ARTICLE

Factors associated with central line-associated bloodstream infection (CLABSI) among children in a tertiary government hospital: a case-control study

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OBJECTIVE: The study aims to determine the factors associated with central line-associated bloodstream infection (CLABSI) among children admitted in a tertiary government hospital.

MATERIALS AND METHODS: This was a retrospective case-control study which utilized records review of pediatric patients admitted from January 2018 to December 2022. Random sampling was employed to include confirmed cases of patients with CLABSI and controls who did not develop CLABSI. Patients were matched in terms of unit of admission. Data were collected through chart review and odds ratio was used to determine the factors associated with CLABSI using univariate and multivariate regression analysis.

RESULTS: A total of 92 cases and 184 controls were included in the study. Results of multivariate regression analysis revealed that the age group of 6 to 12 years old (OR=18.91, 95% CI 2.32 to 153.9) had the highest odds of acquiring CLABSI. Blood transfusion as indication for central line insertion increased the risk of CLABSI (OR=5.24, 95% CI 1.67 to 16.48). Those more likely to acquire CLABSI were patients with duration of CVC use of more than 14 days (OR=25.68, 95% CI 2.77 to 238.4), those who received total parenteral nutrition (OR=13.44, 95% CI 2.67 to 67.56) and chemotherapeutic or immunosuppressive drugs (OR=3.07, 95% CI 1.2 to 7.85).

CONCLUSION: This study revealed that age, blood transfusion as indication for central line use, receipt of total parenteral nutrition, receipt of chemotherapeutic and immunosuppressive drugs, and duration of CVC utilization of more than 14 days were found to increase the risk of CLABSI. Careful consideration of these factors in patients with CVCs should be observed to prevent the occurrence of CLABSI.

KEYWORDS: *Central line-associated bloodstream infection, CLABSI, associated factors, children*

INTRODUCTION

Central venous catheterization is an indispensable procedure in treating children with life-threatening conditions. The process involves inserting a central venous catheter (CVC) at a peripheral location, advancing and coursing through a major vein, such as the internal jugular, subclavian, brachiocephalic, or femoral vein,[1] until the distal tip of the catheter reaches the superior vena cava, inferior vena cava or the junction with the right atrium. Vascular access in hospitalized, critically ill neonates and children are often needed for monitoring hemodynamics, antibiotic therapy, parenteral nutrition, fluid administration and other indications.[2,3] However, the usefulness of central lines for these patients suffers significant drawbacks as microbial contamination can lead to central line-associated bloodstream infection (CLABSI).[4]

CLABSI is a common hospital-acquired infection that may lead to severe sepsis, increased risk for intensive care unit (ICU) admission, prolonged hospitalization, increased mortality and morbidity, and overinflated healthcare costs.[5] Previous studies have found varying CLABSI rates in tertiary care settings across regions, ranging from 0.28 to 24.73 per 1000 catheter days.[6–8] Most studies, however, involved pediatric patients admitted in ICUs. Factors found to be linked to CLABSI development have been explored, such as duration of catheterization, catheter replacement, multiple catheterizations, and total parenteral nutrition.[9,10] Younger age, birth weight, type of CVC, dwell time, and number of central lines were found to be insignificant.[11,12] In a retrospective cohort study among neonatal ICU patients with percutaneously inserted CVCs at the Philippine Children's Medical Center (PCMC), See Tsai[13] found that patients with CLABSI had a significantly longer median duration of catheterization than those who did not develop CLABSI. The most frequent organisms isolated among ICU-admitted children and neonates were coagulase-negative *Staphylococcus* (CONS), *Candida spp.,* and *Staphylococcus aureus,*[14,15] while for non-ICU patients, coagulase-negative *Staphylococcus* (CONS) was also the most common organism identified.[15]

Despite the advances in the prevention and management of CLABSI, its incidence in critically ill neonates and children remains unchanged.[16] On the other hand, CLABSI is also a preventable hospital-acquired infection. Revealing the characteristics of patients at risk for developing CLABSI can aid physicians in making suitable clinical decisions in managing and recommending preventive approaches applicable in the local study setting. This study aims to determine the associated risk factors of CLABSI among hospitalized children below 18 years old admitted at PCMC from January

2018 to December 2022. Specifically, it aims to describe the demographic and clinical characteristics of children who developed and did not develop CLABSI; determine the factors associated with CLABSI in children who developed CLABSI; and lastly, describe the microbiologic profile and antibiotic susceptibility of CLABSI in children who developed CLABSI.

Materials and Methods

Research Design. This study utilized a case-control design, approved by the Institutional Review-Ethics Committee of PCMC. All patients with central venous catheters under 18 years old admitted at PCMC between January 2018 and December 2022 were included.

Inclusion Criteria. To be included as a subject, the study required patients to meet these requirements: (1) admitted in-patients at PCMC between January 2018 to December 2022; (2) all genders below 18 years old; (3) admitted to the ward or ICU (neonatal, pediatric, septic); (4) with at least one central venous catheter; (5) any place of CVC insertion (ward, ICU, operating room, emergency room); (6) with or without peripheral intravenous line. For cases: (7) CLABSI should have occurred 48 hours after admission and CLABSI diagnosis was confirmed by blood culture according to the Centers for Disease Control and Prevention (CDC) criteria. For controls: (8) presence of CVC for at least 48 hours and did not develop CLABSI or had negative blood culture results for CLABSI suspicion.

