Epidemiology of Bacterial Infections in Pediatrics Intensive Care Unit (PICU) at Zagazig University

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ABSTRACT

Background: Infections are one of the commonest causes of mortality in the pediatric intensive care unit (PICU), with a mortality of up to 50%, depending on the origin of the infection. At our study death rate was 35.8% and survival was 64.2%. **Objective:** This study aimed to identify the most common bacterial infections in pediatric intensive care unit (PICU) at Zagazig University and to describe their epidemiologic and microbiologic characteristics, and determine other risk factors for developing bacteremia.

Patients and Methods: This cross-sectional study was conducted over a period of 6 months from June 2017 to November 2017; it included 240 pediatric patients admitted at Pediatric Intensive Care Unit (PICU), Faculty of Medicine, Zagazig University Hospitals.

Results: Prolonged hospital stay, urinary catheter (UC) non-significantly increased risk of infection. On the other hand, central venous catheter (CVC), mechanical ventilation (MV) significantly increased risk of infection. There was statistically non-significant relation between outcome and type of organism.

Conclusion: MV and UC were significantly associated with healthcare-associated infections (HAIs). Patients with HAIs had significantly longer length of stay (LOS).

Keywords: Bacterial Infections, Epidemiology, Pediatrics Intensive Care Unit

INTRODUCTION

In hospitals the incidence of infection is highest in the intensive care units, adult and children and these would seem suitable areas for targeting efforts to reduce bacteremia **(1).** Although the number of cases of bacteremia in hospital is small in comparison with urinary and respiratory tract infections, the morbidity and mortality rates are high. Identification of those at risk could help focus efforts on prevention and early diagnosis should lead to earlier and more appropriate therapy for those in whom the diagnosis is suspected **(2).**

Blood culture remains the gold standard in diagnosing causative pathogens; however, the average time to detection of positive cultures is16 hours and may be as long as 24 to 48 hours. Blood cultures are used to identify microorganisms in blood and to assist in guiding antimicrobial therapy. Common sources of bacteria including genitourinary tract, respiratory tract, abscesses, surgical wounds, biliary tract and prosthetic cardiac valves **(3).**

Blood stream infection (BSIs) caused by commensal species play important roles in infection in the PICU, which poses difficulties in determining true pathogens from contaminants. It also served as the single most important type of infection because of their high frequency (59%) and potential life threatening consequences **(3).**

The aim of this study was to identify the most common bacterial infections in Pediatric Intensive Care Unit (PICU) at Zagazig University and to describe their epidemiologic and microbiologic characteristics, and determine other risk factors for developing bacteremia.

PATIENTS AND METHODS

This cross-sectional study was conducted over a period of 6 months from June 2017 to November 2017; it included (240 patients). This study was carried out in Pediatric Intensive Care Unit and Medical Microbiology and Immunology Department, Faculty of Medicine, Zagazig University Hospitals.

Inclusion Criteria: All children admitted to Pediatric Intensive Care Unit (PICU) at Zagazig University Hospitals within 6 months and stayed for 48 hours or more.

Exclusion criteria: Absence of informed consent, immunodeficiency, and age <1 month or >16 years.

All patients were subjected to the following:

1) **Complete history taking,** with stress on risk factor of infection like mechanical ventilation, central venous catheterization and urinary catheterization.
2) **Complete physical examination.**
3) **Investigations:** including CBC, CRP, liver function, kidney function and chest X-ray.
4) **Bacteriologic cultures** from different sites were collected from blood, urine, sputum, and cerebrospinal fluid if needed. On suspicion, cultures were taken per suspected site(s) of infection. Samples from different sites might be collected from same patient.
5) **Patients were divided according to blood culture results to 2 groups:** culture +ve and culture –ve group.
6) **Catheter-associated urinary tract infection (CAUTI):** 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**

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bloodstream infection (CLABSI): It is a laboratory-confirmed bloodstream infection where central line (CL) 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 was identified by using a combination of imaging, clinical, and laboratory criteria.

