.4% (5/7)	16.6% (1/6)

Patients who left against medical advice and with >1 episode of HCAI were excluded from attributable mortality and attributable mortality rate assessment; HCA-BSI- Health care-associated Blood stream infection, HCAI- Health care-associated infection; LAMA- Left against medical advice; HCA-UTI- Health care-associated Urinary tract infection; UC-urinary catheters; VAP- Ventilator associated pneumonia.

Table 5: Distribution of microorganism in Health care-associated infections.

Microorganism	VAP	BSI	UTI	Others*	n (total)
Acinetobacter spp.	16	1	-	1	18
Pseudomonas spp.	7	6	-	-	13
Yeast	2	4	6	-	12
Escherichia coli	3	2	2	1	8
Klebsiella spp.	3	1	-	1	5
Stenotrophomonas	1	-	-	-	1
Enterobacter cloacae	1	-	-	-	1
Sphingomonas spp.	1	1	-	-	2
Burkholderia cepacia	-	1	-	-	1
Aeromonas spp.	-	1	-	-	1
Serratia rubidaea	1	-	-	-	1
Total	**35**	**17**	**8**	**3**	**63**

* Acinetobacter spp. was isolated from 1 case of LRI-LUNG; Klebsiella spp. was isolated from 1 case of SSI-MED and *Escherichia coli* was isolated from 1 case of GI-IAB; BSI- Blood stream infection; UTI- Urinary tract infection; VAP- Ventilator associated pneumonia

HCA-BSI

Of the 324 study patients, 17 were diagnosed as HCA-BSI. These 17 patients had 17 episodes of HCA-BSI. All HCA-BSI were laboratory-confirmed bloodstream infection. The crude infection rate of HCA-BSI was 5.24/100 patients and incidence density was 5.5/1,000 patient-days (Table 4). During the study period, 60 patients had central venous catheterization for ≥48 hours. The total central venous catheter days were 737 (Table 4). Out of these 17 HCA-BSI, one episode of central line associated (CLA-BSI) was diagnosed. The crude infection rate of CLA-BSI was 1.66/100 patients with CVC for ≥48 hours and incidence density was 1.35/1000 central line days. The attributable mortality of HCA-BSI was 71.4%. Pseudomonas spp. were the most common organism isolated in 6 cases (Table 5).

CA-UTI

Out of 324 patients 8 episodes of HCA-UTI occurred in eight patients. All HCA-UTI were catheter associated (CA-UTI). During the study period, 86 (26.54%) patients had urinary catheterization for ≥48 hours. The total urinary catheter days were 924 (Table 3). The crude infection rate of CA-UTI was 9.3/100 patients with UC ≥48 hours and incidence density was 8.6/1,000 UC-days. The attributable mortality of CA-UTI was 16.6% (1/6) (Table 4).

Antimicrobial susceptibility profile

All the isolates were found susceptible to colistin. Higher susceptibility rates to carbapenems were observed among *Enterobacteriaceae* members (*Escherichia coli* and *Klebsiella pneumoniae*) than non-fermenting gram negative bacteria (*Acinetobacter, Pseudomonas spp.* etc). When we compared the antimicrobial susceptibility pattern between organisms causing HCAIs with non HCAIs, it was noticed that majority of organisms of HCAI had lesser susceptibility than non-HCAI isolates (Table 6).

Table 6: Percentage distribution of antimicrobial susceptibility among bacterial isolates.