Exclusion Criteria. The following patients were excluded from the study: (1) with incomplete data on medical records (2) with laboratory confirmed sepsis before inserting the CVC based on medical records; (3) referred from another hospital with CVC already inserted; (4) transferred to another hospital or went home against medical advice.

Finding Potential Cases and Controls. Children with CVCs inserted during their hospitalization within the retrospective period of this study were identified by reviewing the Neonatology and Surgery services logbooks. The records of the Microbiology section and Section of Pediatric Infectious Diseases were also reviewed to determine patients who have had growths on their central line blood cultures during their hospitalization. Meanwhile, patients with CVCs who did not have blood culture testing for CLABSI or had negative results during their hospitalization were also recorded in a logbook.

Patients diagnosed with CLABSI were cross validated to confirm that they met the study's criteria for the case definition per the CDC guidelines and for the inclusion of the patient as a case in the present study. Neonates with growth of a common commensal pathogen with only a single blood

culture obtained were included as potential cases since obtaining paired samples in neonates is not commonly practiced in PCMC, provided that the patient had at least one of the following signs or symptoms: fever (>38.0°C), hypothermia (<36.0°C), apnea, or bradycardia and the organism identified in blood is not related to an infection at another site. To focus on hospital-acquired CLABSIs, we only considered CLABSI which occurred after 48 hours from admission. For multiple CLABSIs of a single CVC, only the first episode was included in the analysis. Likewise, for patients with multiple CVCs, only the first documented CLABSI was included in the analysis. A patient with more than one CLABSI incidence was used as a case subject only once and only the first admission was included. The same was done for patients who did not develop CLABSI or had negative results to ensure they met the inclusion criteria for controls. Patients who satisfied the criteria after the cross-validation proceedings were categorized into two groups according to their CLABSI diagnosis.

Sample Size Calculation and Sampling. The study required a sample size of at least 62 cases and 124 controls (ratio of 1:2) at a 95% confidence interval and 80% power of the test. The computation was based on the findings of the study of Wylie, et al.,[17] where three factors were shown, including duration of ICU central venous catheterization, use of parenteral nutrition, and blood product transfusion.

Based on the hospital admission date, the cases were sorted sequentially from one to the last. Case units were chosen by drawing random numbers from the patients who developed CLABSI. Potential controls were sorted by the unit of admission and admission date. The two controls who were admitted to the same unit of admission and closest to the admission date of the case (within three months) were selected purposively. This was done to control confounding factors that may be related to the unit of admission, such as the severity of illness, and to account for potential temporal trends in the exposure and outcome among cases and controls. The process was repeated until the minimum sample size required was reached. We did not limit the sample size to 62 cases and 124 controls so as to accommodate more entries from the records, as well as to increase the statistical power of the study.

Data Collection Procedure. A standardized data collection form and coding manual was used during the data collection proceedings. The following were the independent variables collected and analyzed as potential risk factors for CLABSI: age (0-29 days, 1-12 months, 2-5 years, 6-12 years, 13-18 years), sex, nutritional status based on height/length and weight (normal, wasted/ severely wasted, overweight/obese), underlying diagnosis (cardiovascular, respiratory, gastrointestinal, renal, hematologic/oncologic, neurologic, surgical, infectious, other neonatal pathology),

indication for central line placement (fluid resuscitation, blood transfusion, drug infusion, nutrition, hemodialysis), type of central line inserted (non-tunneled, tunneled, totally implanted, umbilical, peripherally inserted central catheter), place of CVC insertion (general ward, ICU, operating room, emergency room), site of central line placement (internal jugular vein, subclavian vein, femoral vein, umbilical vein, arm or leg), receipt of blood products, receipt of total parenteral nutrition (TPN), receipt of chemotherapeutic or immunosuppressive drugs, duration of central line use (number of days from the date of CVC insertion to the date of CVC removal). The following data were also collected: the onset of CLABSI (number of days from the date of CVC insertion to the date of symptom onset), length of hospital stay (number of days from the date of patient's admission to the date of discharge or demise, whichever comes first), outcome if with CLABSI (died or recovered) and the microbiologic profile of CLABSI cases. A unique alphanumeric identification code was assigned to each study subject to maintain their anonymity and protect their information.

Statistical analysis. Data collected using the standardized data collection form were encoded into the study's data sheet in Microsoft Excel. Descriptive statistics, such as mean standard deviation, median and interquartile range were used to describe continuous variables. On the other hand, frequency and percentage were used to present categorical data. Odds ratio was obtained to determine the factors associated with CLABSI using univariate and multivariate regression analysis (among variables with p <0.20). Moreover, for variables that resulted in 0 cells, Fisher's exact test was then utilized. The level of significance was at 5%. Medcalc statistical software was used to carry out statistical calculation.

RESULT

A total of 92 CLABSI cases and 184 controls were included in the study. Table 1 shows the characteristics of CLABSI patients at PCMC from January 2018 to December 2022. The majority (82.6%) of patients only had a single episode of CLABSI. CLABSI recurrence was noted in 18.5% of cases, most of which occurred in a different CVC site. The prevalence of mortality is 10.9%.

