Antimicrobial Stewardship & Healthcare Epidemiology (2023), **3**, e12, 1–4
doi:10.1017/ash.2022.370

SHEA

Concise Communication

Trends in pediatric community-onset *Staphylococcus aureus* antibiotic susceptibilities over a five-year period in a multihospital health system

Erica C. Prochaska MD[1], Shaoming Xiao MSPH[1], Pranita D. Tamma MD, MHS[1], Anna Sick-Samuels MD, MPH[1,2], Christina Schumacher PhD, MHS[3], Avinash Gadala PhD, MS[2], Karen C. Carroll MD[4] and Aaron M. Milstone MD, MHS[1,2]

[1]Division of Pediatric Infectious Diseases, Department of Pediatrics, Johns Hopkins University School of Medicine, Baltimore, Maryland, [2]Department of Hospital Epidemiology and Infection Control, Johns Hopkins Health System, Baltimore, Maryland, [3]Division of General Pediatrics, Department of Pediatrics, Johns Hopkins University School of Medicine, Baltimore, Maryland and [4]Division of Medical Microbiology, Department of Pathology, Johns Hopkins University School of Medicine, Baltimore, Maryland

Abstract

The epidemiology of community-onset *Staphylococcus aureus* infections is evolving. We performed a multihospital, retrospective study of pediatric community-onset *S. aureus* susceptibilities between 2015 and 2020. Oxacillin and clindamycin susceptibility remained lower at 67% and 75%, respectively. Tetracycline and trimethoprim-sulfamethoxazole susceptibility remained high at >90%. Oxacillin susceptibility was highest in invasive infections.

(Received 19 September 2022; accepted 30 November 2022)

Staphylococcus aureus remains the most common cause of invasive bacterial infections in children.[1] Hospital-onset methicillin-resistant *S. aureus* (MRSA) rates have decreased in the United States, whereas community-onset MRSA infections have decreased to a lesser extent.[2,3] Although most epidemiologic studies have focused on adults, MRSA rates appear to be declining in children as well.[4,5] In the United States, pediatric hospitalizations due to *S. aureus* decreased by 35% between 2009 and 2016,[6] and pediatric outpatient visits for purulent skin and soft-tissue infections (SSTIs) decreased between 2011 and 2015.[7] Although the decrease in pediatric infections due to *S. aureus* is encouraging, the epidemiology of pediatric *S. aureus* antibiotic resistance in the community remains incomplete in the United States. Several studies have shown that MRSA susceptibility to clindamycin declined in the 2010s,[4,5] and concurrently, trimethoprim-sulfamethoxazole prescriptions for SSTIs have increased nationally.[7] Pediatric *S. aureus* infections continue to be a public health problem for children, and clinicians require contemporary *S. aureus* susceptibility data to guide antibiotic decision making. Most pediatric *S. aureus* antibiotic data available describe hospital-based trends and antibiotic susceptibilities. Here, we describe recent trends in *S. aureus* susceptibilities within a multihospital health system with a focus on pediatric community-onset infections and infections managed in the outpatient setting.

Author for correspondence: Erica C. Prochaska, MD, Johns Hopkins University School of Medicine, Department of Pediatrics, 200 North Wolfe St, Rubenstein 3141, Baltimore, MD 21287. E-mail: eprocha1@jhmi.edu

PREVIOUS PRESENTATION: Preliminary findings from this study were presented as a poster at IDWeek 2022 on October 20, 2022, in Washington, DC.

Cite this article: Prochaska EC, *et al.* (2023). Trends in pediatric community-onset *Staphylococcus aureus* antibiotic susceptibilities over a five-year period in a multihospital health system. *Antimicrobial Stewardship & Healthcare Epidemiology*, https://doi.org/10.1017/ash.2022.370

Methods

We performed a multihospital, retrospective study of temporal trends in *S. aureus* antibiotic susceptibility. Using electronic medical record (EMR) data (Epic Systems, Verona, WI), we identified bacterial cultures growing *S. aureus* obtained from patients aged <18 years between January 1, 2015, and December 31, 2020, from the Johns Hopkins Hospital (JHH) microbiology laboratory. The JHH microbiology laboratory services an urban academic medical center, an urban midlevel teaching hospital, a suburban community hospital, and hospital-affiliated outpatient clinics. We only included the first clinical culture per patient per year. We excluded cultures that likely represented colonization, such as nasal swabs or throat swabs. Invasive infections were defined as positive blood, bone, joint, and central nervous system cultures. Respiratory cultures included tracheal, sputum, bronchoalveolar lavage, pulmonary tissue, and pulmonary abscess cultures. Soft-tissue cultures were defined as skin, abscess, vesicle, and nonsurgical wound cultures. Community-onset infections were defined as cultures obtained within 3 calendar days of hospitalization or from children who were not hospitalized. Infections managed in the outpatient setting were cultures from patients with community-onset