	***Acinetobacter spp.* (40)**		***Pseudomonas spp.* (39)**		***Enterobacteriaceae***				**Other* gram negative bacteria (16)**	
					***Escherichia coli* (24)**		***Klebsiella spp.* (16)**			
	Non HCAI (n = 22)	HCAI (n = 18)	Non HCAI (n = 26)	HCAI (n = 13)	Non HCAI (n = 16)	HCAI (n = 8)	Non HCAI (n = 11)	HCAI (n = 5)	Non HCAI (n = 9)	HCAI (n = 7)
Ceftriaxone	6.67% (1/15)	0 (0/9)	5% (1/20)	0 (0/13)	0 (0/12)	0 (0/8)	25% (2/8)	0 (0/4)	14.3% (1/7)	50% (3/6)
Ceftazidime	50% (4/8)	0 (0/2)	43.8% (7/16)	50% (4/8)	40% (4/10)	0 (0/5)	16.7% (1/6)	0 (0/3)	40% (2/5)	0 (0/1)
Cefepime	25% (2/8)	0 (0/3)	42.9% (6/14)	57.1% (4/7)	18.2% (2/11)	0 (0/4)	71.4% (5/7)	33.3% (1/3)	33.3% (1/3)	0 (0/2)
Meropenem	10% (2/20)	0 (0/ 13)	50% (12/24)	46.2% (6/13)	68.8% (11/16)	57.2% (4/7)	90.1% (10/11)	80% (4/5)	50% (3/6)	50% (2/4)
Imipenem	18% (4/ 22)	5.6% (1/18)	52% (13/25)	46.2% (6/13)	75% (12/16)	50% (4/8)	81.9% (9/11)	60% (3/5)	33.3% (2/6)	42.9% (3/7)
Piperacillin - tazobactam	14.3% (2/14)	0 (0/ 8)	42.1% (8/19)	37.5% (3/8)	15.4% (2/13)	20% (1/5)	11.1% (1/9)	25% (1/4)	25% (1/4)	0 (0/3)
Amikacin	9% (2/ 22)	0 (0/ 18)	50% (13/26)	30.8 % (4/13)	62.5% (10/16)	37.5% (3/8)	81.9% (9/11)	60% (3/5)	14.3% (1/7)	57.1% (4/7)
Netilmicin	14.3% (1/ 7)	20% (2/ 10)	53.8% (7/13)	0 (0/6)	28.6% (2/7)	14.3% (1/7)	50% (1/2)	50% (1/2)	50% (2/4)	50% (2/4)
Colistin	100% (22/22)	100% (18/18)	100% (16/16)	100% (11/11)	100% (11/11)	100% (8/8)	100% (8/8)	100% (5/5)	100% (7/7)	100% (6/6)
Ciprofloxacin	11.8% (2/ 17)	0 (0/13)	55.6% (10/18)	50% (4/8)	0 (0/15)	0 (0/6)	25% (2/8)	50% (2/4)	25% (1/4)	25% (1/4)
Levofloxacin	45.5% (5/11)	0 (0/3)	53.8% (7/13)	42.9% (3/7)	0 (0/10)	0 (0/1)	71.4% (5/7)	100% (2/2)	40% (2/5)	33.3% (1/3)
Cotrimoxazole	-	-	-	-	0 (0/15)	20% (1/5)	25% (2/8)	0 (0/ 4)	42.9% (3/7)	42.9% (3/7)

HCAI- Health care-associated infection; *Other gram negative bacteria isolated were Stenotrophomonas spp. (4 isolates); *Burkholderia cepacia* (3 isolates); Achromobacter spp. (2 isolates); Sphingomonas spp. (2 isolates); Aeromonas sp. (1 isolate); Enterobacter sp. (1 isolate); *Salmonella Typhi* (1 isolate); *Serratia rubidaea* (1 isolate); Sphingobacterium sp. (1 isolate); Numerator - Number of susceptible isolates among exposed; Denominator - Total number of isolates exposed to particular antibiotic.

Acinetobacter spp. isolates were resistant to majority of antibiotics tested except colistin. All isolates of *Acinetobacter spp.* were susceptible to colistin (100%) but showed very low susceptibility to most of the other antibiotics (i.e.) amikacin (5%), netilmicin (17%), carbapenems (10%), third and fourth generation cephalosporins (10%), piperacillinm tazobactam (9%) and levofloxacin (35%) (Table 6).

Isolates of *Pseudomonas spp.* were susceptible to colistin (100%) and showed higher susceptibilities than Acinetobacter spp. to other antimicrobials i.e. ciprofloxacin (54%), levofloxacin (50%), carbapenems (49%), amikacin (44%), netilmicin (37%) and piperacillin-tazobactam (41%). None of the isolates of *Pseudomonas spp.* were susceptible to ceftriaxone but 50% of the isolates were found susceptible to ceftazidime and cefepime. Non-HCAI isolates showed better susceptibility to aminoglycosides (51.3% versus 21%) (Table 6).

