

Staphylococcus aureus antibiotic susceptibility patterns in pediatric atopic dermatitis

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Abstract

Background/Objectives: *Staphylococcus aureus* is the most prevalent bacterial pathogen in atopic dermatitis (AD) patients presenting with skin infections. Despite the known association between *S aureus* and AD, guidance on empiric antibiotics for skin infections in pediatric AD patients is limited.

Methods: We conducted a retrospective study over a five-year period to characterize the *S aureus* strains recovered from pediatric AD patients with clinically apparent bacterial skin infections treated in an academic medical center. We assessed patient demographics and dilute bleach bath usage to determine whether these factors were correlated with methicillin resistance. Culture results from our AD cohort were also compared to those from pediatric patients presenting to the Saint Louis Children's Hospital emergency department (ED) with *S aureus* skin abscesses from 2013 to 2015.

Results: Methicillin-sensitive *S aureus* (MSSA) was more prevalent (77.8%) than methicillin-resistant *S aureus* (MRSA) (22.2%). There was no correlation between MRSA and age, sex, race, or dilute bleach bath use. In comparison with pediatric patients presenting to the ED, AD patients had lower rates of MSSA susceptibility to doxycycline and MRSA susceptibility to trimethoprim-sulfamethoxazole (TMP-SMX).

Conclusions: First-generation cephalosporins remain appropriate empiric therapy for most pediatric AD patients. In patients with a history of MRSA, empiric doxycycline or TMP-SMX could be considered, given their high MRSA susceptibility rates.

KEYWORDS

atopic dermatitis, pediatrics, SSTI, *Staphylococcus aureus*

1 | INTRODUCTION

Atopic dermatitis (AD) is one of the most common pediatric skin disorders, affecting up to 18% of the pediatric population in the United States.¹ *Staphylococcus aureus* is the most prevalent bacterial pathogen in AD patients presenting with skin infections, and studies have demonstrated that higher *S aureus* bioburden correlates with increased AD severity.²

Despite the known association between *S aureus* and AD, guidance on the optimal empiric antibiotic for skin infections in pediatric AD patients is limited. Thus, we conducted a retrospective study to characterize the *S aureus* strains recovered from pediatric AD patients with clinically visible bacterial skin infections treated in an academic medical center. With these data, we can better understand *S aureus* susceptibility trends in pediatric AD patients presenting with an acute skin infection and examine factors associated with

methicillin-resistant *S aureus* (MRSA) infection, ultimately informing empiric antibiotic therapy.

2 | MATERIALS AND METHODS

The Washington University in St. Louis Institutional Review Board approved this retrospective cohort study of patients seen at Saint Louis Children's Hospital (SLCH) and its associated dermatology clinics during the five-year period from September 1, 2012, to August 31, 2017 (the "study period"). Included patients were under 18 years of age, had a diagnosis of AD, were evaluated by a dermatologist, and had a cutaneous aerobic bacterial culture obtained from a clinically infected site during the study period. Patients were excluded if they were immunosuppressed at the time of infection (not including medications for AD [eg, methotrexate]), including a history of solid organ or hematopoietic stem cell transplant or human immunodeficiency virus infection, or had other (non-AD) significant skin disease.

A query using ICD-9 and ICD-10 codes for AD and bacterial skin infection flagged potential patients. Electronic medical records were reviewed to identify patients with clinical signs of infection and positive bacterial cultures; 118 patients with a total of 182 cultures met our inclusion criteria. Date of birth, race, sex, body sites affected by AD (face, scalp, neck, trunk, upper extremities, lower extremities,

and groin/buttocks), patient-reported use of dilute bleach baths, and bacterial culture results were collected for each patient through chart abstraction. The specific body site of each culture was not recorded, as clinicians may swab multiple sites for a single culture. Data from AD patients with MRSA infections were compared to those with methicillin-sensitive *S aureus* (MSSA) infections. Culture results from our AD cohort were also compared to those from pediatric patients presenting to the SLCH emergency department (ED) with *S aureus* skin abscesses from 2013 to 2015.

Of the 118 study patients, four were excluded because their cultures did not grow *S aureus*. Cultures from 8 patients grew MSSA and MRSA during the study period, and these patients were excluded from the analyses directly comparing patient factors (ie, sex, race, age, dilute bleach bath usage) between patients with MRSA vs MSSA infections unless otherwise noted. All *S aureus* isolates were included in the antibiotic susceptibility analysis, with the exception of three cultures that simultaneously grew both MSSA and MRSA.