7) **Material for culture:** (A) Blood culture bottles (Egyptian diagnostic media" Egypt). (B) Nutrient agar (Oxoid, UK): for preparation of blood and chocolate agar. (C) MacConkey agar (Oxoid, UK). (D) Blood agar. (E) Chocolate agar. (F) BD GASPAK EZ Anaerobic container system.

Samples Collection:
Blood and others (urine, sputum, CSF)

Methods for Cultivation:
(1) The protective cover was removed from the top of the culture then the top of the bottle was wiped using an ethanol-ether.
(2) The collected blood was dispensed in the culture bottle by inserting the needle through the rubber liner.
(3) The top of the culture bottle was wiped with ethanol swab and the protective cover was replaced. (
4) The blood was mixed with the broth without delay.
(5) The bottles were labeled with the name "the number of the patient and the date of collection.
(6) The blood culture bottles were incubated at 37°C.
(7) Blind subculture was done after the first night incubation on: (i) Blood agar: two blood agar plates were cultivated, the first plate was incubated at 37°C for 48 hours aerobically using gas generation kit anaerobic system and placed in anaerobic gas jar. (ii) Chocolate agar: the chocolate agar plate was incubated aerobically in 5-10% CO_2 incubator at 37°C for 48 hours. (iii) MacConkey Agar: MacConkey agar plate was incubated aerobically at 37°c for 48 hours [(4)]. (8) All plates were examined after the incubation period for growth.

Negative blood culture bottles were checked daily for evidence of macroscopic growth (e.g., hemolysis "turbidity" gas production and the presence of visible colonies or a layer of growth over the fluid surface). If no evidence of microbial growth after 10 days of incubation, Gram satins and blind subcultures were done before considering the culture as negative [(5)].

Ethical consent:
This study was ethically approved from, Institutional Reviewer Board (IRB) in Faculty of Medicine, Zagazig University Hospital. A written consent from parents or caregivers of every case that participated in this research was taken. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis
Data were checked, entered and analyzed using SPSS version 23 for data processing. Data were expressed as number and percentage for qualitative variables and as median, range, and mean ± standard deviation (SD) for quantitative one. Chi- square test (X^2) was used to compare qualitative data. Binary logistic regression analysis was used to calculate odds ratio (OR). P value < 0.05 was considered significant.

RESULTS
This table shows that 57.5% of patients were of age between 1-5 years and shows that percent of male to female admitted to PICU were nearly equal **(Table 1)**.

Table (1): Descriptive data of the studied group

Variables	Studied cases (n=240)	
	N	%
Age (years):		
Median	1.5	
Range	2 months – 13 years	
Age groups:		
1 month – 1 year	74	30.8
1 – <5 years	138	57.5
5 – 13 years	28	11.7
Sex:		
Male	117	48.8
Female	123	51.2
Length of stay (days)		
Mean ± SD	12±2.81	
Min – max	2-365	
Weight (Kg)		
Mean ± SD	11.13±2.76	
Min – max	1.5-78	
Heart rate/min		
Mean ± SD	133.2±13.01	
Min – max	99-174	
Respiratory rate/min		
Mean ± SD	38.7±8.01	
Min – max	20-62	

This table shows that (30.4%) of the study group had positive blood culture, (11.3%) had positive urine culture, and (4.2%) had positive sputum culture **(Table 2)**.

Table (2): Type of culture in studied group

Variables	Frequency (240)	%
Cultures		
Blood	73	30.4%
Urine	48	20%
Sputum	10	4.2%
Cerebrospinal fluid (CSF)	3	1.3%
Central venous catheter (CVC)	23	8.3%

This table demonstrates that the most frequent isolated organism was Staphylococcus aureus (58.9%) of blood cultures, while the least frequent one was Enterobacter bacteria (2.7%) of blood cultures **(Table 3)**.

Table (3): Type of organisms from different cultures

Organisms	Frequency (240)	%
Blood	73	
Acinetobacter	3	4.1
Enterobacter	2	2.7
Klebsiella	17	23.3
Pseudomonas	8	11.0
Staphylococcus aureus	43	58.9
Urine	48	
Klebsiella	16	33.3
Staphylococcus aureus	32	66.7
Sputum	10	
Acinetobacter	1	10.0
Enterobacter	1	10.0
Klebsiella	1	10.0
Pseudomonas	2	20.0
Staphylococcus aureus	5	50.0
CSF	3	
Klebsiella	2	66.7
Staphylococcus aureus	1	33.3
CVC	23	
Klebsiella	8	34.5
Staphylococcus aureus	15	65.5

About 41% of patients with positive culture had VAP, 31.5% had CLBSI, and 65.7% had CAUTI **(Table 4)**.

