

Report

Prevalence of community-acquired methicillin-resistant *Staphylococcus aureus* and antibiotic resistance in patients with atopic dermatitis in Porto Alegre, Brazil

Vanessa Petry¹, MD, Caroline Lipnharski¹, MD, Giancarlo R. Bessa¹, MD, Vera B. Silveira¹, MD, Magda B. Weber¹, PhD, Renan R. Bonamigo¹, PhD, and Pedro A. d'Azevedo², PhD

¹Department of Dermatology, and

²Department of Microbiology, Federal University of Health Sciences of Porto Alegre, Porto Alegre, Rio Grande do Sul, Brazil

Correspondence

Vanessa Petry, MD
Rua Mostardeiro 291/305
CEP 90430-000 Moinhos de Vento
Porto Alegre, Rio Grande do Sul
Brazil
E-mail: vpetry@hotmail.com

Funding: This study was supported by the Conselho Nacional de Tecnologia e Desenvolvimento Científico (CNPq) and Fundação de Amparo à Pesquisa do Estado do Rio Grande do Sul (FAPERGS).

Conflicts of interest: None.

doi: 10.1111/ijd.12020

Abstract

Background Atopic dermatitis (AD) is a skin manifestation of atopy caused by hyperreactivity to various antigens. Studies have shown that 60–100% of patients with this condition present with colonization by *Staphylococcus aureus*. Given increasing rates of antimicrobial resistance, the sensitivity to antimicrobials of *S. aureus* colonizing atopic patients has been investigated. Cross-sectional studies worldwide suggest that the prevalence of methicillin-resistant *S. aureus* infection (MRSA) in the AD population varies from 0% to 30.8%.

Objectives The objectives of this study were to determinate the prevalence of *S. aureus* and MRSA in patients with AD in two dermatologic centers in Porto Alegre, Brazil.

Methods A total of 91 patients with AD attending two dermatologic centers in Porto Alegre were enrolled in this study from December 2009 to July 2011. Two skin swabs were taken from each patient, one from the nares and the other from a non-infected eczematous skin lesion. The swabs were sent to the laboratory, where standard procedures to isolate bacteria and identify *S. aureus*, antimicrobial resistance, and sensitivity patterns were carried out. The severity of AD was defined using the Eczema Area and Severity Index (EASI).

Results Of the 91 patients sampled, 67 (73.6%) patients were found to be positive for *S. aureus* colonization. Nasal swabs were positive in 55 (60.4%) patients, lesional swabs in 44 (48.4%) patients, and both lesional and nasal swabs were positive in 32 (35.2%) patients. Patients with positive swabs had a higher mean $\pm$ standard deviation EASI score [mean (9.1 $\pm$ 8.8)] compared with patients with negative swabs (3.9 $\pm$ 3.6) ($P = 0.002$). None of the 91 patients showed any evidence of MRSA infection. Overall, nearly 32% of the *S. aureus* isolated from nasal swabs and 36.40% of the *S. aureus* isolated from lesional swabs was resistant to erythromycin.

Conclusions The results of this study confirm a high rate of *S. aureus* colonization in pediatric patients with AD and indicate a relevant association between colonization and high EASI score. No MRSA was found in cultures from this sample of patients in southern Brazil. Nearly one-third of isolates were identified as resistant to erythromycin, an antibiotic that is commonly used in pediatric patients.

Introduction

Atopic dermatitis (AD) is the skin manifestation of atopy and occurs in 10–20% of children and 1–3% of adults.^{1–3} Patients with AD are subject to a combination of genetic predisposition to skin barrier dysfunctions and alterations in the innate and adaptive immune responses that leads to a higher frequency of bacterial skin colonization and infection.⁴

Staphylococcus aureus is a colonizer of the skin microbiota and can become pathogenic under certain conditions, such as the breakdown of the skin barriers or in diminished immunity.^{5–7} Individuals with AD are more than usually susceptible to staphylococcal skin infections.^{8,9} Studies have shown that 60–100% of patients with this condition present with *S. aureus*, whereas individuals without AD show colonization prevalences of 5–30%.^{9,10}

Given increasing rates of antibiotic resistance, studies to identify sensitivity to antibiotics in strains of *S. aureus* that colonize atopic patients have been conducted.^{10–26} Farajzadeh *et al.*¹⁰ analyzed swabs from non-infected eczematous lesions in 50 patients with AD in Iran and found a positive culture in 74.0% and *S. aureus* in 66.0% of cases. Bacterial resistance, at least to one of the antimicrobials tested, was found in 94.0% of samples.¹⁰ Penicillin resistance was detected in 90.0% of samples, erythromycin resistance in 66.7%, and cephalexin resistance in 13.8%.¹⁰

Reports on methicillin-resistant *S. aureus* (MRSA) infections in AD patients have been published since 2005.^{27–29} Cross-sectional studies carried out around the world suggest that prevalences of MRSA in AD populations vary from 0% to 30.8%.^{11–26} This large variation in prevalence suggests that real prevalences of MRSA may vary among countries. The objectives of the present study were to determine the prevalences of *S. aureus* and MRSA infections in patients with AD in two dermatology centers in Porto Alegre in southern Brazil.

