

RISK FACTORS FOR RECURRENT BACTEREMIA IN CHILDREN UNDERGOING CHEMOTHERAPY OR HEMATOPOIETIC STEM CELL TRANSPLANTATION

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BACKGROUND

- Septicemia is one of the leading causes of death worldwide, and 6–10% of the patients who experience one episode of Gram-negative bacteremia will have another recurrent episode.
- Recurrent bacteremia by the same pathogen may be due to ineffective therapy caused by the failure to eliminate the source of infection due to insufficient duration of therapy, antibiotic choice, or inducible antibiotic resistance by the pathogen.
- The host's immunity status and the presence of indwelling catheters may also be important risk factors for recurrent bacteremia.
- Sepsis is a complication frequently encountered in children underlying treatment of hematopoietic stem cell transplant (HSCT) for malignancies, especially due to a majority of patients with indwelling venous catheters.
- Indications for catheter removal among children with central-line associated blood stream infection (CLABSI) should follow the recommendations for adults, however, difficulties in vascular access often leads to attempting treatment without catheter removal.
- Therefore, the primary aim of this study was to find risk factors for recurrent sepsis in children undergoing chemotherapy of HSCT and examine whether more aggressive catheter removal after CLABSI in children is necessary.

METHODS

- In the Pediatric Bone Marrow Transplant Center of Seoul St. Mary's Hospital, positive blood culture are prospectively monitored, to control and prevent outbreaks.
- The date of culture, culture results, symptoms presented, category of blood stream infections (by the CDC/NHSN surveillance definition (2021) of Bloodstream Infections), and whether bloodstream infections were central-line associated blood stream infection (CLABSI) were collected prospectively.
- The definition for positive differential time to positivity (DTP) suggesting CLABSI was the detection of bacterial growth from a blood culture drawn from a central venous catheter (CVC) 2 hours prior to detection of bacterial growth from a blood culture drawn from the peripheral vein.
- For blood cultures, at least 5–10 mL of blood was drawn from the peripheral vein and CVC of the patient. The culture bottles were then inserted into the incubators at the same time.
- When the alarm went off for a presumptive bacterial growth in any of the culture bottles, the time was recorded to monitor differential time to positivity.
- The Vitek-2 (bioMérieux, Marcy l'Etoile, France) was used for species identification and antimicrobial susceptibility tests. The Clinical and Laboratory Standards Institute (CLSI) guideline was used to determine the cutoff for antibiotic susceptibilities and the presence of ESBL-producing *K. pneumoniae*.

RESULTS

- During September 2016 to February 2021, a total 280 cases of laboratory confirmed bloodstream infections (LBCT) or Mucosal Barrier Injury Laboratory-Confirmed Bloodstream Infection (MBI-LBCT) were diagnosed in children below 18 years old with underlying hematologic malignancies or solid tumors. Of these, 52.9% (n=148) were male, and the mean age was 9.7 (SD±6.1) years old.