Table (4) Distribution of the studied patients according to site of infection

Site of infection	N (73)	%
Ventilator acquired pneumonia **(VAP)**	30	41.1
Central line associated blood stream infection **(CLBSI)**	23	31.5
Catheter association urinary tract infection **(CAUTI)**	48	65.7

Out of cases with positive culture of Klebsiella 94.1% had CAUTI. Out of cases with positive culture of staph, 74.4% had CAUTI. All patients with positive culture with pseudomonas, enterobacter and acinetobacter had VAP **(Table 5).**

Table (5) Isolated organisms according to site of infection

	N=73	%
Klebsiella (n=17):		
VAP	7	41.2
CLBSI	8	47.1
CAUTI	16	94.1
Staph aureus (n=43):		
VAP	10	23.3
CLBSI	15	34.9
CAUTI	32	74.4
Pseudomonas (n=8): VAP	8	100%
Acinetobacter (n=3): VAP	3	100%
Enterobacter (n=2): VAP	2	100%

VAP: Ventilator acquired pneumonia.
CLBSI: Central line associated blood stream infection.
CAUTI: Catheter association urinary tract infection.

There was statistically significant relation between the studied groups regarding prolonged PICU stay, mechanical ventilation, or urinary catheter. However, there was non-significant relation between them regarding gender, or age group. Female gender and age from 5 to 13 years non-significantly protected from infection. Prolonged stay>15 days, mechanical ventilation, urinary catheter, use of CVC, increased risk of infection by 1.83, 2.99, 2.96, and 2.8 folds respectively **(Table 6)**.

Table (6) Comparison between patients with positive and negative blood culture regarding risk factors

Factor	Culture		Total	Test		Odds ratio (95% CI)
	Positive	Negative		χ^2	p	
	N=73(%)	N=167(%)	N=240(%)			
Age groups:						
1month-1year	23 (31.1)	51 (68.9)	74 (30.9)	6.015	0.049*	1.15 (0.63-2.12)
1 - <5 year	47 (34.1)	91 (65.9)	138 (57.5)			0.27 (0.06-0.91)
5 – 13 years	3 (10.7)	25 (89.3)	28 (11.6)			
Gender:						
Female	33 (27)	89 (73)	122 (50.4)	1.329	0.249	0.72 (0.42-1.26)
Male	40 (33.9)	78 (66.1)	118 (49.6)			
Length of Stay :						
≤15 day	40 (25.8)	115 (74.2)	155 (64.6)	4.395	0.036*	1.83 (1.04-3.21)
>15 days	33 (38.8)	52 (61.2)	85 (35.4)			
MV:						
Yes	51 (41.1)	73 (58.9)	124 (51.7)	13.91	<0.001**	2.99 (1.66-5.36)
No	22 (19)	94 (81)	116 (48.3)			
CVC:						
Yes	37 (32.2)	43 (53.8)	80 (33.3)	14.214	<0.001**	2.96 (1.67-5.27)
No	36 (22.5)	124 (77.5)	160 (66.7)			
Urinary catheter:						
Yes	48 (41.4)	68 (58.6)	116 (48.3)	12.749	<0.001**	2.8 (158-4.96)
No	25 (20.2)	99 (79.8)	124 (51.7)			

* Statistically significant, ** Statistically highly significant, CI confidence interval

Age and weight were significantly lower in patients with positive blood culture. On the other hand, they reported significantly longer PICU stay **(Table 7)**.

