Original Article

A study on microbial profile and antibiotic resistance in pediatric intensive care unit in a tertiary care hospital

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ABSTRACT

Objective: The objective of the study was to compare the microbial profile and antibiotic resistance pattern of isolates from pediatric intensive care unit (PICU) after dividing them as isolates detected within 48 h of admission and isolates detected after 48 h in PICU. **Materials and Methods:** This retrospective observational study was performed in a single tertiary care hospital's PICU for a period of 3 years from July 2016 to June 2019. The total number of cultures sent, type of specimen, number of positive cultures in different specimens, culture isolates and their antibiotic resistance, and sensitivity pattern were noted. Positive cultures were divided as admission isolates if detected from cultures sent within 48 h of admission and as PICU acquired isolate if detected from cultures sent after 48 h of admission to PICU. The epidemiological characteristics of these isolates and their antibiotic susceptibility were compared. **Results:** A total of 3157 cultures were sent and positive cultures were 345 (10.8%). Admission isolates were 147 (4.6%) and PICU-acquired isolates were 198 (6.2%). Tracheal secretions had the highest yield with 35.6% of the cultured specimen being positive. The most common admission isolates were *Escherichia coli* (18.3%), *Staphylococcus aureus* (15.3%), and *Klebsiella pneumoniae* (12.2%). The most common PICU acquired isolates were *K. pneumoniae* (19.1%), *E. coli* (16.6%), *Pseudomonas aeruginosa* (15.6%), and *Acinetobacter baumannii* (9.6%). The number of drug-resistant strains multidrug-resistant (MDR) (MDR *Acinetobacter*, MDR *E. coli*, and MDR *Klebsiella*) was significantly higher in PICU-acquired isolates ($p<0.05$) when compared to admission isolates. **Conclusion:** When starting empirical antibiotics in PICU; especially, after 48 h of admission, pediatric intensivists should be aware that the organisms are most likely to be less susceptible and also should be guided by the local microbiological data.

Key words: Antibiotic resistance, Intensive care unit acquired infections, Multidrug resistance

Health care-associated infections (HCAI) also known as nosocomial infections or hospital infections are one of the most frequent adverse events of health care [1-2]. The prevalence of infections in intensive care units (ICUs) varies among different studies, with adult studies reporting 37–51% while a pediatric study reported a prevalence of 8.2% of severe sepsis in pediatric ICUs (PICUs) [3-5]. The organisms isolated from ICUs not only differ from those isolated from the community or wards but also those isolated after the patient's prolonged stay in ICU. Archibald *et al*. in their study found the highest resistance rates in organisms isolated from ICU which were then reduced in a step-wise manner in organisms isolated from non-ICU patients and outpatients [6].

Monitoring for the prevalence of bacteria and their susceptibility pattern is necessary for developing and modifying hospital antibiotic policy. Those who come to PICU with infection might have acquired it in the community, ward, or from other referral hospitals. ICU-acquired infection is said to have occurred conventionally if the patient develops features of infection after 48 h of ICU stay. It is highly plausible that the bacteria and their susceptibility pattern might be different depending on whether the patient was admitted with infection or acquired infection during PICU stay.

The study aimed to divide all the isolates from PICU into those detected from cultures sent within 48 h of admission (PICU admission isolate) and those detected from cultures sent after 48 h of admission (PICU acquired isolates). The microbial profile and antibiotic susceptibility pattern between the two groups were compared to look for any differences.

MATERIALS AND METHODS

This retrospective observational study was conducted in a tertiary care PICU at Mazumdar Shaw Medical Centre, Narayana Health

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City, Bengaluru from July 2016 to June 2019. All cultures which were sent from PICU during the study period were traced. The total number of cultures sent, type of specimen sent for culture, the number of positive cultures in different specimens, culture isolates, and their antibiotic susceptibility and resistance pattern was noted. Positive isolates were divided as admission isolates if detected from cultures sent within 48 h of admission and PICU acquired isolates if detected from cultures sent after 48 h of admission to PICU.

Cultures were collected based on clinical indications only. Bacterial isolates were identified and *in-vitro* susceptibility testing was done using Vitek–2 Compact system which uses a fluorogenic methodology for organism identification and a turbidimetric method for susceptibility. Antibiograms were retrospectively collected for the most frequent Gram-positive and Gram-negative bacteria and for the most commonly prescribed antibiotics in the institution.

