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Trends in Nosocomial Blood Stream Infection in PICU of a Tertiary Care Hospital

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ABSTRACT

Objective: To determine the antimicrobial sensitivity pattern for local pathogens in the Pediatric Intensive Care Unit of Children's Hospital, Lahore, Pakistan, and its impact on patient outcomes.
Study Design: Analytical cross-sectional.
Place and Duration of Study: Children's Hospital, Lahore, Pakistan, from Feb 2021 to Feb 2022.
Methodology: We enrolled all the children meeting our inclusion criteria and who were admitted to Pediatric Intensive Care Unit. Blood cultures were sent after 48 hours of admission with those having positive blood cultures considered to have nosocomial bloodstream infection. Demographic, microbiological, and other variables were documented on a data collection form. All data was analyzed on Statistical Package for Social Sciences (SPSS) version 26.0.
Results: We enrolled 1,157 pediatric patients with a median age of 3.0 years. Bloodstream Infection was confirmed in 14.7% of patients, with significantly younger patients experiencing bloodstream infection (median age 1.4 years vs. 4.0 years, p=0.002). Bloodstream Infection patients demonstrated markedly longer hospital stays (15.0 vs. 7.0 days, p<0.001) and extended mechanical ventilation duration (9.0 vs. 3.0 days, p=0.003). Microbiological analysis of positive cultures revealed predominance of gram-negative organisms (145(86%), with gram-positive organisms accounting for 14%.
Conclusion: The frequency of nosocomial bloodstream infection in Pediatric Intensive Care Unit was found to be quite high, leading to longer duration of stay and poorer outcomes. The emergence of highly resistant organisms is alarming, which underscores the need for rational use of antibiotics and strict infection control programs.

Keywords: Bloodstream infections, Community-acquired infections, Gram positive, Nosocomial.

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INTRODUCTION

Nosocomial bloodstream infections (BSI) in pediatric population is a major, preventable infectious complication in critically sick patients due to which these are a major health problem resulting in high morbidity, mortality, and increased burden of health costs.[1,2] Hospital-acquired infections are often caused by invasive procedures, monitoring devices and lapses in infection control policies.[3] According to the Centers for Disease Control and Prevention, a nosocomial infection is defined as an infectious event that is diagnosed more than 48 hours after admission without evidence that the pathogen was already in the incubation phase1 especially as most common nosocomial infections are bloodstream infections resulting in a threefold increased risk of death.[4,5] These infections are usually caused by multidrug resistant organisms where empiric antibiotic treatment, started within the first hour, reduces mortality.[6] Thus, knowing local pathogens and their antimicrobial sensitivity pattern is necessary before starting treatment especially as coagulase-negative staphylococci were the most prevalent pathogens in the United States,[7] while in Pakistan, the majority of isolates were Gram-negative bacteria and Klebsiella was the most common pathogen.[3] Additionally, emerging antibiotic resistance to treat nosocomial infections is alarming with great difficulty encountered in treating multidrug-resistant pathogens, resulting in higher mortality,[8] due to which continuous surveillance of pathogens and their antimicrobial susceptibility is essential.[3] As there is limited data from Pakistan, the aim of this study was to find out local pathogens and their antimicrobial sensitivity pattern.

METHODOLOGY

This cross-sectional study was conducted at the PICU of Children's Hospital, Lahore, Pakistan, from February 2021 to February 2022, after obtaining ethics approval from the Institutional Review Board vide certificate number 2021-212-CHICH. A total of 1148 admitted patients were included in our study using purposive sampling technique. The sample size was calculated using OpenEpi, with confidence level of

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95% and assumed frequency of 31.2 cases per 1000, as reported in literature.[9]

Inclusion Criteria: All children admitted to the PICU from February 2021 to February 2022 under the age of 12 years, with no previous history of comorbidities or chronic infections were included.

Exclusion Criteria: Patients with positive blood culture at the time of admission, patients who were discharged or expired within 48 hours of admission were excluded.

Blood samples of all study participants were sent for culture on admission. Those children who were culture positive were considered as nosocomial bloodstream infections. Variables including demographic data, organism isolated on blood culture and its sensitivity pattern, length of PICU stay, need and duration of mechanical ventilation, and outcome, in terms of fatality or discharge, were documented on a predesigned data collection tool. All data was analyzed using Statistical Package for the Social Sciences (SPSS) version 26.0 and a *p*-value of ≤0.05 was considered statistically significant.