Materials and methods

We conducted a prospective, observational, cross-sectional study. A total of 91 patients with AD who attended outpatient clinics in Porto Alegre, southern Brazil, between December 2009 and July 2011 were invited to participate in the study. The diagnosis of AD was made by the treating dermatologist according to the criteria of Hanifin and Rajka.⁴

Using a standardized questionnaire, the patient's demographic details, medical history, and current and previous systemic and topical treatments were documented. Physical examination included the evaluation of eczema severity according to the Eczema Area and Severity Index (EASI) guideline.³⁰ Patients with acute infection or a history of oral antibiotic use within the previous 30 days were excluded.

A swab was taken from the nares of each patient and another from a non-infected eczematous skin lesion and sent to the Microbiology Laboratory of the Federal University of Health Sciences of Porto Alegre, where standard procedures for bacterial isolation and the identification of microorganisms present in the lesions were followed. *Staphylococcus aureus* was identified according to Gram's stain, and growth and fermentation on mannitol agar, coagulase, and DNase. A disk diffusion test (*D*-test) was performed according to the recommendations of the Clinical and Laboratory Standards Institute,³¹ with disks containing the following antimicrobial agents: cefoxitin (30 µg); ciprofloxacin (5 µg); clindamycin (2 µg); chloramphenicol (30 µg); erythromycin (15 µg); gentamicin (10 µg); linezolid (30 µg); oxacillin (1 µg); and trimethoprim-sulfamethoxazole (25 µg). Resistance to macrolides and lincosamides was assessed by *D*-test, with a

distance of 15–26 mm between the clindamycin (2 µg) and erythromycin (15 µg) disks as previously described.³²

Informed consent was obtained from patients and parents for participation in this study. The study was approved by the Institutional Ethics Committee of the Federal University of Health Sciences of Porto Alegre.

Statistical analysis was conducted using SPSS Version 16.0 (SPSS, Inc., Chicago, IL, USA). Continuous variables were reported as means with standard deviations (SDs) and analyzed using analysis of variance (ANOVA). Categorical data were analyzed using the chi-squared test. A *P*-value of <0.05 was considered to indicate statistical significance.

Results

This study involved 91 patients with AD aged between three months and 30 years (median age: 6 years). Of these, 53.2% were male and 46.8% were female. The mean duration of disease in this population was 4.7 years.

Sixty-seven patients had at least one positive culture for *S. aureus*. The distribution of positive cultures is presented in Table 1.

There was no statistical difference between patients with and without positive cultures in terms of gender, age, time with disease, previous use of antimicrobials, previous hospitalization, and living with or not living with healthcare workers. Patients with positive cultures presented a higher EASI score compared with patients with negative cultures (Table 2). The results of antimicrobial susceptibility testing are summarized in Figures 1 and 2.

Discussion

Of the 91 patients sampled, 67 (73.6%) were found to be positive for *S. aureus* colonization. Fifty-five (60.4%)

Table 1 Results of culture for *Staphylococcus aureus* (*n* = 91)

Variable	<i>n</i> (%)
All	
Negative	24 (26.4)
Positive	67 (73.6)
Nasal swabs	
Negative	36 (39.6)
Positive	55 (60.4)
Lesional swabs	
Negative	47 (51.6)
Positive	44 (48.4)
Classifications (lesional swabs/nasal swabs)	
Negative/negative	24 (26.4)
Negative/positive	23 (25.3)
Positive/negative	12 (13.2)
Positive/positive	32 (35.2)

Table 2 Comparison of general characteristics and Eczema Area and Severity Index scores in patients with positive and negative findings for *Staphylococcus aureus* ($n = 91$)