Data are presented as number of isolates and their percentages. Comparative analysis was performed using the Chi-square test for categorical variables. For those variables for which the expected value was <5, Fischer's exact test was employed. Tests were performed with the significance set at the $p<0.05$. The software used for analysis was SPSS 17.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

A total of 3147 cultures were sent from PICU during the study period. Out of the total cultures, 345 (10.8%) identified an organism. Admission isolates were 147 (4.6%) and PICU acquired isolates were 198 (6.2%). The distribution of culture positive specimens is depicted in Table 1. The positivity rate was very high for tracheal secretions (35.6%) as compared to blood (4.8%) and urine (9.7%).

Table 2 shows the isolates and their distribution as PICU admission isolates and PICU acquired isolates. Gram-negative isolates were significantly higher in both PICU admission (66.6%) and PICU acquired isolates (86.4%). Although the bacterial profile was almost similar in the two groups, *Staphylococcus aureus* was isolated significantly more in the PICU admission group. Furthermore, *Pseudomonas* and *Stenotrophomonas* were significantly more isolated in the PICU acquired group.

The most common isolates in our study were *Escherichia coli* (17.4%), *Klebsiella pneumoniae* (16.2%), and *Pseudomonas aeruginosa* (12.2%). The most common PICU acquired isolates were *K. pneumoniae* (19.1%), *E. coli* (16.6%), and *P. aeruginosa* (15.6%). Among the admission isolates, the most common were *E. coli* (18.3), *S. aureus* (15.6%), and *K. pneumoniae* (12.2%). Table 3 shows the distribution of culture isolates among blood, tracheal secretions, and urine. The table shows PICU acquired isolates in blood were all Gram-negative organisms and no Gram-positive organism.

Antibiogram of selected isolates between the 2 groups are compared in Table 4. There were no significant differences in the antibiograms of the Gram-positive strains (*S. aureus* and *Enterococcus* spp.) between PICU admission and PICU acquired isolates. Even though the number of methicillin resistant *S. aureus* (MRSA) was more in the PICU admission group compared to PICU acquired, it was not statistically significant. The number of vancomycin resistant enterococci (VRE) was more in PICU acquired group compared to the PICU admission group but there was no statistical significance.

Antibiograms of commonly isolated Gram-negative organisms (*A. baumannii, P. aeruginosa, K. pneumoniae,* and *E. coli*) in two groups were compared. PICU acquired *A. baumannii* and *E. coli* were significantly ($p<0.05$) more resistant to meropenem and imipenem as compared to PICU admission isolates. PICU acquired *K. pneumoniae* was more resistant to ceftazidime, cefepime, meropenem, and colistin. There was no statistically significant difference between susceptibility of PICU admission and PICU acquired strains of *P. aeruginosa* to any of the antibiotic tested. Multidrug resistant (MDR) strains such as MDR *E. coli*, MDR *Acinetobacter*, and MDR *Klebsiella* were significantly higher in the PICU acquired group compared to the PICU admission group

Table 1: Description of specimens-number and type of specimens and positivity rate

Type of specimen	Total cultures (3157)	Positive culture (n,%)(n=345–10.8%)	PICU admission isolate (n=147, 4.6%)	PICU acquired isolate (n=198, 6.2%)
Blood	1556	75 (4.8)	43	32
Tracheal secretions	348	124 (35.6)	29	95
ET secretions	252	104 (41.2)	23	81
Sputum/BAL	46	6 (13)	4	2
Tracheostomy	50	14 (28)	2	12
Urine	567	55 (9.7)	29	26
CSF	246	11 (4.4)	5	6
Stool	85	17 (20)	8	9
Pus	99	18 (18.1)	13	5
Pleural fluid	69	16 (23)	8	8
Peritoneum fluid	43	7 (16)	2	5
CVP tip	41	3 (7.3)	1	2
Others	103	15 (16.5)	9	6

CVP: Central venous pressure; CSF: Cerebrospinal fluid; BAL: Bronchoalveolar lavage; ET: Endotracheal; PICU: Pediatric intensive care unit

Table 2: Distribution of culture isolates as PICU admission and PICU acquired isolate