Descriptive statistics were used to characterize the study population and the proportion of AD patients with MRSA and MSSA infections. Comparison of the factors associated with MRSA and MSSA infection was made with SPSS (IBM SPSS version 25, Chicago, IL) using Fisher's exact test for categorical data and Student's *t* test for continuous data. All tests for significance were two-tailed, and *P*-values of < 0.05 were considered significant.

TABLE 1 Patient demographics

	All patients AD (n = 106)	MSSA AD (n = 83)	MRSA AD (n = 23)	P-value
Sex, n (%)				
Male	69 (65)	55 (66)	14 (61)	0.63
Female	37 (35)	28 (34)	9 (39)	
Age in y, mean (standard deviation)	5.6 (4.9)	5.7 (5.1)	5.2 (4.2)	0.66
Race, n (%)				
Caucasian	54 (51)	40 (48)	14 (61)	0.66
African American	42 (40)	34 (41)	9 (39)	
Other ^a	10 (9)	9 (11)	1 (4)	
Dilute bleach baths used, n (%) ^b				
Yes	27 (25)	20 (24)	7 (30)	1.00
No	35 (33)	27 (33)	8 (35)	
Body site of AD involvement, n (%)				
Scalp	37 (35)	26 (31)	11 (48)	0.22
Face	90 (85)	71 (86)	19 (83)	0.75
Neck	42 (40)	38 (46)	4 (17)	0.02
Trunk	90 (85)	73 (88)	17 (74)	0.11
Upper extremities	105 (99)	82 (99)	23 (100)	1.00
Lower extremities	101 (95)	79 (95)	22 (96)	1.00
Groin or buttocks	25 (24)	22 (27)	3 (13)	0.27

^aDocumented as Indian, unknown, "other."

^bNot documented for 44 patients.

TABLE 2 Antibiotic susceptibilities

Isolates (n; %)	Antibiotic, % susceptible (n tested)							
	Cefazolin	Clindamycin	Erythromycin	TMP-SMX	Doxycycline	Vancomycin	Rifampin	Linezolid
<i>All S aureus</i>								
AD (167; 100)	78 (167)	84 (166)	59 (167)	98 (166)	90 (62)	100 (167)	100 (28)	100 (27)
ED (4077; 100)	56	81	42	98	97	98	100	100
<i>MSSA</i>								
AD (130; 78)	100 (130)	86 (129)	70 (130)	100 (129)	89 (47)	100 (130)	100 (20)	100 (20)
ED (2296; 56)	100	82	65	99	97	98	100	100
<i>MRSA</i>								
AD (37; 22)	0 (37)	76 (37)	22 (37)	92 (37)	93 (15)	100 (37)	100 (8)	100 (7)
ED (1781; 44)	0	80	12	98	98	98	99	100

3 | RESULTS

Of the 182 cultures obtained from skin infections during the study period, 170 (93.4%) grew *S aureus* and 12 grew other species (four *Streptococcus pyogenes* and the remainder with mixed skin flora). Excluding the three cultures that grew both MSSA and MRSA, 130 (77.8%) of the *S aureus* cultures grew MSSA and 37 (22.2%) grew MRSA.

3.1 | Patient demographics

The prevalence of MRSA vs MSSA did not differ significantly by age at first culture ($P = 0.66$), sex ($P = 0.63$), or race ($P = 0.66$; Table 1). There were 69 total *S aureus* cultures from Caucasian patients (1.2 per patient) and 86 from African American patients (1.8 per patient; $P < 0.003$).

3.2 | Body site involvement by AD

The upper extremities were the body sites most commonly affected by AD (99%), followed by the lower extremities (95%) and then the trunk and the face (both 85%). Least commonly involved was the groin or buttocks (24%). All but one of the patients had more than one site affected by AD (99%), and the median number (range) of sites affected was 5 (1-7).

3.3 | Dilute bleach baths

Twenty-seven patients reported using dilute bleach baths during the study period, while 35 reported they did not (dilute bleach bath usage was not recorded in the remainder). There was no significant difference in MRSA prevalence in patients taking and not taking dilute bleach baths ($P = 1.00$).