Table 1. Characteristics of Pediatric Patients and Cultures Positive for Community-Onset *Staphylococcus aureus* Infections, 2015–2020

Characteristics	No.	%
Patient characteristics		
Total patients	2,220	
Race		
Black	958	43.2
White	813	36.6
Asian	92	4.1
Other/Unknown	357	16.0
Ethnicity		
Non-Hispanic	1,916	86.3
Hispanic	267	12.0
Other	37	1.7
Age, mean y (SD)	6.9 (±5.7)	
Sex		
Male	1,176	53.0
Female	1,043	47.0
Other	<5 patients	
Culture characteristics		
Total cultures	2,387	
MRSA	780	32.7
Culture Source		
Abdomen	7	0.3
Soft tissue	1,508	63.2
Soft tissue, surgical	75	3.1
Central nervous system	5	0.2
Urinary	72	3.0
Deep respiratory	63	2.6
Respiratory	252	10.6
Blood	130	5.4
Bone/Joint	72	3.0
Ear, sinus, nasal	134	5.6
Other	69	2.9
Collection department		
Emergency department	1,323	55.4
Hospital	662	27.7
Clinic	361	15.1
Other	39	1.6
Collection location		
Academic medical center	1,762	73.8
Mid-level teaching hospital	331	14.0
Community hospital	294	12.3
No. of cultures per year		
2015	456	
2016	436	
2017	453	
2018	410	

(*Continued*)

https://doi.org/10.1017/ash.2022.370 Published online by Cambridge University Press

Table 1. (*Continued*)

Characteristics	No.	%
2019	395	
2020	237	
Management		
Inpatient	1,035	43.4
Outpatient	1,352	56.6

Note. SD, standard deviation.