TABLE 1. CHARACTERISTICS OF CLABSI PATIENTS AT THE PHILIPPINE CHILDREN'S

MEDICAL CENTER FROM JANUARY 2018 TO DECEMBER 2022

Variables	**CASE (n = 92)**	
	n	**%**
Unit of admission		
Neonatal ICU	21	22.8
Pediatric ICU	20	21.7
Septic ICU	7	7.6
General ward	44	47.8
Number of CLABSI experienced		
One	76	82.6
Multiple (2-3)	16	17.4
CLABSI re-occurrence		
None	75	81.5
Yes, same CVC site	1	1.1
Yes, different CVC site	16	17.4
Outcome		
Recovered	82	89.1
Died	10	10.9
Onset of CLABSI (days), median	17 (13 to 20.0)	

Table 2 presents the demographic and clinical characteristics of patients with and without CLABSI during the study period. Cases and controls were matched in terms of unit of admission. The proportion of CLABSI cases was significantly higher among those aged 1-12 months old, in contrast to the control group (34.8% vs 14.1%, p<0.0012). Male to female split, nutritional status, and median number of central lines placed were not significantly different between the two groups. The underlying diagnosis differed substantially, as a higher proportion of cases had underlying neurologic conditions than controls (31.5% vs 14.7, p=0.0161). In terms of indication for central line use, among the cases, the following had significantly higher proportion of CLABSI compared to controls: fluid resuscitation (85.9% vs 69.6%, p<0.0032), drug infusion (85.9% vs 72.3%, p<0.0001), blood transfusion (44.6% vs 22%, p<0.0001), nutrition (29.3% vs 8.7%, p<0.0001), other indication (13% vs 5.4%, p<0.0281). A significantly higher proportion of CLABSI cases than controls had non-tunneled catheters (92.4% vs 78.8%, p<0.0042) and had central lines inserted in the internal jugular vein (85.9% vs. 82.1%, p=0.0077) or the femoral vein (7.6% vs. 2.7%, p=0.0077). Majority of CVC insertion were done in the operating room for both groups. Receipt of blood products, TPN and chemotherapeutic or immunosuppressives were significantly higher in those with CLABSI than controls. The median duration of CVC utilization was significantly longer among those with CLABSI than controls (19 days vs 10.5 days, p<0.0001). Median duration of hospital stay was also significantly longer among those with CLABSI than controls (49 days vs 21 days, p<0.0001).

TABLE 2. DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF CHILDREN WITH CLABSI AND WITHOUT CLABSI AT THE PHILIPPINE CHILDREN'S MEDICAL CENTER FROM JANUARY 2018 TO DECEMBER 2022

Variables	CASE (n = 92) With CLABSI		CONTROL (n = 184) Without CLABSI		p-value
	n	%	n	%	
Age (years)					
0 – 29 days	9	9.8	39	21.2	
1 – 12 months	32	34.8	26	14.1	0.0012*
2 – 5 years	13	14.1	33	17.9	
6 – 12 years	18	19.6	42	22.8	
13 – <18 years	20	21.7	44	23.9	
Sex					
Male	44	47.8	93	50.5	0.6709
Female	48	52.2	91	49.5	

Underlying primary diagnosis					
Cardiovascular	1	1.1	9	4.9	
Respiratory	10	10.9	14	7.6	
Gastrointestinal	12	13.0	16	8.7	
Renal	18	19.6	52	28.3	
Hematologic/Oncologic	8	8.7	32	17.4	
Neurologic	29	31.5	27	14.7	0.0161*
Surgical	2	2.2	6	3.3	
Infectious	11	12.0	27	14.7	
Other Neonatal Pathology	1	1.1	1	0.5	
Others	0	0.0	0	0.0	
Weight, median (IQR)	12.75 (3.75 to 32)		15 (4 to 34)		0.3108
Nutritional status					
Normal	45	48.9	100	55.6	
Wasted/Severely wasted	38	41.3	68	37.8	0.7305
Overweight/Obese	9	9.8	16	8.9	
Indication for central line					
Fluid resuscitation	79	85.9	128	69.6	0.0032*
Blood transfusion	41	44.6	22	12.0	0.0001*
Drug infusion	79	85.9	133	72.3	0.0118*
Nutrition	27	29.3	16	8.7	0.0001*
Hemodialysis	22	23.9	61	33.2	0.1153
Others	12	13.0	10	5.4	0.0281*
Type of central line inserted					
Non-tunneled catheter	85	92.4	145	78.8	0.0042*
Tunneled catheter	0	0.0	2	1.1	
Totally implanted (port-a-cath)	1	1.1	14	7.6	
Umbilical catheter	0	0.0	15	8.2	
Peripherally inserted central catheter	6	6.5	8	4.3	
Place of CVC insertion					
NICU	12	13.0	23	12.5	0.5654
PICU	0	0.0	0	0.0	
Septic ICU	0	0.0	0	0.0	
General Ward	1	1.1	0	0.0	
Operating Room	76	82.6	155	84.2	
Emergency Room	3	3.3	6	3.3	
Number of central lines placed, median (IQR)	1.0 (1.0 to 1.0)		1.0 (1.0 to 1.0)		0.4771
Site/s of central lines insertion					
Internal jugular vein	79	85.9	154	83.7	0.0077*
Subclavian vein	0	0.0	2	1.1	
Femoral vein	7	7.6	5	2.7	
Umbilical vein	0	0.0	15	8.2	
Arm (PICC line)	3	3.3	1	0.5	
Leg (PICC line)	3	3.3	7	3.8	
Duration of CVC utilization, median (IQR)	19.0 (15 to 23)		10.5 (7.0 to 14.0)		0.0001*
Duration of CVC utilization					
<7 days	1	1.1	42	22.8	
7 to 14 days	21	22.8	97	52.7	0.0001*
>14 days	70	76.1	45	24.5	
Receipt of blood products	60	65.2	49	26.6	0.0001*
Receipt of total parenteral nutrition	47	51.1	19	10.3	0.0001*
Receipt of chemotherapeutic or immunosuppressive drugs	51	55.4	66	35.9	0.0112*
Length of hospital stay (days), median (IQR)	49 (37.5 to 71.5)		21 (13 to 36)		0.0001*

