Staphylococcus aureus bacteremia in children: Antibiotic resistance and mortality

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Background: *Staphylococcus aureus* (SA) is a major cause of bacteremia in children. Methicillin-resistant SA (MRSA) is considered a public health threat; however, difference in prognosis of children suffering of Methicillin-sensitive SA (MSSA) vs. MRSA bacteremia is not well defined.

Methods: Data of all SA bacteremia events in children (0-16 years), from 2002 to 2016, in a single tertiary center were Collected. Positive cultures within 48 hours of hospitalization were considered community

associated (CA). Those obtained afterwards or from children hospitalized within the previous year, were considered Health-care associated (HA).

Results: We recorded 427 events, 284 (66%) were HA, 64 (15%) were MRSA and 9 (2%) were CA-MRSA (Table 1). There was no increase in MRSA during the study period (Figure 1). In-hospital, 30-day and one-year mortality were 3% (12 cases), 3.5% (16 cases) and 12% (50 cases) respectively. Prior diagnosis and current site of infection was available for 335 (78%) children (Table 2). Children with HA bacteremia had a much higher

rate of prior diagnosis of chronic disease. The Kaplan-Meier survival curves in the first year after positive blood culture is shown in Figure 2A. Comparing 47 pairs of HA-MSSA and HA-MRSA bacteremia events, matched according to length of stay prior bacteremia, showed similar survival rate (Figure 2B). On multivariate analysis controlling for demographics, admitting department and prior morbidity, HA bacteremia and prior chronic disease were associated with increased one-year mortality: HR (95% CI) 4.1 (1.3-12) and 3.4 (1.2 to 9.0), respectively. MRSA was not significantly associated with increase one-year mortality compared to MSSA: HR (95%CI) 1.4 (0.6 to 3.1).

Figure 1. Pediatric *Staphylococcus aureus* bacteremia, 2002-2016

Table 1. Pediatric *Staphylococcus aureus* bacteremia, 2002-2016, Hadassah medical center, Jerusalem, Israel (N=427).

	HA-MSSA	HA-MRSA	CA-MSSA	CA-MRSA	p-value
Number (%)	226 (53%)	55 (12.9%)	137 (32.1%)	9 (2.1%)	
Female, n (%)	87 (38%)	22 (40%)	37 (27%)	5 (55%)	0.06
Mean Age, years (SD)	3.5 (4.0)	2.9 (3.4)	5.5 (4.7)	3.6 (4.0)	<0.001
Mean duration of hospitalization before positive culture, days (SD)	10.3 (14.4)	20.1(20.3)	0.71 (0.49)	0.76 (0.48)	<0.001
Mean duration of hospitalization after positive culture, days (SD)	16 (17.3)	23 (23)	5.74 (8.8)	7.2 (12.7)	<0.001
Mortality after 30 days, n (%)	7 (3%)	6 (11%)	3 (2%)	0 (0%)	
In hospital death, n (%)	7 (3%)	4 (7%)	1 (1%)	0 (0%)	

Table 2. Prior diagnosis and current site of infection (N=335)

	HA_MSSA	HA_MRSA	CA_MSSA	CA_MRSA	p-value
Total	160 (48%)	48 (14%)	119 (36%)	8 (2%)	
Prior chronic disease	119 (74%)	38 (79%)	28 (24%)	1 (13%)	<0.001
Hemato-oncology and Immune suppression	60 (38%)	11 (23%)	5 (4%)	0 (0%)	<0.001
Congenital malformation	39 (24%)	22 (46%)	16 (13%)	1 (13%)	<0.001
Any concurrent infection	58 (36%)	15 (31%)	81 (68%)	2 (25%)	<0.001
Osteomyelitis and Arthritis	18 (11%)	1 (2%)	46 (39%)	1 (13%)	<0.001
Endocarditis	5 (3%)	0 (0%)	3 (3%)	0 (0%)	0.62
Skin and soft tissue infection	9 (6%)	3 (6%)	13 (11%)	0 (0%)	0.3

MSSA- Methicillin-sensitive *Staphylococcus aureus*, MRSA- Methicillin-resistant *Staphylococcus aureus*, CA- Community associated, HA-Health care associated. See Methods for definitions.

Figure 2. Survival following pediatric *Staphylococcus aureus* bacteremia

Conclusions: Short term pediatric mortality after SA bacteremia is low. HA-SA bacteremia bares an increased long-term risk for mortality, particularly in children suffering chronic disease. Mortality was not increased for MRSA compared to MSSA bacteremia. The very low rate of CA-MRSA bacteremia justifies our current practice not to include Glycopeptides in the empiric treatment of CA bacteremia.