RESULTS

We enrolled 1148 patients for this study, where the median (IQR) age of patients was 3.0(7.0) years with age ranges from 0 to 14 years. Among these, 734(63.9%) were males and 423(36.1%) were females. Nosocomial BSI was suspected in 389(33.9%) patients, however, this was confirmed by a positive blood culture report in only 169(14.7%) patients. Median (IQR) age of patients with BSI was 1.4(5.5) as compared to non-BSI of 4.0(8.0) years (*p*-value=0.002). The median (IQR) duration of stay of children with nosocomial BSI was 15.0(28) days compared to 7.0(11) days in those without nosocomial BSI (*p*-value<0.001). The median (IQR) days of mechanical ventilation in children with nosocomial BSI were 9.0(22) as compared to 3.0(10) in those without nosocomial BSI (*p*-value<0.003) Table-I. Out of 169 nosocomial BSI-positive patients, 77(45.5%) were lost either because of death or leaving against medical advice. Among 979 patients without nosocomial BSI, 339(34.6%) expired or left against medical advice (*p*-value=0.006) (Table-II) Among the 169 positive cases of BSI, only 24(14%) cultures showed gram-positive organisms whereas 145(86%) cultures showed gram-negative organisms. No fungi were isolated from the blood cultures. The most common organism detected was *Pseudomonas spp*. 59(35%), followed by *Serratia spp*. 28(16.5%), Klebsiella 19(11%), *Staphylococcus epidermidis* 19(11%), *Acinetobacter spp*. 18(10.5%), *Enterobacter spp*. 12(7%), *Staphylococcus aureus* 5(3%), *Escherichia Coli* 4(2.5%), *Citrobacter spp*. 3(2%), Salmonella 2(1%), as shown in Table-III while the susceptibility pattern of the isolated organisms is shown in Table-IV. Gram-negative organisms were resistant to commonly used first-line antibiotics like Co-amoxiclav and Ceftriaxone, however, both gram-positive and negative organisms showed good sensitivity to Amikacin. Klebsiella was found to be the most resistant organism, sensitive only to Colistimethate. Gram-positive organisms showed good sensitivity to Vancomycin, Linezolid, Teicoplanin, and even Amikacin.

Table-I: Comparison of Age, Length of PICU Stay and Mechanical Ventilation (n=1148)

Variable	Culture	Median (IQR)	*p*-value (≤ 0.05)
Age (years)	Positive	1.4(5.5)	<0.002
	Negative	4.0(8.0)	
Length of PICU stay (days)	Positive	15.0(28)	<0.001
	Negative	7.0(11)	
Duration of Mechanical Ventilation (days)	Positive	9.0(22)	<0.003
	Negative	3.0(10)	

Table-II: Comparison of Outcome in Both Groups (n=1148)

Outcome	Nosocomial BSI		Total	*p*-value (≤ 0.05)
	Positive	Negative		
Discharge/ Shift out	92(12.6%)	640(87.4%)	732(100.0%)	.006
Expired/ LAMA	77(18.5%)	339(81.5%)	732(100.0%)	
Total	169(14.7%)	979(85.3%)	1148(100.0%)	

LAMA: Left Against Medical Advice

Table-III: Pattern of Micro-organisms in Blood Culture Positive Cases (n=169)

Type of Organisms	Organisms	n(%)
Gram Negative	Pseudomonas Spp.	59(35%)
	Serratia Spp.	28(16.5 %)
	Klebsiella Spp.	19(11%)
	Acinetobacter	18(10.5%)
	Enterobacter Spp.	12(7%)
	Escherichia Coli	4(2.5%)
	Citrobacter Spp.	3(2%)
	Salmonella	2(1%)
Gram Positive	Staphylococcus Epidermidis	19(11%)
	Staphylococcus Aureus	5(3%)

DISCUSSION

Table-IV: Sensitivity Pattern of Microorganisms in Blood Culture (n=169)