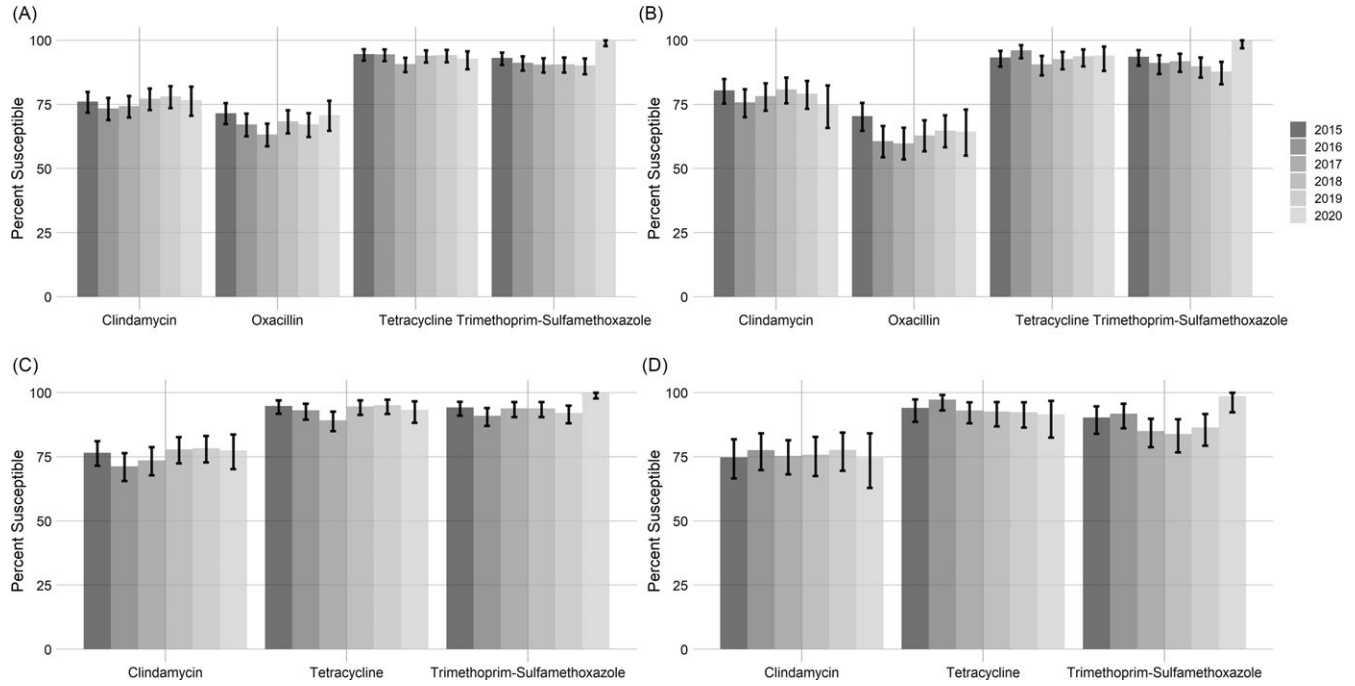

Fig. 1. Percentage with antibiotic susceptibility with 95% confidence intervals during the study period in (A) community-onset *S. aureus* cultures; (B) community-onset, outpatient-managed *S. aureus* cultures, (C) community-onset MSSA cultures; and (D) community-onset MRSA cultures.

infections who were not admitted to a hospital. The Cochran-Armitage test was used to analyze trends in antibiotic susceptibilities. $P < .05$ was considered statistically significant. Data were analyzed using R software (R Center for Statistical Computing, Vienna, Austria). This study was approved by the Johns Hopkins University Institutional Review Board.

Results

In total, 2,220 patients and 2,387 cultures were identified and met eligibility criteria. Children with a *S. aureus* culture had a mean age of 6.9 years (SD, ±5.7); 53.0% were male; and 36.6% were white (Table 1). The number of overall clinical cultures per year was stable during 2015–2019 and ranged from 395 to 456. Notably, a 40% decrease occurred in the number of cultures in 2020 (n = 237) compared to 2019 (n = 395). Overall, 1,508 cultures (63.2%) were from soft-tissue sources, and 1,352 (56.6%) were managed in the outpatient setting.

Of the 2,387 community-onset *S. aureus* cultures, 1607 (67.3%) were oxacillin susceptible, and oxacillin susceptibility was 71.5% in 2015 and 70.8% in 2020 ($P = .71$) (Fig. 1). Within all community-onset cultures, clindamycin susceptibility was stable at ~75% ($P = .27$). Trimethoprim-sulfamethoxazole and tetracycline susceptibility remained >90% ($P = .21$ and $P = .50$). In cultures of community-onset infections managed in the outpatient setting, oxacillin susceptibility was 70.4% in 2015 and 64.4% in 2020 ($P = .38$). Oxacillin susceptibility was lowest in SSTIs, with 67.1% oxacillin susceptibility in 2015 and 65.2% in 2020 ($P = .75$) (Supplementary Fig. 1). Invasive cultures were 75.5% oxacillin susceptible in 2015 and 84% susceptible in 2020 ($P = .90$).

Within MRSA cultures, tetracycline susceptibility remained ≥90% ($P = .15$). Trimethoprim-sulfamethoxazole susceptibility did not change between 2015 and 2020 ($P = .90$); however, trimethoprim-sulfamethoxazole susceptibility decreased from 90.3% to 84% between 2015 and 2018 and then increased to 99% in 2020. Clindamycin susceptibility in MRSA clinical cultures remained ~75% throughout the study period ($P = .92$). Among MSSA cultures, trimethoprim-sulfamethoxazole and tetracycline susceptibility remained ≥90% ($P = .84$ and $P = .07$). Clindamycin susceptibility remained ~75% in MSSA cultures during the study period ($P = .21$).

Discussion

Within this multihospital health system, MRSA continues to cause 30% of community-onset infections among pediatric patients.

https://doi.org/10.1017/ash.2022.370 Published online by Cambridge University Press

MRSA prevalence is particularly high among patients managed in the outpatient setting and those who present with SSTIs. Overall, 84% of invasive infections were MSSA. The stability in methicillin resistance among *S. aureus* cultures of community-onset infections differs from other epidemiologic studies that have reported decreases in methicillin resistance in pediatric *S. aureus* infections.[4–6] Most prior studies analyzed trends in hospitalized children, which may account for this difference and would align with our finding of MSSA predominance in invasive infections. The cause of national increases in invasive MSSA is unclear. Studies describing a rise of MSSA within invasive pediatric *S. aureus* infections have reported differing molecular characteristics, with the *lukSF*-PV gene detected in 6%[8]–30%[9] of community-onset invasive MSSA isolates. The increase in invasive MSSA infections nationally may be due to the rise of a virulent methicillin-susceptible strain versus community immunity to USA300.[9] Further immunologic and molecular epidemiology studies are required to understand national trends in invasive MSSA infections.

