

STREPTOCOCCUS MITIS/ORALIS SEPSIS IN PATIENTS WITH NEUTROPENIA AFTER CHEMOTHERAPY



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BACKGROUND

- Streptococci are the dominant species in the human oral cavity and upper respiratory tract.
- Oral mucositis affects 30–40% of the patients receiving chemotherapy and 80% undergoing HSCT. During episode of oral mucositis, patients are at a risk for invasive infections caused by opportunistic pathogens in the oral cavity.
- The purpose of this study was to investigate the clinical characteristics of *S. mitis/oralis* invasive infection and find patients at high risk for with *S. mitis/oralis* infection in order to prevention of *S. mitis/oralis* bacteremia.

METHODS

- Patients receiving chemotherapy or stem cell transplant for malignancies and primary immunodeficiencies at the pediatric bone marrow transplant center of Seoul St. Mary's hospital admitted during January 2017 to December 2020 for blood stream infections were included in this study. Chart review (Demographics, underlying disease, laboratory, fever duration, etc) of the patients were done retrospectively
- Inclusion criteria were as follows:
 - Underlying malignancies or stem cell transplant recipients
 - Fever (Axillary T $\geq 37.5^{\circ}\text{C}$, tympanic T $\geq 38.0^{\circ}\text{C}$)
 - Blood stream infection.
- Prospectively collected database of patients with bloodstream infections (BSI) in the pediatric Hematology ward.
- Bacterial identification: MALDI-TOF MS (VITEK[®] MS, bioMerieux) for bacterial identification
- Antimicrobial susceptibility testing: Vitek 2 AST (bioMerieux)