Significant @ p-value ≤ 0.05; IQR – interquartile range

Table 3 presents the univariate logistic regression analysis of factors associated with CLABSI. Results showed that 10 factors were significantly associated with CLABSI. Children aged 1 to 12 months were 5 times more likely to acquire CLABSI than those 0-29 days old (OR=5.33, 95% CI 2.19 to 13.23). Those with underlying neurologic diagnosis were also 9 times more likely to acquire CLABSI (OR=9.67, 95% CI 1.15 to 81.46). Indication for central line was also significantly associated with CLABSI, specifically, fluid resuscitation (OR=2.66, 95% CI 1.37 to 5.17), blood transfusion (OR=5.92, 95% CI 3.23 to 10.85), drug infusion (OR=2.33, 95% CI 1.19 to 4.55), nutrition (OR=4.36, 95% CI 2.21 to 8.62), as well as other indications (OR=2.61, 95% CI 1.08 to 6.29). Moreover, those with non-tunnel type of CVC were 3 times more likely to acquire CLABSI as compared to other types of central line (OR=3.27, 95% CI 1.40 to 7.63). Site of CVC insertion was also significant, as those with femoral vein insertion were 8 times more likely to acquire CLABSI (OR=8.4, 95% CI 1.57 to 44.92). Those with duration of CVC use of more than 14 days and 7 to 14 days were 65 times (OR=65.33, 95% CI 8.68 to 491) and 9 times (OR=9.09, 95% CI 1.18 to 69.83) more likely to acquire CLABSI than those with less than 7 days of use, respectively. Receipt of TPN (OR=9.07, 95% CI 4.85 to 16.97), receipt of blood products (OR=5.17, 95% CI 3.01 to 8.86) and chemotherapeutic or immunosuppressive drugs (OR=1.94, 95% CI 1.16 to 3.25) were all significantly associated with higher odds of acquiring CLABSI. Furthermore, patients with a median duration of hospital stay exceeding 49 days are at higher risk of CLABSI (OR=1.03, 95% CI 1.02 to 1.04).

TABLE 3. Univariate Logistic Regression Analysis of Factors Associated With CLABSI At The Philippine Children's Medical Center from January 2018 to December 2022

Variables	COR	95% CI		p-value
		Lower	Upper	
Age (years)				
0 – 29 days		*Reference*		
1 – 12 months	5.33	2.19	13.23	0.0002*
2 – 5 years	1.71	0.65	4.39	0.279
6 – 12 years	1.86	0.75	4.62	0.183
13 – <18 years	1.97	0.8	4.83	0.1386
Sex				
Male	1.11	0.68	1.84	0.6704
Female		*Reference*		

Cardiovascular		*Reference*		
Respiratory	6.43	0.7	59.17	0.1004
Gastrointestinal	6.75	0.75	60.76	0.0885
Renal	3.12	0.37	26.33	0.2967
Hematologic/Oncologic	2.25	0.25	20.44	0.4713
Neurologic	9.67	1.15	81.46	0.0370*
Surgical	3	0.22	40.93	0.4100
Infectious	3.67	0.41	32.49	0.2431
Other Neonatal Pathology	9	0.28	285.5	0.2129
Nutritional status				
Normal		*Reference*		
Wasted/Severely wasted	1.24	0.73	2.11	0.4235
Overweight/Obese	1.25	0.51	3.04	0.6228
Indication for central line				
Fluid resuscitation	2.66	1.37	5.17	0.0040*
Blood transfusion	5.92	3.23	10.85	0.0001*
Drug infusion	2.33	1.19	4.55	0.0133*
Nutrition	4,36	2.21	8.62	0.0001*
Hemodialysis	0.63	0.36	1.12	0.1161
Others	2.61	1.08	6.29	0.0326*
Type of central line inserted				
Others		*Reference*		
Non-tunneled catheter	3.27	1.40	7.63	0.0062*
Place of CVC insertion				
Others (ER/General ward)		*Reference*		
Operating Room	0.74	0.2	2.68	0.6418
NICU	0.78	0.18	3.32	0.7395
Number of central lines placed	2.02	0.28	14.59	0.4849
Site/s of central lines insertion				
Others		*Reference*		
Internal jugular vein	3.14	0.9	10.98	0.0734
Femoral vein	8.4	1.57	44.92	0.0128*
Arm (PICC line)	1.8	0.3	10.64	0.5168
Duration of CVC utilization				
<7 days		*Reference*		
7 to 14 days	9.09	1.18	69.83	0.0338*
>14 days	65.33	8.68	491	0.0001*
Receipt of blood products	5.17	3.01	8.86	0.0001*
Receipt of total parenteral nutrition	9.07	4.85	16.97	0.0001*
Receipt of chemotherapeutic or immuno-suppressive drugs	1.94	1.16	3.25	0.0115*
Length of hospital stay	1.03	1.02	1.04	0.0001*