Table (7) Comparison between the studied groups regarding age, weight, length of stay and vital signs

Parameters	Culture					
	Positive		Negative		Mann-Whitney/t test	p
	Mean±SD	Median (range)	Mean±SD	Median (range)		
Age (years)	1.74±1.56	1.5 (0.17- 10)	2.78±3.01	2 (0.17– 13)	-2.136	0.033*
Weight (kg)	11.13±2.76	9 (4 – 45)	14.71±3.71	11 (1.5 – 78)	-2.341	0.019*
Heart rate (/min)	133.67±14.13	99 – 170	133±12.51	99 - 174	0.367	0.714
Respiratory rate	39.12±8.34	21 - 55	38.52±7.98	20 - 62	0.531	0.596
Length of stay	26.25±5.83	14 (1 - 365)	18.48±4.63	11 (1 – 365)	-2.332	0.02*

*Statistically significant

Mechanical ventilation, and CVC were independent risk factor for infection among the studied groups. Mechanical ventilation increased the risk of infection by 2.15 folds while CVC were associated with 3.35 fold elevated risk of infection. On the other hand, prolonged hospital stay, and urinary catheter were non-significantly associated with developing infection **(Table 8)**.

Table (8): Binary logistic regression for the risk factors of infection among the studied group

Risk factors	β	Odds ratio	95% C.I.		p
			Lower	Upper	
Prolonged LOS (>15 days))	0.553	1.738	0.939	3.216	0.078
MV	0.765	2.15	1.065	4.339	0.033*
Urinary Catheter	0.688	1.989	0.988	4.006	0.054
CVC use	1.21	3.353	1.81	6.211	<0.001**

* Statistically significant, ** Statistically highly significant

DISCUSSION

The prevalence of HAIs in our PICU was 30.4%, which constitutes a significant cause of illness and expense. Our results are higher than results found by **Hassan *et al.*** [6] who found incidence of HAIs were 8% and 21.1% respectively.

As regard length of PICU stay, it was significantly longer in culture +ve group than culture –ve group and increased LOS>15 days was associated with increased risk of infection 1.83 fold. This comes in agreement with **Rosenthal *et al.*** [7] who found that prolonged LOS increased incidence of HAIs up to 96.3%. Previous studies also consider prolonged LOS as a risk factor for HAIs, as longer hospitalization leads to colonization of patients by pathologic organisms and longer duration invasive procedures which favors the development of HAIs [8]**.** Also, we found that MV, CVC, UC increased risk of infection by 2.99, 2.8 and 2.96 folds respectively, when comparing between culture +ve and culture –ve groups. Although we found length of stay >15 days and UC increased risk of infection when comparing between the two groups of patients. However, when we analyzed data using binary logistic regression we observed that MV and CVC were considered as independent risk factors of infection [OR 2.1 and 3.3] while length of stay >15 days and UC were non-significantly associated with developing infection.

Our result regarding increased infection in mechanically ventilated patient agrees with **Moustafa *et al.***[9] and is also comparable to many studies in the USA and China [10, 11].

Out of 240 cases, 73 cases had positive blood culture, the commonest organism was staphylococcus aureus (58.9%) followed by Klebsiella (23.3%) and pseudomonas (11%). This comes in agreement with **Hassan *et al.*** [6] who observed that the most frequent gram positive organism associated with HAIs was Staphylococcus aureus with a rate of 37%. On the contrary, **Moustafa *et al.*** [9] found that 72% of isolated organisms were gram positive bacteria and 28% were gram negative bacteria. Also, **Alotaibi *et al.*** [12] showed Klebsiella species as the commonest organism in their PICU. CAUTI was the most frequent reported site of infection in this study (65.7%) followed by VAP (41.1%) and CLBSI 31.5%. Also, **Hassan *et al.*** [6] found UTI was the most common HAIs in their PICU (55.6%). These results are different from a study by **Moustafa *et al.*** [9] who reported that VAP was the most frequent episodes in their study. CLBSI rate (31.5%) was lower than that reported by other studies (47% and 48%) [13,14] and higher than **Moustafa *et al.*** [9] who found CLBSI rate was (24%). Discrepancy of results of site of infection may be due to different types of patients and different risk factors.

In agreement with literature available on PICU[8], the mortality rate in the current study was higher for the patients with HAIs than those free of HAIs.

CONCLUSION

MV and UC were significantly associated with HAIs. Patients with HAIs had significantly longer LOS.

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