Bacteria	PICU admission isolate (n=147) (%)	PICU acquired isolate (n=198) (%)	Total isolates (n=345) (%)	p-value
Gram-positive bacteria	49 (33.3)	29 (14.6)	78 (22.6)	<0.001
S. aureus	23 (15.6)	10 (5.1)	33 (9.5)	<0.001
Streptococcus pneumoniae	8 (5.4)	4 (2)	12 (3.5)	0.08
CONS	5 (3.4)	3 (1.5)	8 (2.3)	1(F)
Enterococcus faecalis	2 (1.3)	4 (2)	6 (1.7)	1(F)
Enterococcus faecium	11 (7.4)	8 (4)	19 (5.5)	0.1
Gram-negative bacteria	98 (66.6)	169 (86.4)	267 (77.3)	<0.001
E. coli	27 (18.3)	33 (16.6)	60 (17.4)	0.6
K. pneumoniae	18 (12.2)	38 (19.1)	56 (16.2)	0.08
Acinetobacter baumannii	9 (6.1)	19 (9.6)	28 (8.1)	0.2
P. aeruginosa	11 (7.4)	31 (15.6)	42 (12.2)	0.02
Stenotrophomonas maltophilia	2 (1.3)	12 (6.1)	14 (4.1)	0.02(F)
Enterobacter	6 (4)	4 (2)	10 (2.9)	0.3
Serratia	0	3 (1.5)	3 (0.01)	0.2
Burkholderia cepacia	4 (2.7)	4 (2)	8 (2.3)	0.7
Candida species	5 (3.4)	12 (7)	17 (4.9)	0.2

F: Fischer's test was used; PICU: Pediatric intensive care unit; *S. aureus: Staphylococcus aureus; E. coli: Escherichia coli; K. pneumoniae: Klebsiella pneumoniae; P. aeruginosa: Pseudomonas aeruginosa*

Table 3: Distribution of culture isolates among different specimens

Organism	PICU admission isolate			PICU acquired isolate		
	Blood	Tracheal secretions	Urine	Blood	Tracheal secretions	Urine
Gram-positive organisms						
S. aureus	8	5			4	
CONS	3				2	
E. faecalis			4			
E. faecium	2		10		2	11
S. pneumoniae	7				3	
Gram-negative organisms						
E. coli	9	4	12	8	10	5
K. pneumonia	4	4	2	8	17	5
A. baumannii	1	2		4	11	1
P. aeruginosa	1	4	1	2	18	1
S. maltophilia		2		3	8	
Enterobacter species	2			1	2	
Serratia				1	1	
B. cepacia	3			2		
Candida species	3	2		3	3	3

PICU: Pediatric intensive care unit; *S. aureus: Staphylococcus aureus; E. coli: Escherichia coli; K. pneumoniae: Klebsiella pneumoniae; P. aeruginosa: Pseudomonas aeruginosa; E. faecalis: Enterococcus faecalis; E. faecium: Enterococcus faecium; S. pneumoniae: Streptococcus pneumoniae; A. baumannii: Acinetobacter baumannii; S. maltophilia: Stenotrophomonas maltophilia; B. cepacia: Burkholderia cepacia*

(Table 5). Two pan-resistant *Klebsiella* were isolated during the study period in the PICU on admission group. The source of the strain was from outside hospitals.

DISCUSSION

Our PICU is situated in a tertiary care center. Most of our patients (70%) are referred from surrounding hospitals and 30% of patients are admitted through emergency. The profile of patients admitted in our PICU is as follows: Infectious diseases (30%) mainly, dengue, rickettsial and bacterial sepsis, respiratory diseases (23%) mainly asthma, viral lower respiratory infections, bacterial pneumonia, and central nervous system diseases (25%). PICU has about 12% of hemato-oncology cases who are severely immuno compromised. These patients are managed in separate isolation beds in PICU. Furthermore, the respiratory cases are cohorted as per the diagnosis. Bed occupancy rates vary between 50 and 75% depending on the timing of the year, busiest being July to November.

Our study showed that PICU admission isolates were 42.6% and PICU acquired isolates were 57.4%. Tan *et al*. in their study has

Table 4: Comparison of antibiograms of selected isolates between PICU admission and PICU acquired group