***Significant @ p-value ≤ 0.05*; COR – Crude odds ratio

Table 4 summarizes the results of multivariate logistic regression analysis where the following factors were analyzed: age, underlying diagnosis, indication for central line insertion, type of central line inserted, site of central line insertion, duration of CVC utilization, receipt of blood products, receipt of TPN, receipt of chemotherapeutics or immunosuppressive and length of hospital stay. Five factors were found to be significantly associated with CLABSI. Results revealed that age groups of 1 to 12 months (OR=11.58, 95% CI 2.16 to 62.04), 1 to 5 years (OR=9.3, 95% CI 1.13 to 76.4), 6 to 12 years (OR=18.91 95% CI 2.32 to 153.9) and 13 to 18 years old (OR=15.45, 95% CI 1.83 to 130.6) were associated with higher odds of acquiring CLABSI as compared to children aged 0 to 1 month old. Indication for central line, specifically blood transfusion, was also associated with higher odds of CLABSI (OR=5.24, 95% CI 1.67 to 16.48). Those with duration of CVC use of more than 14 days were 25 times (OR=25.68, 95% CI 2.77 to 238.4) more likely to acquire CLABSI than those with less than 7 days of use. Receipt of total parenteral nutrition (OR=13.44, 95% CI 2.67 to 67.56) and receipt of chemotherapeutic or immunosuppressive drugs (OR=3.07, 95% CI 1.2 to 7.85) were also significantly associated with CLABSI.

TABLE 4. MULTIVARIATE LOGISTIC REGRESSION ANALYSIS OF FACTORS ASSOCIATED WITH CLABSI AT THE PHILIPPINE CHILDREN'S MEDICAL CENTER FROM JANUARY 2018 TO DECEMBER 2022

Variables	AOR	95% CI		p-value
		Lower	Upper	
Age (years)				
0 – 29 days		*Reference*		
1 – 12 months	11.58	2.16	62.04	0.0041*
2 – 5 years	9.30	1.13	76.40	0.0378*
6 – 12 years	18.91	2.32	153.9	0.0060*
13 – <18 years	15.45	1.83	130.6	0.0119*
Indication for central line				
Fluid resuscitation	-	-	-	-
Blood transfusion	5.24	1.67	16.48	0.0046*
Drug infusion	-	-	-	-
Nutrition	1.87	0.26	13.63	0.5362
Hemodialysis	1.19	0.36	4.01	0.7737
Others	1.72	0.38	7.79	0.4827
Duration of CVC utilization				
<7 days		*Reference*		
7 to 14 days	7.66	0.83	71	0.0733
>14 days	25.68	2.77	238.4	0.0043*
Receipt of total parenteral nutrition	13.44	2.67	67.56	0.0016*
Receipt of chemotherapeutic or immunosuppressive drugs	3.07	1.2	7.85	0.0193*

Significant @ p-value ≤ 0.05; AOR – Adjusted odds ratio

Table 5.1. summarizes the microorganisms isolated among patients with CLABSI. There was a total of 92 organisms isolated (56 were grown from both the central line and a peripheral venipuncture site, 17 were grown from two peripheral venipuncture sites, 19 were grown from a single peripheral venipuncture site). About 48.9% of isolates were gram-negative organisms followed by gram-positive organisms with 44.6%, and fungal organisms with 6.5%. Among the four gram-positive species isolated, around 63.4% were coagulase-negative staphylococci (CONS), followed by 17.1% methicillin-sensitive *Staphylococcus aureus* (MSSA). Among the 13 gram-negative species isolated, *Klebsiella pneumoniae (K. pneumoniae)* accounted for 31.1%, followed by *Acinetobacter baumannii (A. baumannii),* with 24.4%. On the other hand, *Candida spp.* was the most common fungal organism in the study (83.3%).

TABLE 5.1. CLABSI MICROBIAL ISOLATES AT THE PHILIPPINE CHILDREN'S MEDICAL CENTER FROM JANUARY 2018 TO DECEMBER 2022

Microorganisms	n (%)
Gram-positive	41 (44.6)
Coagulase-negative Staphylococci	26 (63.4)
Methicilin-sensitive *Staphylococcus aureus*	7 (17.1)
Methicilin-resistant *Staphylococcus aureus*	6 (14.6)
Enterococcus faecalis	2 (4.9)
Gram-negative	45 (48.9)
Klebsiella pneumoniae	14 (31.1)
Acinetobacter baumannii	11 (24.4)
Enterobacter cloacae	3 (6.7)
Pseudomonas aeruginosa	3 (6.7)
Serratia marcescens	3 (6.7)
Achromobacter xylosoxidans	2 (4.4)
Sphingomonas paucimobilis	2 (4.4)
Stenotrophomonas maltophilia	2 (4.4)
Burkholderia cepacia	1 (2.2)
Escherichia coli, ESBL	1 (2.2)
Pantoea spp.	1 (2.2)
Pseudomonas putida	1 (2.2)
Pseudomonas stutzeri	1 (2.2)
Fungi	6 (6.5)
Candida spp.	5 (83.3)
C. albicans	1 (16.7)

ESBL – extended spectrum beta-lactamase

Table 5.2 presents the antibiotic susceptibility of gram-positive organisms. Results revealed that CONS were mostly resistant to the different antibiotics, except for vancomycin to which 100% of the isolates were sensitive. All isolates of MRSA were 100% sensitive to vancomycin and linezolid. Among two patients with *Enterococcus faecalis (E. faecalis),* both were still sensitive to the drug of choice, penicillin, while no resistance to vancomycin was documented.