Variable	Culture		P-value
	Negative ($n = 24$)	Positive ($n = 67$)	
Gender, n (%)			
Male	10 (41.7)	39 (58.2)	0.248 ^a
Female	14 (58.3)	28 (41.8)	
Age, years			
Mean $\pm$ SD	6.2 $\pm$ 4.1	7.3 $\pm$ 5.6	0.384 ^b
Median (IQR)	6.0 (2.1–10.0)	6.0 (3.0–10.0)	
Range	0.3–13.0	0.5–30.0	
Age 0–13 years, n	24	62	
Age 13–30 years, n	0	5	0.320 ^b
Time with disease, years			
Mean $\pm$ SD	4.1 $\pm$ 3.5	4.9 $\pm$ 5.1	0.574 ^c
Median (IQR)	2.3 (1.2–6.4)	4.0 (1.5–6.0)	
Range	0.1–12.0	0.3–30.0	
Antibacterial use in the past, n (%)			
No	6 (25.0)	12 (17.9)	0.653 ^a
Yes	18 (75.0)	55 (82.1)	
Hospitalization in the past, n (%)			
No	23 (95.8)	61 (91.0)	0.671 ^b
Yes	1 (4.2)	6 (9.0)	
Live with healthcare workers, n (%)			
No	23 (95.8)	63 (94.0)	1.000 ^b
Yes	1 (4.2)	4 (6.0)	
Eczema Area and Severity Index score			
Mean $\pm$ SD	3.9 $\pm$ 3.6	9.1 $\pm$ 8.8	0.002 ^c
Median (IQR)	2.3 (1.2–6.4)	6.1 (2.4–11.6)	
Range	0.4–12.8	0.6–40.5	

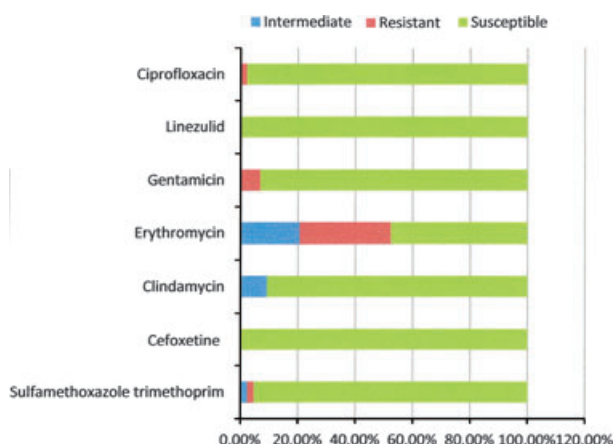
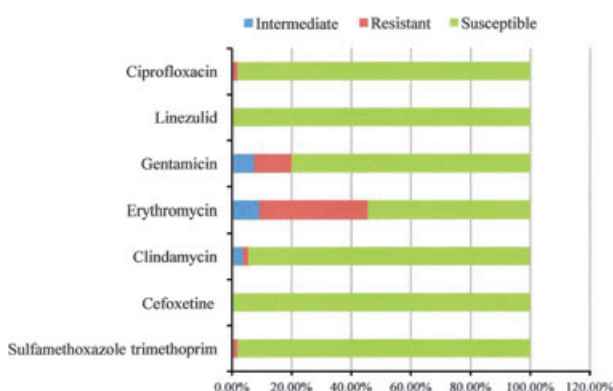
SD, standard deviation; IQR, interquartile range.

^aPearson's chi-squared test.^bFisher's exact test.^cMann–Whitney U-test.

gave positive nasal swabs, 44 (48.4%) gave positive lesional swabs, and 32 (35.2%) gave both lesional and nasal positive swabs.

These findings confirm the high rates of *S. aureus* colonization in patients with AD compared with prevalences reported in normal individuals (5–30%).^{9,10,33} The 73.6% prevalence of *S. aureus* colonization in atopic patients identified in the present study is consistent with recently published data reporting rates of 66–80%.^{13,17,21,24}

We found an association between EASI score and *S. aureus* colonization. Mean $\pm$ SD scores were higher in patients with *S. aureus*-positive swabs (9.1 $\pm$ 8.8) than in patients with *S. aureus*-negative swabs (3.9 $\pm$ 3.6) ($P = 0.002$). These results are similar to those found by Farajzadeh *et al.*¹⁰ using the SCORAD (SCORing of Atopic Dermatitis) index. Farajzadeh *et al.*¹⁰ suggested

**Figure 1** Antimicrobial susceptibility and resistance in lesional swabs**Figure 2** Antimicrobial susceptibility and resistance in nasal swabs

that the higher the rate of colonization, the more severe the dermatitis.