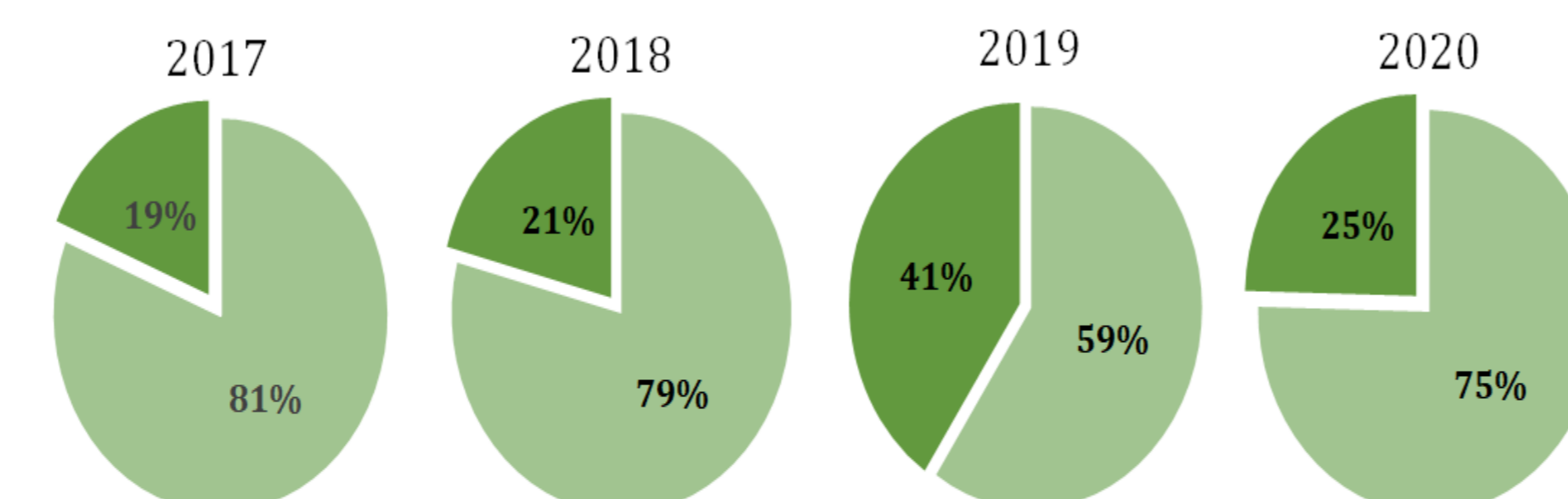
RESULTS

- During the four-year study period, there were 4,647 admissions, and 2,358 (50.7%) experienced at least 1 episode of fever. Overall, the incidence of bacteremia was 10.9% of all febrile children (N=258).
- The most common pathogen causing bacteremia was *S. mitis/oralis* (24%, n=62), followed by *E. coli* (14.3%, n=37), *Klebsiella* spp. (10.5%, n=27), and *S. epidermidis* (7.4%, n=19) (Table 1). *Candida* sepsis occurred in 3.5% (n=9) of the children. Four patients were diagnosed with *S. mitis/oralis* bacteremia plus another bacteria (*S. aureus*, *E. coli*, *R. ornitholytica*, and *C. freundii*).
- By year, the proportion of bacteremia caused by *S. mitis/oralis* was 19% in 2017, 21% in 2018, 41% in 2019, and 25% in 2020. 51% of *S. mitis/oralis* bacteremia occurred 8-14 days after day 0 of chemotherapy (Fig. 1).
- Of the 66 patients with *S. mitis/oralis* bacteremia, 77.3% (n=51) were diagnosed between 8-14 days (2nd week) after initiating chemotherapy, and 89.4% of the regimens contained cytarabine (DNA analogue causing the mucositis and hair loss) (Fig. 2).

Table 1. Incidence of bacteremia

	No. of cases N=258	% of Total		No. of cases N=258	% of Total
Gram positive	135	52.3	Gram negative	108	41.9
<i>Streptococcus mitis/oralis</i>	62	24.0	<i>Escherichia coli</i>	37	14.3
<i>Staphylococcus epidermidis</i>	19	7.4	<i>Klebsiella</i> spp.	27	10.5
<i>Enterococcus faecium</i>	14	5.4	<i>Pseudomonas aeruginosa</i>	13	5
<i>Rothia mucilaginosa</i>	9	3.5	<i>Enterobacter cloacae</i>	6	2.3
<i>Corynebacterium</i> spp	7	2.7	<i>Neisseria</i> spp.	5	1.9
<i>Staphylococcus aureus</i>	6	2.3	<i>Capnocytophaga sputigena</i>	5	1.9
<i>Bacillus</i> spp.	5	1.9	<i>Stenotrophomonas maltophilia</i>	5	1.9
<i>Staphylococcus haemolyticus</i>	3	1.2	<i>Acinetobacter baumannii</i>	3	1.2
<i>Streptococcus pneumoniae</i>	2	0.8	<i>Citrobacter</i> spp.	2	0.8
<i>Streptococcus sanguinis</i>	2	0.8	<i>Haemophilus</i> spp.	2	0.8
<i>Paenibacillus</i> spp.	2	0.8	<i>Camphylobacter jejuni</i>	1	0.4
<i>Granulicatella adiacens</i>	1	0.4	<i>Proteus mirabilis</i>	1	0.4
<i>Streptococcus salivarius</i>	1	0.4	<i>Raoultella ornitholytic</i>	1	0.4
<i>Staphylococcus capitis</i>	1	0.4			
<i>Dermabacter hominis</i>	1	0.4			

Figure 1. Proportion of bloodstream infections caused by *S. mitis/oralis*



- Patients with Acute myeloid leukemia had a significantly higher rate of bacteremia with *S. mitis/oralis* (P<0.001) compared to patients with Acute lymphoid leukemia, solid tumors, and other malignancies (Table 2).
- A multivariate analyses on risk factors for *S. mitis/oralis* bacteremia was the underlying disease AML (OR, 4.6; 95% CI, 2.4-8.7; P<0.001), and the use of cytarabine (OR, 4.5; 95% CI, 2.4-8.5; P<0.001). Compared to ALL, AML has a HR 3.7(95% CI 1.9-7.2) of bacteremia with *S. mitis/oralis* (Table 3).