TABLE 5.2. ANTIBIOTIC SUSCEPTIBILITY OF CLABSI-CAUSING GRAM-POSITIVE ORGANISMS AT THE PHILIPPINE CHILDREN'S MEDICAL CENTER FROM JANUARY 2018 TO DECEMBER 2022

Variables	**CONS n=26 (63.4%)**		**MSSA n=7 (17.1%)**		**MRSA n=6 (14.6%)**		***E. faecalis* n=2 (4.9%)**	
	S	**R**	**S**	**R**	**S**	**R**	**S**	**R**
Cefazolin	0(0.0)	26 (100)	7 (100)	0 (0.0)	0 (0.0)	6 (100)	-	-
Oxacillin	0 (0.0)	26 (100)	7 (100)	0 (0.0)	0 (0.0)	6 (100)	-	-
Clindamycin	0 (0.0)	26 (100)	7 (100)	0 (0.0)	6 (100)	0 (0.0)	-	-
Erythromycin	0 (0.0)	26 (100)	6 (85.7)	1 (14.3)	6 (100)	0 (0.0)	-	-
Gentamicin	0 (0.0)	26 (100)	7 (100)	0 (0.0)	6 (100)	0 (0.0)	-	-
Linezolid	0 (0.0)	26 (100)	7 (100)	0 (0.0)	6 (100)	0 (0.0)	-	-
Trimethoprim sulfamethoxa-zole	1 (3.8)	25 (96.2)	7 (100)	0 (0.0)	1 (16.7)	5 (83.3)	-	-
Vancomycin	26 (100)	0 (0.0)	7 (100)	0 (0.0)	6 (100)	0 (0.0)	-	-
Ciprofloxacin	0 (0.0)	26 (100)	7 (100)	0 (0.0)	6 (100)	0 (0.0)	2 (100)	0 (0.0)
Levofloxacin	0 (0.0)	26 (100)	7 (100)	0 (0.0)	6 (100)	0 (0.0)	2 (100)	0 (0.0)
Ampicillin	-	-	-	-	-	-	2 (100)	0 (0.0)
Penicillin	-	-	-	-	-	-	2 (100)	0 (0.0)

Gram-Positive Microorganisms: CONS - Coagulase-negative staphylococci, *E. faecalis* - *Enterococcus faecalis*, MRSA – Methicillin-resistant *Staphylococcus aureus*, MSSA - Methicillin-sensitive *Staphylococcus aureus*; ***Susceptibility:*** S – Sensitive, R – Resistant, (-) – Not tested

Table 5.3 shows the antibiotic susceptibility of the top five gram-negative organisms. Fourteen patients with *K. pneumoniae* were 100% sensitive to colistin, 92.9% to amikacin, and 71.4% to carbapenems (ertapenem, imipenem, meropenem). Of the 14 isolates of *K. pneumoniae,* 13 were multidrug-resistant (nonsusceptible to at least one antibiotic in three or more drug classes) while 1 was extremely drug-resistant (nonsusceptible to at least one agent in all but two or fewer drug classes). Among 11 patients with *A. baumannii,* 90.9% were sensitive to amikacin, followed by 81.8% to gentamicin and trimethoprim sulfamethoxazole. Of the 11 isolates of *A. baumannii*, 10 were multidrug-resistant while 1 was extremely drug-resistant.

TABLE 5.3. ANTIBIOTIC SUSCEPTIBILITY OF TOP FIVE CLABSI-CAUSING GRAM-NEGATIVE ORGANISMS AT THE PHILIPPINE CHILDREN'S MEDICAL CENTER FROM JANUARY 2018 TO DECEMBER 2022

Variables	***K. pneumoniae*** **n=14 (31.1 %)**		***A. baumannii*** **n=11 (24.4%)**		***E. cloacae*** **n=3 (6.7%)**		***P. aeruginosa*** **n=3 (6.7%)**		***S. marcescens*** **n=3 (6.7%)**	
	S	**R**	**S**	**R**	**S**	**R**	**S**	**R**	**S**	**R**
Cefepime	1 (7.1)	13 (92.9)	3 (26.3)	8 (72.7)	3 (100)	0 (0.0)	1 (33.3)	2 (66.7)	0 (0.0)	3 (100)
Cefotaxime	0 (0.0)	14 (100)	2 (18.2)	9 (81.8)	2 (66.7)	1 (33.3)	-	-	0 (0.0)	3 (100)
Ceftazidime	0 (0.0)	14 (100)	3 (27.3)	8 (72.7)	2 (66.7)	1 (33.3)	1 (33.3)	2 (66.7)	0 (0.0)	3 (100)
Ceftriaxone	0 (0.0)	14 (100)	1 (9.1)	10 (90.9)	2 (66.7)	1 (33.3)	-	-	0 (0.0)	3 (100)
Cefuroxime	0 (0.0)	14 (100)	-	-	2 (66.7)	1 (50)	-	-	0 (0.0)	3 (100)
Gentamicin	2 (14.2)	12 (85.7)	9 81.8)	2 (18.2)	2 (66.7)	1 (33.3)	2 (66.7)	1 (33.3)	0 (0.0)	3 (100)
Piperacillin tazobactam	5 (35.7)	9 (64.3)	3 (27.3)	8 (72.7)	3 (100)	0 (0.0)	1 (33.3)	2 (66.7)	2 (66.7)	1 (33.3)
Trimethoprim-Sulfamethoxa-zole	2 (14.2)	12 (85.7)	9 (81.8)	2 (18.2)	3 (100)	0 (0.0)	-	-	0 (0.0)	3 (100)
Ciprofloxacin	7 (50.0)	7 (50.0)	3 (27.3)	8 (72.7)	3 (100)	0 (0.0)	2 (66.7)	1 (33.3)	0 (0.0)	3 (100)
Levofloxacin	6 (42.8)	8 (57.2)	-	-	-	-	1 (50)	1 (50)	0 (0.0)	3 (100)
Ampicillin	0	14 (100)	-	-	0 (0.0)	3 (100)	-	-	-	-
Amoxicillin clavulanic acid	0	14 (100)	-	-	0 (0.0)	3 (100)	-	-	-	-
Ertapenem	10 (71.4)	4 (28.6)	-	-	3 (100)	0 (0.0)	-	-	3 (100)	0 (0.0)
Imipenem	10 (71.4)	4 (28.6)	2 (18.2)	9 (81.8)	3 (100)	0 (0.0)	2 (66.7)	1 (33.3)	3 (100)	0 (0.0)
Meropenem	10 (71.4)	4 (28.6)	3 (27.3)	8 (72.7)	3 (100)	0 (0.0)	2 (66.7)	1 (33.3)	3 (100)	0 (0.0)
Amikacin	13 (92.9)	1 (7.1)	10 (90.9)	1 (9.1)	3 (100)	0 (0.0)	2 (66.7)	1 (33.3)	3 (100)	0 (0.0)
Colistin	14 (100)	0 (0.0)	-	-	-	-	3 (100)	0 (0.0)	-	-