During the study period, clindamycin susceptibility to MRSA remained relatively low and trimethoprim-sulfamethoxazole and tetracycline susceptibility remained high. During 2015–2019, trimethoprim-sulfamethoxazole susceptibility fell, particularly among MRSA cultures. Surveillance of *S. aureus* susceptibilities within our health system previously showed a recent decrease in trimethoprim-sulfamethoxazole susceptibility as well.[5] Reports have since emerged suggesting that a commercial platform for antibiotic susceptibility testing may overestimate trimethoprim-sulfamethoxazole resistance compared to disc-diffusion testing.[10] In reponse to these reports, the Johns Hopkins Hospital microbiology laboratory transitioned to trimethoprim-sulfamethoxazole disc-diffusion susceptibility testing for *S. aureus* isolates in 2019. Our results show an increase in trimethoprim-sulfamethoxazole susceptibility in 2019–2020. This increase in susceptibility may be due to the concurrent change in microbiology susceptibility testing. Due to increased clindamycin resistance, there has been a national decline in clindamycin prescriptions and an increase in trimethoprim-sulfamethoxazole prescriptions for SSTIs.[7] Our results demonstrate that trimethoprim-sulfamethoxazole susceptibility has remained high despite a national increase in prescriptions; however, this trend requires close monitoring.

This study had several limitations. Culture collection sources were defined by provider-entered orders and may not represent the true source of infection. These data from a multihospital health system may not reflect trends in other geographic regions. Despite these limitations, this study confirms that MRSA continues to cause significant disease burden among pediatric patients within a multihospital health system, particularly those managed in the outpatient setting and those with SSTIs. The divergence between MRSA and MSSA disease severity is consistent with other studies and warrants increased surveillance of community-onset *S. aureus* infections to identify emerging strains and prevalent virulence factors.

Supplementary material. To view supplementary material for this article, please visit https://doi.org/10.1017/ash.2022.370

Acknowledgments. Danielle Koontz, MA, MS, contributed to the study design and data collection.

Financial support. This work was supported in part by the National Institutes of Health (grant nos. T32 AI052071 to E.P. and K24 AI141580 to A.M.).

Conflicts of interest. All authors report no conflicts of interest relevant to this article.

References

1. Cassat JE, Thomsen I. *Staphylococcus aureus* infections in children. *Curr Opin Infect Dis* 2021;34:510–518.
2. Kourtis AP, Hatfield K, Baggs J, *et al.* Vital signs: epidemiology and recent trends in methicillin-resistant and in methicillin-susceptible *Staphylococcus aureus* bloodstream infections—United States. *Morbid Mortal Wkly Rep* 2019;68:214–219.
3. Klein EY, Sun L, Smith DL, Laxminarayan R. The changing epidemiology of methicillin-resistant *Staphylococcus aureus* in the United States: a national observational study. *Am J Epidemiol* 2013;177:666–674.
4. Sutter DE, Milburn E, Chukwuma U, Dzialowy N, Maranich AM, Hospenthal DR. Changing susceptibility of *Staphylococcus aureus* in a US pediatric population. *Pediatrics* 2016;137:e20153099.
5. Khamash DF, Voskertchian A, Tamma PD, Akinboyo IC, Carroll KC, Milstone AM. Increasing clindamycin and trimethoprim-sulfamethoxazole resistance in pediatric *Staphylococcus aureus* infections. *J Pediatric Infect Dis Soc* 2019;8:351–353.
6. Spaulding AB, Thurm C, Courter JD, *et al.* Epidemiology of *Staphylococcus aureus* infections in patients admitted to freestanding pediatric hospitals, 2009–2016. *Infect Control Hosp Epidemiol* 2018;39:1487–1490.
7. Fritz SA, Shapiro DJ, Hersh AL. National trends in incidence of purulent skin and soft-tissue infections in patients presenting to ambulatory and emergency department settings, 2000–2015. *Clin Infect Dis* 2020;70:2715–2718.
8. Crandall H, Kapusta A, Killpack J, *et al.* Clinical and molecular epidemiology of invasive *Staphylococcus aureus* infection in Utah children; continued dominance of MSSA over MRSA. *PLoS One* 2020;15:e0238991.
9. Hulten KG, Mason EO, Lamberth LB, Forbes AR, Revell PA, Kaplan SL. Analysis of invasive community-acquired methicillin-susceptible *Staphylococcus aureus* infections during a period of declining community-acquired methicillin-resistant *Staphylococcus aureus* infections at a large children's hospital. *Pediatr Infect Dis J* 2018;37:235–241.
10. Al-Rawahi GN, Chorlton S, Dhaliwal S, Golding GR, Tilley P. Performance of the BD Phoenix automated microbiology system for trimethoprim-sulfamethoxazole susceptibility testing of *Staphylococcus aureus*. *J Clin Microbiol* 2019;58:e00994–19.