Organism	PICU on admission (X/Y) (%)	PICU acquired (X/Y) (%)	p-value
A. baumannii			
Meropenem	3/8 (37.5)	1/17 (5.8)	0.08(F)
Imipenem	3/8 (37.5)	1/18 (5.5)	0.07(F)
Tigecycline	3/8 (37.5)	8/13 (61.5)	0.38(F)
Colistin	7/7 (100)	16/16 (100)	–
E. coli			
Meropenem	13/16 (81.2)	13/24 (54.1)	0.04
Imipenem	17/19 (89.4)	11/21 (52.3)	0.01
Tigecycline	14/14 (100)	14/14 (100)	–
Colistin	13/13 (100)	15/15 (100)	–
K. pneumoniae			
Ceftazidime	7/13 (53.8)	2/28 (7.1)	0.002(F)
Cefepime	6/14 (42.8)	4/30 (13.3)	0.05(F)
Meropenem	5/13 (38.4)	4/31 (12.9)	0.037(F)
Tigecycline	5/11 (45.4)	12/20 (60)	0.4(F)
Colistin	12/12 (100)	21/28 (75)	0.02(F)
P. aeruginosa			
Ceftazidime	9/12 (75)	15/23 (65.2)	0.7(F)
Cefepime	8/11 (72.7)	11/15 (73.3)	1(F)
Meropenem	7/10 (70)	8/13 (61.5)	1(F)
Colistin	9/9 (100)	13/13 (100)	–
S. aureus			
Cotrimoxazole	14/20 (70)	3/4 (75)	1(F)
Doxycycline	19/21 (90.4)	4/4 (100)	1(F)
Vancomycin	18/18 (100)	4/4 (100)	–
Linezolid	8/8 (100)	1/1 (100)	–
Teicoplanin	18/18 (100)	4/4 (100)	–

X: Number of isolate sensitive to particular antibiotic; Y: Total number of particular isolates; F: Fisher's test was used; PICU: Pediatric intensive care unit; *S. aureus: Staphylococcus aureus; E. coli: Escherichia coli; K. pneumoniae: Klebsiella pneumoniae; P. aeruginosa: Pseudomonas aeruginosa; A. baumannii: Acinetobacter baumannii*

Table 5: Distribution of antibiotic resistant organisms between PICU admission isolates and PICU acquired isolates

Organism	PICU admission isolates (X/Y) (%)	PICU acquired isolate (X/Y) (%)	p-value
MDR *Acinetobacter*	2/9 (22.2)	13/19 (68.4)	0.04 (F)
XDR *Acinetobacter*	0/9	1/19 (5.2)	
ESBL *E. coli*	16/27 (59.2)	11/33 (33.3)	0.04
MDR *E. coli*	2/27 (7.4)	10/33 (30.3)	0.04
XDR *E. coli*	0/27	1/27 (3)	
Carbapenemase producer *E. coli*	1/27 (3.7)	3/33 (9)	0.61 (F)
ESBL *Enterobacter*	0/6	1/4 (25)	
MDR *Enterobacter*	2/6 (33.3)	1/4 (25)	1.0
ESBL *Klebsiella*	5/18 (27.7)	6/38 (15.7)	0.30 (F)
MDR *Klebsiella*	4/18 (22.2)	22/38 (57.8)	0.01
Carbapenemase producing *Klebsiella*	2/18 (11.1)	0/38	
XDR *Klebsiella*	1/18 (5)	3/38 (7.8)	1.0
Pan resistant *Klebsiella*	2/18 (11)	0/38	
MDR *Pseudomonas*	2/11 (18.1)	3/31 (9.6)	0.59 (F)
MRSA	13/23 (56.5)	4/10 (40)	0.3
VRE	2/11 (18.1)	3/8 (37.5)	0.6 (F)

X: Number of isolates with the particular resistance; Y: Total number of particular isolates; F: Fisher's test was used; ESBL: Extended spectrum beta-lactamase producer; MDR: Multidrug resistant strain, defined as acquired non-susceptibility to at least one agent in three or more anti-microbial categories (14), XDR: Extensively drug resistant strain, defined as non-susceptibility to at least one agent in all but two or fewer anti-microbial categories (i.e., bacterial isolates remain susceptible to only one or two categories) (14), VRE: Vancomycin resistant *Enterococcus*. MRSA: Methicillin resistant *S. aureus*

24.9% of isolates as ICU on admission isolates and 75.1% as ICU acquired isolates [7]. Although not a study on similar lines as ours, the study on sepsis in the European ICUs has higher non-ICU acquired sepsis as compared to ICU acquired sepsis (76.3% vs. 23.7%) [3]. The differences between our study and the other two studies are probably explained by different patient profiles in the ICUs.

In our study, Gram-negative isolates predominated overall (77.6%) and also in both PICU admission (66.3%) and PICU acquired isolate group (86.4%). These results indicate that infections by Gram-positive organisms are certainly very less as compared to Gram-negative organisms. Similar findings which indicate predominance of Gram-negative organisms are shown in other studies [4,8,9]. Summary of data reported to the National Healthcare Safety Network (NHSN), 2015-2017 shows a higher number of Gram-positive organisms (44.6%) as compared to our study [10]. The difference may be because NHSN collected data on all pediatric HCAI's including PICU, pediatric wards, and oncology units while our study included PICU only.