3.4 | Antibiotic susceptibility

Antibiotic susceptibility patterns are detailed in Table 2, along with the susceptibility profiles of *S aureus* isolates obtained from skin

abscess cultures from pediatric patients presenting to the SLCH ED. The prevalence of MRSA infection in our cohort of AD patients (22%) was lower than the 44% MRSA prevalence seen in the ED. Susceptibility to doxycycline trended lower in the MSSA isolates collected from AD patients as compared to the ED population (89.4% vs 97%, respectively). Similarly, MRSA isolates from AD patients tended to be less susceptible to TMP-SMX than those from the ED population (92% vs 98%, respectively).

4 | DISCUSSION

Staphylococcus aureus was the primary pathogen recovered from skin infections in our cohort of AD patients, representing 93% of the total positive cultures. The prevalence of MRSA in the *S aureus* skin infections was 22%, higher than the rate seen in other recent U.S. studies specifically examining AD patients, which has ranged from 7.4% to 15.0%.³⁻⁵

In contrast to the increasing community-acquired MRSA (CA-MRSA) rates of the early 2000s, recent studies of *S aureus* trends in the general pediatric population have noted a decline in CA-MRSA.⁶⁻⁸ Historically, the USA300 clone has been responsible for most CA-MRSA infections, and herd immunity to the USA300 clone may be contributing to this decline.⁷ However, there has been a recent increase in USA300 clones of CA-MSSA,^{9,10} which is notable because the USA300 clone has been associated with greater virulence regardless of methicillin susceptibility.

We identified no statistically significant factors for MRSA skin infection as compared to MSSA. However, there were a higher average number of cultures in African American patients as compared to Caucasian patients. The reason for this difference is not obvious, but a higher rate of USA300 has previously been noted in African American populations with CA-MSSA infections.⁹

MSSA was more common than MRSA in our study cohort, and first-generation cephalosporins remain a reasonable empiric option for these pediatric AD patients. Further supporting this choice is a 2012 study of AD patients treated with topical steroids and oral

cephalexin that saw improvement in AD severity in both the MSSA and MRSA groups.³ In patients with a history of MRSA, empiric doxycycline or TMP-SMX could be considered, given their high MRSA susceptibility rates (93 and 92%, respectively). Of note, these antibiotics provide poor streptococcal coverage, and although *S pyogenes* and viridans group streptococci were seen in only 3% of the cultures in our cohort, this may remain clinically significant. Culture results therefore remain critical to directing therapy.

In comparison with pediatric patients presenting to the ED, AD patients had lower rates of MSSA susceptibility to doxycycline and MRSA susceptibility to TMP-SMX. This increased rate of antibiotic resistance is noteworthy and perhaps reflects a greater degree of prior antibiotic exposure in the AD population.

Our study has several limitations. The retrospective, single-center design may limit generalizability. We did not record the body sites from which cultures were obtained, and we cannot draw any conclusions about a predisposition for MRSA or MSSA to infect specific body sites. We were also unable to reliably monitor prior antibiotic exposure in our population; future work could examine whether prior exposure differed significantly in the MRSA and MSSA groups. Moreover, AD severity could not be reliably inferred, limiting our ability to comment on culture results in relation to disease severity. Finally, nearly 60% of our patients did not have information regarding dilute bleach bath use. A decreased severity of AD has previously been observed in patients with bacterial skin infections who used dilute bleach baths,⁴ and further prospective studies on dilute bleach baths are needed.

5 | CONCLUSION

Staphylococcus aureus remains the most common pathogen in pediatric AD patients with bacterial skin infections. The prevalence of MRSA in our cohort was 22%, higher than seen in previous U.S. studies of AD patients. There was no significant correlation between MRSA infection and age, sex, race, or dilute bleach bath usage. However, African American patients had a higher number of cultures per patient, perhaps reflecting increased disease severity or disease refractory to treatment. While obtaining a culture is crucial in guiding final antibiotic therapy, first-generation cephalosporins are appropriate empiric options for most pediatric AD patients presenting with bacterial skin infections. Clindamycin, tetracyclines, or TMP-SMX can be considered in patients suspected to have, or with a history of, MRSA infection, as guided by one's local antibiogram data.

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