Gram Negative Organisms n (%)										
Organisms	**Co-Am oxiclav**	**Amika cin**	**Tobra mycin**	**Ceftaz idime**	**Ceftri axone**	**Cipro floxacin**	**Sulbactam /cefo perazone**	**Tazo bactam**	**Merop enem**	**Co-trimoxaz ole**
Pseudomonas Spp.	8 (14%)	49 (83%)	9 (16%)	12 (20%)	6 (10%)	14 (23%)	18 (30%)	13 (22%)	16 (27%)	31 (53%)
Serratia Spp.	1 (4%)	18 (64%)	3 (12%)	1 (4%)	1 (4%)	1 (4%)	1 (4%)	2 (8%)	2 (8%)	15 (54%)
Klebsiella Spp.	0 (0%)	2 (11%)	0 (0%)	1 (5%)	1 (5%)	2 (11%)	3 (16%)	2 (11%)	2 (11%)	3 (16%)
Acinetobacter	0 (0%)	6 (33%)	4 (22%)	0 (0%)	0 (0%)	0 (0%)	8 (44%)	1 (5%)	1 (5%)	2 (11%)
Enterobacter Spp.	0 (0%)	7 (58%)	2 (17%)	1 (8%)	0 (0%)	2 (17%)	2 (17%)	2 (17%)	3 (25%)	6 (50%)
Escherichia Coli	3 (75%)	4 (100%)	4 (100%)	1 (25%)	1 (25%)	2 (50%)	4 (100%)	4 (100%)	4 (100%)	4 (100%)
Citrobacter Spp.	0 (0%)	2 (67%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (33%)	1 (33%)	0 (0%)	1 (33%)
Salmonella	0 (0%)	1 (50%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (100%)	0 (0%)
Gram Positive Organisms n (%)										
Organisms	Co-Am oxiclav	Amika cin	Vanco mycin	Ceftaz idime	Ceftri axone	Cipro floxacin	Linzolid	Teico planin	Merop enem	Imipe nem
Staphylococcus Epidermidis	3 (16%)	17 (89%)	19 (100%)	8 (42%)	8 (42%)	9(47%)	17 (89%)	19 (100%)	16 (85%)	17 (89%)
Staphylococcus Aureus	1 (20%)	4 (80%)	5 (100%)	1 (20%)	- -	2(40%)	5 (100%)	5 (100%)	3 (60%)	3 (60%)

Nosocomial Bloodstream Infections (BSIs) are a major challenge for the intensivist in PICU because of changing bacterial etiology and the emergence of antimicrobial resistant strains.[10] Among the nosocomial infections, BSI are the most common and have a significant negative impact on morbidity and mortality. BSIs are more common in PICU than in adult ICU or pediatric wards as their younger age makes patients more susceptible to acquiring infections from their surroundings with malnutrition, immune-compromised state, and the use of invasive devices for monitoring and management in PICU also worsening outcomes.[11,12] The prevalence of nosocomial BSI varies in different studies done in the last 5 years from 2 % to 20.9 %.[13-16] A key factor is the length of stay in PICU as patients requiring prolonged stays in PICU will lead to increase rates of nosocomial BSI.[3] Studies done on nosocomial BSI have showed that gram-positive organisms are more common isolates from blood cultures in PICU,[11,16] and similar results have been seen in infection surveillance programs showing gram-positive organisms as the major isolate,[13,17] unlike in our study, similar to other countries from the Middle East, where gram-negative organisms were the major isolate.[1,3,10,12,14,15] As per World Health Organization's (WHO) antimicrobial resistance report, antimicrobial resistance is a significant global threat as drug resistant infections are leading to 5 million deaths worldwide.[18] Consistent with the other studies; most of the organisms in our study were resistant to commonly used first-line antibiotics like penicillin and cephalosporin while gram-negative organisms are showing more resistance compared to gram-positive organisms.[1,3,10-14,16,17] While gram-negative organisms have shown relatively good sensitivity to carbapenems and aminoglycosides in most studies,[1,3,16,17] in our study, gram-negative isolates were resistant to carbapenems and only showed sensitivity to Amikacin, which is consistent with the results of one study.[10] To the best of our knowledge, a pan-resistant Klebsiella organism, as documented in our study, has only been reported by one researcher.[19] Similarly, Extended Drug Resistant (XDR) Salmonella was sensitive to only Meropenem and azithromycin.[20,21] Thus, knowledge regarding AMR, is crucial to making informed and location-specific policy decisions, particularly for infection control policies, access to essential antibiotics, and research and development of new antibiotics.[22]

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LIMITATION OF STUDY

This study was done in only one center and randomization could not be done. Our study only focused on the nosocomial BSIs and the other types of nosocomial infections were not investigated due to which some BSIs could have been missed because of the conventional laboratory techniques for blood culture and single blood culture specimens.

CONCLUSION

We found that the frequency of nosocomial BSI in our PICU is quite high, which in turn is associated with a longer duration of stay and poor outcomes. The emergence of highly resistant organisms, especially Klebsiella, is alarming, which signals urgent need for rational use of antibiotics and strict infection control programs.

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Authors' Contributions:

Following authors have made substantial contributions to the manuscript as under:

UWA & NS: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

MS & GS: Conception, data analysis, drafting the manuscript, approval of the final version to be published.

AJ & SJ: Data acquisition, critical review, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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