Figure 2. Timing of *S. mitis/oralis* bacteremia

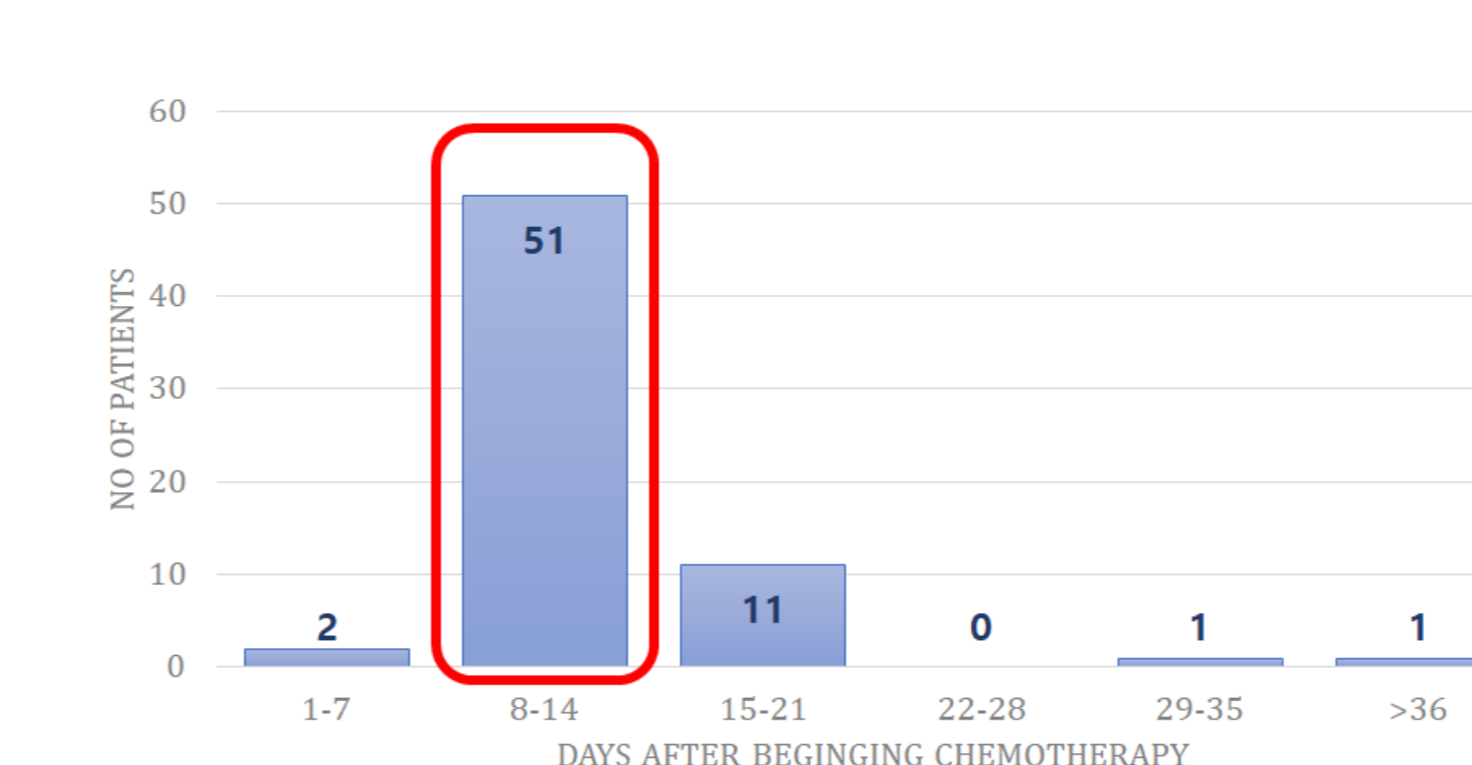


Table 2. Proportion of patients with sepsis caused by *S. mitis/oralis* according to underlying malignancies