In 2008, Suh *et al.*²⁴ published a study in which skin swabs were collected from the nares and lesions of 54 patients with AD and reported a prevalence of 14% for MRSA infection. A recent study in 200 AD patients in Canada¹³ showed a 0.5% prevalence of MRSA infection, which is similar to the finding of no MRSA in the 91 patients reported in the present study.

The reason for the present finding of no MRSA infection despite a high prevalence of *S. aureus* colonization remains unclear. A prospective study conducted in Porto Alegre, southern Brazil, showed an 8.6% prevalence of community-acquired MRSA infection among patients with skin and soft tissue infections presenting in the emergency department.³⁴ This audit confirms that the prevalence of *S. aureus* carriage in pediatric AD patients in Porto Alegre is relatively high.

We also found a high rate (66.7%) of resistance to erythromycin, similar to that demonstrated by Farajzadeh *et al.* in 2008.¹⁰

Conclusions

The results of this study confirm a high rate of *S. aureus* colonization in patients with AD. This *S. aureus* colonization was significantly associated with increasing severity of AD. No other significant differences in demographic or clinical characteristics were found between children who were *S. aureus* culture-positive and those who were culture-negative. A high rate of resistance to erythromycin was identified. No MRSA was found in our cultures; however, this finding requires further investigation in larger studies conducted in multiple centers.

References

- 1 Rothe MJ, Grant-Kels JM. Atopic dermatitis: an update. *J Am Acad Dermatol* 1996; 35: 1–13.
- 2 Ruzicha T. Atopic eczema between rationality and irrationality. *Arch Dermatol* 1998; 134: 1462–1469.
- 3 Wuthrich B. Epidemiology and natural history of atopic dermatitis. *Allergy Clin Immunol Int* 1996; 8: 77–82.
- 4 Hanifin JM, Rajka G. Diagnostic features of atopic dermatitis. *Acta Derm Venereol Suppl (Stockh)* 1980; 92: 44–47.
- 5 Williams HC, Burney PGJ, Pembroke AC, *et al.* The UK Working Party's diagnosis criteria for atopic dermatitis III. *Br J Dermatol* 1994; 131: 406–416.
- 6 Breninkmeijer EE, Schram ME, Leeflang MM, *et al.* Diagnostic criteria for atopic dermatitis: a systematic review. *Br J Dermatol* 2008; 158: 754–765.
- 7 Hanifin JM, Cooper KD, Ho VC, *et al.* Guidelines of care for atopic dermatitis. *J Am Acad Dermatol* 2004; 50: 391–404.
- 8 Breuer K, Kappa A, Werfel T. Bacterial infections and atopic dermatitis. *Allergy* 2001; 56: 1034–1041.
- 9 Guzik TJ, Bzowska M, Kasproicz A, *et al.* Persistent skin colonization with *Staphylococcus aureus* in atopic dermatitis: relationship to clinical and immunological parameters. *Clin Exp Allergy* 2005; 35: 448–455.
- 10 Farajzadeh S, Rahnema Z, Kamyabi Z, *et al.* Bacterial colonization and antibiotic resistance in children with atopic dermatitis. *Dermatol Online J* 2008; 14: 21.
- 11 Kedzierska A, Kapinska-Mrowiecka M, Czubak-Macugowska M, *et al.* Susceptibility testing and resistance phenotype detection in *Staphylococcus* strains isolated from patients with atopic dermatitis, with apparent and recurrent skin colonization. *Br J Dermatol* 2008; 15: 1290–1299.
- 12 Hoeger PH. Antimicrobial susceptibility of skin-colonizing *S. aureus* strains in children with atopic dermatitis. *Pediatr Allergy Immunol* 2004; 15: 474–477.
- 13 Balma-Mena A, Lara-Corales I, Zeller J, *et al.* Colonization with community-acquired methicillin-resistant *Staphylococcus aureus* in children with atopic dermatitis: a cross-sectional study. *Int J Dermatol* 2011; 50: 682–688.
- 14 Breuer K, Haussler S, Kapp A, *et al.* *Staphylococcus aureus*: colonizing features and influence of an antibacterial treatment in adults with atopic dermatitis. *Br J Dermatol* 2002; 147: 55–61.
- 15 Jappe U, Schnuch A, Uter W. Frequency of sensitization to antimicrobials in patients with atopic eczema compared with non-atopic individuals: analysis of multicentre surveillance data, 1995–1999. *Br J Dermatol* 2003; 149: 87–93.
- 16 Arkwright PD, Daniel TO, Sanyal D, *et al.* Age-related prevalence and antibiotic resistance of pathogenic staphylococci and streptococci in children with infected atopic dermatitis at a single-specialty centre. *Arch Dermatol* 2002; 138: 939–941.
- 17 Hill S, Yung A, Rademaker M. Prevalence of *Staphylococcus aureus* and antibiotic resistance in children with atopic dermatitis: a New Zealand experience. *Australas J Dermatol* 2011; 52: 27–31.
- 18 Matiz C, Tom WL, Eichfield LF, *et al.* Children with atopic dermatitis appear less likely to be infected with community-acquired methicillin-resistant *Staphylococcus aureus*: the San Diego Experience. *Pediatr Dermatol* 2011; 28: 6–11.
- 19 Gomes PL, Malavigne GN, Fernando N, *et al.* Characteristics of *Staphylococcus aureus* colonization in patients with atopic dermatitis in Sri Lanka. *Clin Exp Dermatol* 2011; 36: 195–200.
- 20 Tang CS, Wang CC, Huang CF, *et al.* Antimicrobial susceptibility of *Staphylococcus aureus* in children with atopic dermatitis. *Pediatr Int* 2011; 53: 363–367.
- 21 Ortega-Loayza AG, Diamantis SA, Gilligan P, *et al.* Characterization of *Staphylococcus aureus* cutaneous infections in a pediatric dermatology tertiary health care outpatient facility. *J Am Acad Dermatol* 2010; 62: 804–811.
- 22 Lo WT, Wang SR, Tseng MH, *et al.* Comparative molecular analysis of methicillin-resistant *Staphylococcus aureus* isolates from children with atopic dermatitis and healthy subjects in Taiwan. *Br J Dermatol* 2010; 162: 1110–1116.
- 23 Huang JT, Abrams M, Tloughan B, *et al.* Treatment of *Staphylococcus aureus* colonization in atopic dermatitis decreases disease severity. *Pediatrics* 2009; 123: 808–814.
- 24 Suh L, Cofin S, Leckerman KH, *et al.* Methicillin-resistant *Staphylococcus aureus* colonization in children with atopic dermatitis. *Pediatr Dermatol* 2008; 25: 528–534.
- 25 Kedzierska A, Kapinska-Mrowiecka M, Czubak-Macugowska M, *et al.* Susceptibility testing and resistance phenotype detection in *Staphylococcus aureus* strains isolated from patients with atopic dermatitis with