In *Enterobacteriaceae* family all *Escherichia coli* and *Klebsiella* isolates showed susceptibility to colistin (100%). Overall susceptibility of *Klebsiella* isolates was better than *Escherichia coli* isolates for most of the antibiotics tested (Table 6).

Similarly, non-HCAI isolates of *Klebsiella spp.* revealed higher susceptibility than the HCAI isolates to aminoglycosides (77% versus 57%) and carbapenems (86% versus 70%). *Klebsiella* isolates showed better susceptibility to 4th generation cephalosporins (60%) than 3rd generation (11%) and to levofloxacin (77%) than ciprofloxacin (33%). Other gram negative bacteria were found susceptible to colistin (100%), carbapenems (43%) and aminoglycosides (40%). In yeast isolates, all identified species of Candida isolated were susceptible to amphotericin B, fluconazole and flucytosine. Only one strain of *Candida tropicalis* showed resistance to flucytosine (Table 6).

DISCUSSION

HCAI are of important wide-ranging concern in the medical field. Awareness of HCAI is increasing as increasing instrumentation. Now more and more number of ICU are using quality surveillance system to detect and report the HCAI episodes and taking measures to reduce the rates of HCAI episodes. The incidence of HCAI in our study (17.9%) was higher than developed countries and comparable to other developing countries. (13.6-19.5%).[6,9,16-18] The high incidence rates of HCAI in our PICU as in other developing countries could be multi factorial. Our hospital drains the area with poor standards of living. The profile of admitted patients includes predominantly infectious illnesses with malnutrition. Most of the patients present late in advanced stage of disease due to illiteracy and poverty, only the most critically ill children are admitted. When we compare from other Indian PICU our incidences were low may be because of better surveillance system and better resources.[6,19]

Patient who had HCAI were younger, the mean age of patients with HCAI was significantly lower than in patients without HCAI (P <0.05). The mean length of stay in PICU of patients who developed an HCAI was significantly longer (P < 0.01) than non-HCAI (Table 1). Mortality of HCAI patient (50.9%) was significantly higher than in non-HCAI (21.32%). Mortality of HCAI in our study was greater than that reported from PICU of developed countries (7.7-10%).[20,21] It was probably due to younger age of patients, malnutrition, prolonged duration of ICU stay and infections with more resistant strains of organisms.

Site-specific/device-associated infections

The majority of HCAI are associated with the use of invasive devices in critically ill patients. Richards et al4 estimated that in 61 PICU in the USA, 91% of BSI were in patients with a central intravenous line, 95% of episodes of health care-associated pneumonia were in patients on ventilators and 77% of HCA-UTI were in patients with urinary catheters. Similarly in our study, 53 of the 68 (78%) episodes of HCAI were associated with a device use, out of 17 episodes of HCA-BSI, 11 episodes were found in patients with central venous catheters. All 8 cases of HCA-UTI were associated with the use of urinary catheters.

BSI represents the most common HCAI in paediatric patients in developed world but in developing countries VAP exceed BSI.[3,4,6,16-18,20,22,23] Similar to other developing countries VAP was most common HCAI in our study also. NHSN data for 2010 revealed a pooled mean of 1.2 VAP cases per 1000 ventilator-days.[14] However VAP rates from developing countries was higher ranging from 7.9-43.16 in different studies.[3,6,18,24] In our study VAP rate was 31.74 per 1000 ventilator-days with 0.46 DUR. The mortality of VAP patients (46.4%) in our study was significantly higher than non-HCAI. Mortality for VAP seems also be related to the causative pathogen (e.g.) gram negative bacilli (particularly pseudomonas) have > 80% mortality.[25] We found a tendency to greater mortality in VAP, it could be due to highly resistant acinetobacter baumannii which was the most common organism responsible for VAP.