Table 1. Etiology of bacteremia in all patients, and those with recurrent CLABSI

Cultured bacteria	Total		CLABSI		Recurrent sepsis ≥2nd episode	
	N=280	%	n=145	%	n=53	%
<i>Streptococcus mitis/oralis</i>	67	23.9%	38	26.2%	10	18.9%
<i>Escherichia coli</i>	43	15.4%	27	15.7%	9	17.0%
<i>Klebsiella species</i>	31	11.1%	21	14.5%	6	11.3%
<i>Staphylococcus epidermidis</i>	21	7.5%	5	3.4%	3	5.7%
<i>Enterococcus faecium</i>	14	5.0%	8	5.5%	4	7.5%
<i>Pseudomonas aeruginosa</i>	13	4.6%	5	3.4%	5	9.4%
<i>Haemophilus influenzae</i>	10	3.6%	5	3.4%	2	3.8%
<i>Candida species</i>	9	3.2%	5	3.4%	4	7.5%
<i>Corynebacterium species</i>	8	2.9%	5	3.4%	3	5.7%
<i>Enterobacter cloacae</i>	7	2.5%	3	2.1%	2	3.8%
<i>Neisseria species</i>	6	2.1%	3	2.1%	1	1.9%
<i>Staphylococcus aureus</i>	6	2.1%	5	3.4%		
<i>Bacillus cereus</i>	5	1.8%	1	0.7%	1	1.9%
<i>Capnocytophaga species</i>	5	1.8%	1	0.7%		
<i>Stenotrophomonas maltophilia</i>	5	1.8%	3	2.1%	3	5.7%
<i>Staphylococcus haemolyticus</i>	4	1.4%	3	2.1%		
<i>Acinetobacter baumannii complex</i>	3	1.1%	3	2.1%	1	1.9%
<i>Haemophilus species</i>	3	1.1%	1	0.7%	2	3.8%
<i>Streptococcus pneumoniae</i>	3	1.1%	2	1.4%	1	1.9%
<i>Citrobacter freundii</i>	2	0.7%	1	0.7%		
<i>Klebsiella pneumoniae</i>	2	0.7%	1	0.7%	1	1.9%
<i>Pseudomonas aeruginosa</i>	2	0.7%				
<i>Streptococcus sanguinis</i>	2	0.7%	1	0.7%		
<i>Campylobacter jejuni</i>	1	0.4%				
<i>Dermabacter hominis</i>	1	0.4%				
<i>Fusarium species</i>	1	0.4%	1	0.7%		
<i>Granulicatella adiacens</i>	1	0.4%	1	0.7%		
<i>Proteus mirabilis</i>	1	0.4%	1	0.7%		
<i>Raoultella ornitholytic</i>	1	0.4%				
<i>Staphylococcus capitis</i>	1	0.4%				
<i>Streptococcus salivarius</i>	1	0.4%				
<i>Staphylococcus Warneri</i>	1	0.4%				

- CLABSI was diagnosed in 51.8% (n=145), and the most common pathogens cultured were as follows: *S. mitis/oralis* (24.0%, n=67), *E. coli* (15.4%, n=43), and *Klebsiella species* (11.1%, n=31).
- The most common pathogen in recurrent CLABSI episodes were *S. mitis/oralis* (18.9%, n=10), followed by *E. coli* (17.0%, n=9).

Figure 1. Image of a patient with two indwelling central venous catheters

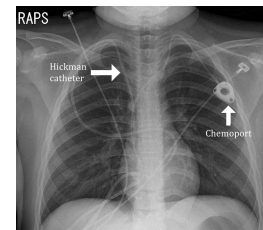
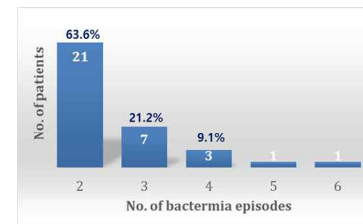


Figure 2. No. of recurrent episodes in patients with CLABSI



- Patients with both hickman catheters and chemoports inserted (two indwelling CVCs, fig. 1) made up 9.6% (n=27), and of the patients with CLABSI, recurrent sepsis (≥2nd episode) events occurred 53 times in 33 patients.
- Of the 33 patients that experienced recurrent CLABSI episodes, 36.4% (n=12) experienced 3 or more episodes (Figure 2).
- In a univariable analyses, duration of indwelling catheters (P=0.001) and no removal of central lines after previous episode (P<0.001) and two indwelling catheters (P=0.092) were factors associated with recurrent bloodstream infections (Table 3).
- However, a multivariable analysis showed that factors associated with recurrent blood stream infections were as follows: duration of indwelling catheter (OR, 1.002; 95% CI, 1.001-1.004; P<0.001) and no removal of central lines after previous episode (OR, 51.143; 95% CI, 6.6-395.0; P<0.001) (Table 3).

CONCLUSION

- The duration of indwelling catheters should be monitored, and central lines should be removed as soon as possible. Furthermore, more aggressive approach in removing permanent catheters after CLABSI in children should be considered.

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Table 3. Univariate and multivariate logistic analyses of Risk factors for recurrent sepsis

Parameters	Univariate			Multivariate		
	OR	95% CI		Adjusted OR	95% CI	
		Lower	Upper		Lower	Upper
Age	0.979	0.9	1.0	0.989		
Underlying disease	1.187	0.7	1.3	0.785		
Days after last chemotherapy	1.423	0.6	2.7	0.879		
Neutropenic state	1.613	0.5	4.2	0.322		
CLABSI	1.011	0.6	1.6	0.933		
duration of indwelling catheter	1.002	1.001	1.003	0.001	1.002	1.001
Hickman change prior to reinfection	39.817	5.2	302.4	<0.001	51.113	6.622
Two indwelling catheters	2.013	0.9	4.4	0.092	1.074	0.422