Gram-Negative Microorganisms: *K. pneumoniae - Klebsiella pneumoniae, A. baumannii - Acinetobacter baumannii, E. cloacae – Entero-bactercloacae, P. aeruginosa - Pseudomonas aeruginosa, S. marcescens - Serratia marcescens* ***Susceptibility:*** S – Sensitive, R – Resistant, (-) – Not tested

Table 5.4 shows the antifungal susceptibility patterns of fungal organisms. All six patients with Candida were 100% sensitive to fluconazole, flucytosine, and voriconazole, while one was resistant to amphotericin B.

TABLE 5.4. ANTIBIOTIC SUSCEPTIBILITY OF CLABSI-CAUSING FUNGAL ORGANISMS AT THE PHILIPPINE CHILDREN'S MEDICAL CENTER FROM JANUARY 2018 TO DECEMBER 2022

Anti-Fungal	*Candida spp.* n=5 (83.3%)		*C. albicans* n=1 (16.7%)	
	S	R	S	R
Amphotericin B	4 (80.0)	1 (20.0)	1 (100)	0 (0.0)
Fluconazole	5 (100)	0 (0.0)	1 (100)	0 (0.0)
Flucytosine	5 (100)	0 (0.0)	1 (100)	0 (0.0)
Voriconazole	5 (100)	0 (0.0)	1 (100)	0 (0.0)

DISCUSSION

Although the use of CVCs has been widely recognized as an essential part of medical care in critically-ill neonates and children, they carry the risk of CLABSI which may lead to increased morbidity, mortality, length of hospital stay and healthcare cost.[17] As there is limited data regarding CLABSI in children in the local setting, this study aimed to identify factors associated with the development of CLABSI involving children admitted in a tertiary government hospital. The risk factors for CLABSI encompass a wide range of variables. In this study, age, blood transfusion as indication for central line use, receipt of TPN and chemotherapeutics/ immunosuppressives, and duration of CVC use of more than 14 days were found to be significant risk factors for CLABSI.

CLABSI can occur in individuals of all ages, but certain age groups may have specific risk factors that contribute to their vulnerability. This study showed that children belonging to the 6–12-year-old age group had the highest odds of acquiring CLABSI (OR=18.91 95% CI 2.32 to 153.9) when compared to children less than 1 month old. This contrasts with a study done by Broudic, et al.,[18] where neonates were identified to be at highest risk of CVC related infection due to their underdeveloped skin barrier and immune system, which make them more susceptible to infections. In another study by Advani, et al., younger age (<1 year) has also been identified as a risk factor for CLABSI.[15] Due to the poor skin integrity of this age group, their skin can be easily damaged during repeated catheter manipulation leading to increased risk of infection. Maintenance of CVCs in this age group can also be more challenging due to their small veins which may increase the risk of complications such as dislodgement or leakage which can provide opportunities for

opportunities for infection.[15] The unanticipated result in this study, however, may be explained by other factors, including the possible predominance of complex medical conditions in older children that may require longer treatment duration and longer duration of central line use, which is also a known risk factor for CLABSI.

The study highlighted underlying medical conditions as a contributing risk factor for CLABSI development. Although no significant association was identified on multivariate analysis, the majority (31.5%) of CLABSI cases occurred in those with underlying neurologic diagnosis. This may be attributed to the possibility that neurological conditions are chronic in nature. Neurologic patients commonly have comorbid medical conditions that compromise their immune system and make them more susceptible to infections. Prolonged hospitalization due to brain injury is also common in these patients which subsequently increases the utilization of external devices such as CVCs, ventricular drains, and ventilators, among others, thus, increasing the risk of bacteremia and catheter infections.[19]

Several medical interventions and patient-level characteristics were significantly associated with the emergence of CLABSI. In the current study, blood transfusion as an indication for CVC insertion, receipt of total parenteral nutrition, receipt of chemotherapeutic or immunosuppressive therapies, and duration of catheter use. These factors are also similar to the results of a previous study done by Wylie, et al.[17]

Previous prospective and retrospective studies have recognized transfusion of blood products as a risk factor for CLABSI.[20,21] Immune suppression, increased frequency of line access, and pathogen multiplication with transfusion are some potential mechanisms to explain the risk associated with blood transfusion. These mechanisms may also explain as to how administration of parenteral nutrition increases CLABSI rate. Other studies suggest that the risk of CLABSI may also be influenced by lipid contamination, glycemic alterations, and gastrointestinal mucosal breakdown brought about by inadequate enteral nutrition which poses more risk of infection.[15,22,23] Moreover, TPN solutions contain high concentrations of glucose that promote bacterial growth when central lines are contaminated.[23] With this, early switch to enteral feeding is suggested to probably decrease the risk of CLABSI.[17] Immediate replacement of tubings used to administer these products should be observed within 24 hours of initiating the infusion to avoid contamination.[24]