The HCA-BSI rates of our study (5.4%) were consistent with studies reported from many developed countries (3.1-14.6%).[12-14,20] The CLA-BSI rate in our study was 1.35/1000 CVC days. Data of CLA-BSI across United States from NHSN reports showed a trend of decline in CLA-BSI rates in PICU of United States, from 3.0 in 2006-2008 to 1.8/1000 central line days in.[12-14] Our results were in concordance with NHSN 2010 report.[14] However, different studies from developing world reported CLA-BSI rate from 7.7 -18.1 per 1000 CVC days.[3,6,16-18,20]

Microorganisms

Gram-negative rods were the most common pathogens identified in our setting. The spectrum of pathogens in our unit is similar to that reported from developing countries in both neonatal and paediatric intensive care patients but quite different from that observed in developed regions of the world, where gram-positive cocci, in particular coagulase-negative Staphylococci, were the predominant pathogens.[4,16,21,22,26-28] We found *Acinetobacter spp.* and *Pseudomonas aeruginosa* as the two most common bacterial micro-organisms implicated in VAP (48%) and BSI (35%) (Table 5). Since they are inherently resistant to the commonly used antibiotics and able to colonise the mucosa of patients and surfaces of various devices, they are particularly common in hospital settings.[29,30]

All the bacterial isolates were multidrug-resistant showing resistant to more than two different classes of antibiotics in their study. We also found a high rate of antibiotic resistance. We found 50-80% of Pseudomonas in children with HCAI were resistant to ceftazidime, amikacin, and ciprofloxacin. Similar resistance pattern was found in study by Becerra et al where they found around 80% of *Pseudomonas spp.* in children with VAP were resistant to ceftazidime, amikacin, ciprofloxacin.[3] We believe that this is due to the extensive use of antibiotics.

However our study had many limitations, like the lack of inclusion of data on re-intubation, which could be relevant for VAP. We did not search for viral agents. We did not stratify cases according to severity of disease, which could influence the appearance of HCAI, mortality and stay. In addition, we did not do long term follow up of HCAI patients to find out HCAI associated morbidity. In our study the incidence of HCAI other than VAP, BSI and UTI were less, so comparative analysis could not be done.

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Annexure 1: VAP score sheet.[10]

Parameter	Range	Score
Temperature	>99.7°F- ≤101.3° F	0
	> 101.3°F- ≤102°F	1
	< 96.8°F or >102°F	2
Leukocytes count	>4000 - <11,000 /mm^3	0
	< 4000 or >11,000 /mm^3 or >5000 mm^3 with band forms	1
Tracheal aspirates	Absence of secretion	0
	Non-purulent secretion	1
	Purulent secretion	2
Oxygenation PaO_2(mmHg)/FIO_2	> 240 or ARDS	0
	≤ 240 with no evidence of ARDS	2
Pulmonary radiography	No infiltrate	0
	Diffuse infiltrate	1
	Localised infiltrate	2
Progression of pulmonary infiltrate	No radiographic progression	0
	Radiographic progression (excluding CHF and ARDS)	2
Culture and gram staining of tracheal aspirate	No pathogenic bacteria cultured	0
	Pathogenic bacteria cultured or Some pathogenic bacteria seen on Gram staining	1

ARDS- Acute respiratory distress syndrome; CHF- congestive heart failure; OF- degree Fahrenheit; FiO2- fraction inspired oxygen; PaO2- Partial pressure of oxygen.

Annexure 2: Formulas for calculation of different rates/ratio.[13,14]

1. Crude infection rate $= \frac{\text{Total number of patients with HCAI}}{\text{Total number of patient}} \times 100$

2. Incidence density $= \frac{\text{Total number of HCAI episodes}}{\text{Total number of patient days}} \times 1000$

3. BSI rate $= \frac{\text{Total number of BSI identified}}{\text{Total number of patient days}} \times 1000$

4. CLA-BSI rate $= \frac{\text{Total number of CLA–BSI episodes}}{\text{Total number of central–line days}} \times 1000$

5. Central line utilization ratio $= \frac{\text{Total number of central–line days}}{\text{Total number of patients days}}$

6. CA-UTI rate $= \frac{\text{Total number of CA–UTI episodes}}{\text{Total number of urinary catheter days}} \times 1000$

7. Urinary catheter utilization ratio $= \frac{\text{Total number of urinary catheter days}}{\text{Total number of patients days}}$

8. VAP rate $= \frac{\text{Total number of VAP episodes}}{\text{Total number of ventilator days}} \times 1000$

9. Ventilator utilization ratio $= \frac{\text{Total number of ventilator days}}{\text{Total number of patients days}}$