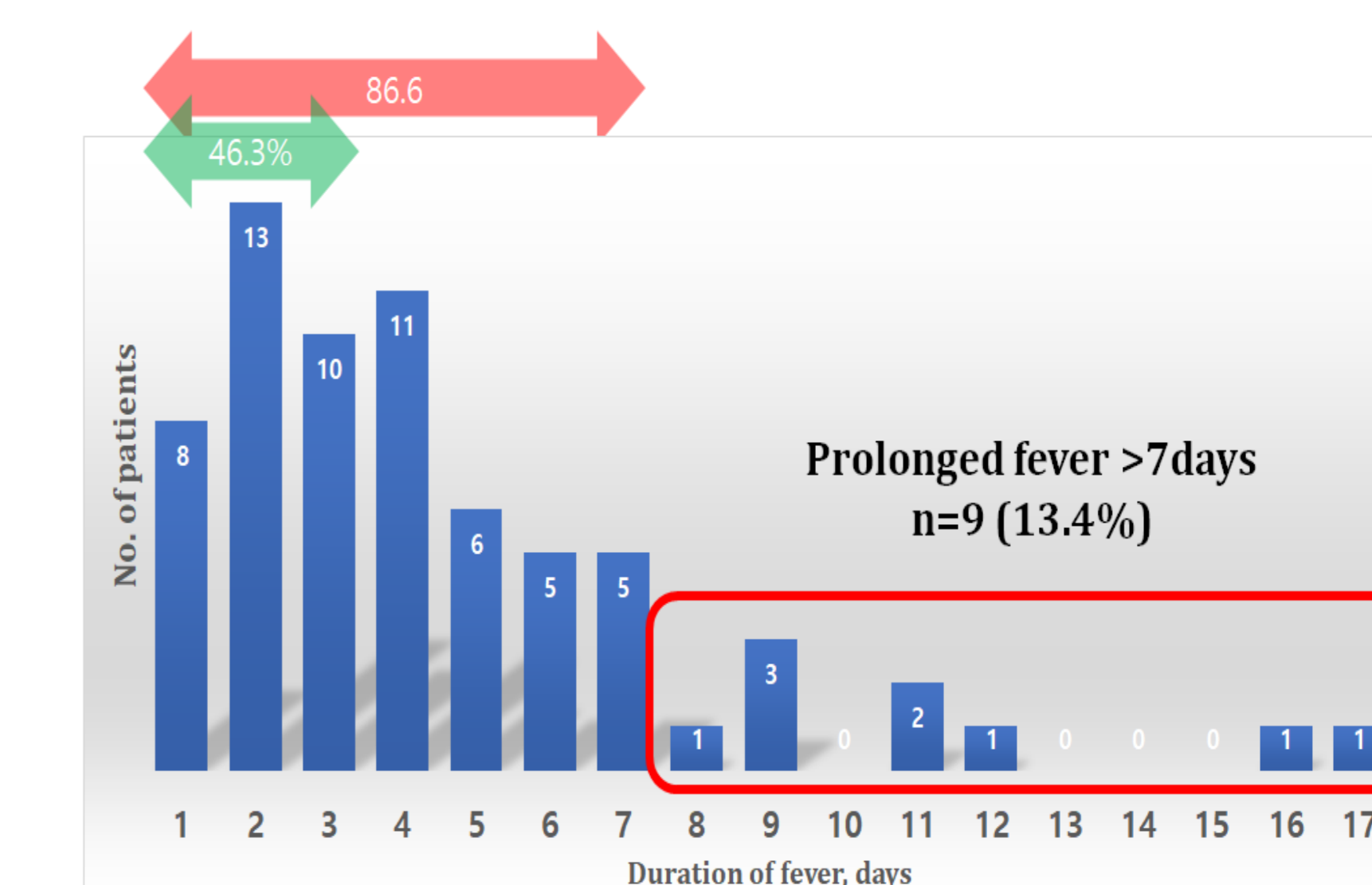
	Total N=258	Other Pathogen n=191	<i>S. mitis/oralis</i> n=67	P
ALL	99 (38.4)	85 (44.5)	14 (20.9)	
AML	137 (53.1)	85 (44.5)	52 (77.6)	<0.001
Solid tumor	11 (4.3)	10 (5.2)	1 (1.5)	
Others	11 (4.3)	11 (5.8)	0	

Table 3. Multivariate analyses on risk factors for *S. mitis/oralis* bloodstream infection

	OR	95% CI	P	OR	95% CI	P
Sex	1	0.9-1.0	0.462			
Age	0.9	0.5-1.7	0.855			
AML	4.6	2.5-8.7	<0.001	4.6	2.4-8.7	<0.001
Neutropenia	7.1	0-71.7	0.997			
Cytarabine	4.5	2.4-8.5	<0.001	-	-	-
Idarubicin	0.9	0.3-1.6	0.986			
Mitoxantrone	1.1	0.6-1.3	0.456			
Fludarabine	0.7	0.3-6.1	0.864			

- Prolonged duration of fever (>7 days) was observed in 13.4% of the patients, and a fever duration >14 days was observed in 2 patients (Fig. 3).
- Although no mortality was observed as a result of *S. mitis/oralis* infections, 23.9% (n=16) had complications such as septic shock and infective endocarditis.

Figure 3. Fever duration in patients with *S. mitis/oralis*



CONCLUSION

- S. mitis/oralis* sepsis causes significant morbidity in patients undergoing treatment for malignancies.
- Patients with AML are at the highest risk, especially after induction or consolidation chemotherapy including cytarabine.
- Further studies are needed to understand the mechanism for *S. mitis/oralis* in the invasion of the oral mucosa to prevent *S. mitis/oralis* sepsis

References >

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