- apparent and recurrent skin colonization. *Br J Dermatol* 2008; **159**: 1290–1299.
- 26 Chung H, Jeon H, Sung H, *et al.* Epidemiological characteristics of methicillin-resistant *Staphylococcus aureus* isolates from children with eczematous atopic dermatitis lesions. *J Clin Microbiol* 2008; **46**: 991–995.
 - 27 Roesch A, Linde HJ, Landthaler M, *et al.* Elimination of a community-acquired methicillin-resistant *Staphylococcus aureus* infection in a nurse with atopic dermatitis. *Arch Dermatol* 2005; **141**: 1520–1522.
 - 28 Hon KL, Leung AK, Kong AY, *et al.* Atopic dermatitis complicated by methicillin-resistant *Staphylococcus aureus* infection. *J Natl Med Assoc* 2008; **100**: 797–800.
 - 29 Suh LM, Honig PJ, Yan AC. Methicillin-resistant *Staphylococcus aureus* skin abscesses in a pediatric patient with atopic dermatitis: a case report. *Cutis* 2006; **78**: 113–116.
 - 30 Hanifin JM, Thurston M, Omoto M, *et al.* The eczema area and severity index (EASI): assessment of reliability in atopic dermatitis. *Exp Dermatol* 2001; **10**: 11–18.
 - 31 Clinical and Laboratory Standards Institute. *Performance Standards for Antimicrobial Susceptibility Testing*. 15th Informational Supplement. Approved standard M100-S15. Wayne, PA: CLSI, 2007.
 - 32 Fiebelkorn KK, Crawford SA, McElmell ML, Jorgensen JH. Practical disk diffusion method for detection of inducible clindamycin resistance in *Staphylococcus aureus* and coagulase-negative staphylococci. *J Clin Microbiol* 2003; **41**: 4740–4744.
 - 33 Nakamura MM, Rohling KL, Shashty M, *et al.* Prevalence of methicillin-resistant *Staphylococcus aureus* nasal carriage in the community pediatric population. *Pediatr Infect Dis J* 2002; **21**: 917–922.
 - 34 Gelatti LC, Sukiennik T, Becker AP, *et al.* Sepsis due to community-acquired methicillin-resistant *Staphylococcus aureus* in southern Brazil. *Rev Soc Bras Med Trop* 2009; **42**: 458–460.