Receipt of chemotherapeutic or immunosuppressive medications was also seen as a significant risk factor for CLABSI development in this study. This association may be related to the increased susceptibility to infection brought about by cytostatic

drug-induced neutropenia.[25,26]

Infection prevention efforts on the prompt removal of CVCs have been emphasized in many guidelines since the length of central line access has been identified as a consistent risk factor for bloodstream infection. This study identified the duration of CVC use of more than 14 days as an independent risk factor for CLABSI. This confirms the findings of previous studies that prolonged catheter dwell times increase the risk of CLABSI. [15,17] The development of CLABSI in patients with prolonged CVC use may be attributed to the degradation and dysfunctionality that CVCs acquire over time from repeated manipulations.[27] Long-term central venous access, however, is frequently unavoidable particularly in critically ill children admitted in government hospitals. In addition, immediate replacement of the central line is not always possible due to their high cost. Nonetheless, periodic assessment of CVCs should be done to determine if these can be removed or if an alternative and less invasive access line can be used.

In contrast to other studies, this study found no significant association between the types of central line inserted and the development of CLABSI, as well as the site of central line insertion and the odds of acquiring CLABSI. The non-significant findings could be attributed to the limitations of a relatively small sample size, as well as the potential influence of other confounding factors, such as variations in catheter insertion techniques and patient characteristics. However, it is worth noting that majority of the central lines inserted in PCMC were non-tunneled catheters. These catheters are associated with an increased risk of CLABSI due to several reasons. Direct insertion of non-tunneled CVCs provides a direct pathway for bacteria to enter the bloodstream, increasing the risk of contamination during the insertion process.[15,24] Moreover, non-tunneled CVCs often are less securely anchored in place as compared to tunneled or totally implanted catheters which can lead to instability and increased risk of contamination at the insertion site.[24] Considering these factors, it is still advisable to limit the use of non-tunneled CVCs for short-term purposes when possible.

As in other studies,[11,28,29] the most frequent microorganism isolated in CLABSI cases were gram-positive cocci, specifically, CONS. This may be attributed to the colonization of the patient's skin flora or a result of several healthcare providers manipulating the device.[27] Increasing rates of gram-negative organisms are also being reported globally. Of note, this study showed a higher proportion of gram-negative (n=45, 48.9%) compared to gram-positive organisms (n=41, 44.6%), particularly *K. pneumoniae* and *A. baumannii.* This can be a cause for concern as gram-negative organisms are associated with higher morbidity and

mortality rates and are prone to antibiotic resistance, making them more difficult to treat.[30] Thus, empiric use of antibiotics based on the antibiotic susceptibility of these organisms should be considered to ensure that effective treatment is given to patients at the onset.

For the clinical outcome of CLABSI cases, 10.9% of those who developed CLABSI died. However, it was not possible to determine whether death was a direct consequence of CLABSI in those patients.

This study also revealed that in PCMC, the majority of CLABSI cases occurred in patients admitted at the general wards. Hence, efforts to prevent infection of CVCs, not only in the ICUs but also in general wards should be strictly implemented. Care bundles to prevent CLABSI beginning from insertion to site care should be made available to healthcare workers in all areas and should be reviewed on a regular basis. Knowledge of the different risk factors associated with CLABSI can help healthcare providers in identifying patients who are at higher risk of developing CLABSI. Enhanced infection control measures should be practiced in patients who are likely to need blood transfusion, parenteral nutrition and chemotherapeutics to prevent or reduce CLABSI occurrence. Adjunctive interventions to prevent CLABSI in these patients such as antiseptic dressings and antibiotic lock therapy may also be considered.[31] More importantly, frequent hand hygiene, personnel training, use of skin antiseptics, provision of barrier methods, daily evaluation of catheters and removal of the CVCs when no longer needed are practices that should always be implemented.[24] Continued surveillance of CLABSI is also important to document changes in the epidemiological features and antibacterial resistance.

Discussion

This study has some limitations. First, the study only involved patients with hospital-acquired CLABSIs which limited the study sample size and limited the generalizability to only hospitalized cases. As this is a single-center study, the results may not be representative of the entire pediatric population. A wide confidence interval was also observed in some of the risk factors identified, hence, it is difficult to make precise predictions or draw definitive conclusions based on the results of this study. Therefore, the researcher recommends that a prospective study with a larger sample size be conducted in the future to validate these risk factors. Research focused on evaluating and comparing different prevention strategies aimed at reducing CLABSI rates may also be explored.

Conclusion

This study showed that age, blood transfusion as indication for central line use, receipt of total parenteral nutrition, receipt of chemotherapeutic and immunosuppressive drugs, and duration of CVC utilization of

more than 14 days were found to be independent risk factors for CLABSI among children admitted in PCMC during the study period. The diagnosis of CLABSI should be considered in symptomatic patients with central lines who have the abovementioned risk factors. Coagulase-negative *Staphylococcus* (CONS), *K. pneumoniae* and *A. baumannii* were the most commonly isolated organisms in patients with CLABSI. Hence when considering CLABSI empiric antibiotic coverage in our institution should include coverage for both gram-negative and gram-positive organisms.

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