Most of the organisms isolated from ICUs usually are *E. coli, Klebsiella, Pseudomonas, Acinetobacter, Enterobacter*, and *S. aureus*. Ling *et al*. in their meta-analysis on burden of HCAIs in Southeast Asia found *P. aeruginosa, Klebsiella* species, and *A. baumannii* as the most common organisms causing HCAI [8]. Singhi *et al*. in a study on nosocomial bloodstream infection in PICU concludes that Gram-negative organisms are predominant isolates and *K. pneumoniae* (20.1%), *S. aureus* (16.4%), *Enterobacter* spp. (16.6%), and *Acinetobacter* (8.6%) being commonest [9]. In the international study on prevalence and outcomes of infection in ICUs, of the positive cultures, 62% detected Gram-negative organisms with *S. aureus* (20%) being commonest Gram-positive organism and *Pseudomonas* species (19.9%) and *E. coli* (16%) being most common Gram-negative bacteria [4]. Our study also showed a similar pattern of the organisms (*E. coli* – 17.4%, *K. pneumoniae* – 16.2%, *P. aeruginosa* – 12.2%, and *S. aureus* – 9.5%).

Our study showed predominance of Gram-negative bacteria such as *E. coli*, *Klebsiella,* and *Pseudomonas* in both the groups, *S. aureus* showed higher presence in PICU admission group. In a similar study by Tan *et al*., most common ICU acquired strains were *A. baumannii* (19.5%), *P. aeruginosa* (15.6%), and *S. maltophilia* (11.5%), while the ICU on admission strains were *P. aeruginosa* (19.6%), *A. baumannii* (15.6%), and *K. pneumoniae* (13.3%). *S. aureus* was present in both the groups in 10.7% and 10.6% cultures, respectively [7].

In our study, PICU acquired *A. baumannii*, *E coli,* and *K. pneumoniae* were more resistant than admission isolates. Similar finding was reported by Tan *et al*., where in apart from the above-mentioned organisms *P. aeruginosa* is also resistant to meropenem and imipenem [7]. Significantly higher carbapenem resistant *Klebsiella* species is noted in central line associated blood stream infections (CLABSIs) in PICU as per summary of data reported to NHSN 2015-2017 [10]. Haque *et al*. in their overview mention Gram-negative organisms causing HCAI's have higher (20–40%) resistance and also device associated HCAI's have highest antimicrobial resistant organisms [11]. In an Indian study conducted in adult respiratory ICU, in patients with prior antibiotic use, Gram-negative infections were common with *Acinetobacter* and *Klebsiella* spp. having higher resistance [12].

Our study has some limitations. First, it was a single center study. Every hospital and every ICU has its own microbiological profile and susceptibility rates; hence, our findings may not be similar to other PICUs. Second, we did not collect the demographic data, clinical findings, and use of devices such as ventilator and central line, which would have enabled us to identify ventilator associated pneumonia, CLABSI, and catheter associated urinary tract infection. Thus, our study does not differentiate the organisms between colonization and causative organism. Third, our PICU has lot of admissions from hemato-oncology wards including post-bone marrow patients and post-operative surgical patients who may have had prolonged hospital stay and exposure to multiple antibiotics before admission to PICU thus affecting the profile of PICU admission isolates. Finally, we did not analyze the data with respect to patient coming from community, ward or from referring hospital which would have helped to know the profile of the organisms in a better way.

Our study found that the Gram-negative organisms from PICU acquired isolates were significantly resistant to antibiotics including carbapenems. Initiation of appropriate antibiotic therapy is essential in sick children admitted in PICU, if not morbidity and mortality increase significantly. Carbapenems are frequently used in PICUs for infections but with the advent of carbapenem resistant *Acinetobacter*, *E coli*, *Klebsiella,* and *Pseudomonas*, use of carbapenems in PICU acquired infection will lead to failure of initial empiric antibiotic therapy leading to increased morbidity and mortality. New class of antibiotics is not being developed and very few are in the pipeline; hence, strict infection control measures are needed to reduce the prevalence of MDR strains otherwise we may go back to pre-antibiotic era [13].

CONCLUSION

Although the organisms in PICU admission and the PICU acquired group were almost similar, the resistance among PICU acquired isolates was significantly high. Hence, while starting empirical antibiotics in PICU; especially, after 48 h of admission, pediatric intensivists should be aware that the organisms are most likely to be less susceptible.

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