

## ORIGINAL ARTICLE

# Prevalence of *Staphylococcus aureus* and antibiotic resistance in children with atopic dermatitis: A New Zealand experience

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### ABSTRACT

**Background/Objectives:** Children with atopic dermatitis often have infective exacerbations which are treated with antibiotics and/or antiseptics. The most common infective cause is *Staphylococcus aureus* with a worldwide trend towards antibiotic resistance. This prospective observational audit aimed primarily to establish the prevalence of *S. aureus* colonisation in New Zealand children with atopic dermatitis attending a specialised paediatric dermatology clinic. Secondary aims were to assess whether *S. aureus* colonisation correlated to clinical severity, the sensitivity patterns to antibiotics (in particular methicillin-resistant *S. aureus*, and to identify any demographic or management risk factors.

**Methods:** Subjects were children aged 18 years or younger attending a tertiary public hospital dermatology clinic with a diagnosis of atopic dermatitis. Demographic and social data, as well as current and previous systemic and topical treatments, were recorded. Patients were examined and the extent of atopic dermatitis determined using a standardised scale (Scoring Atopic Dermatitis (SCORAD)). Two skin swabs were taken for culture and standard sensitivities; one from the left antecubital fossa and one from the worst area of atopic dermatitis. Microbiological cultures and density of *S. aureus* colonisation were recorded. SCORAD and density of *S. aureus* culture were correlated. Demographic and clinical data from children with *S. aureus* was analysed.

**Results:** One hundred children were recruited from March 2007 to May 2008. *S. aureus* was isolated from

68 patients. There was a positive correlation between the density of *S. aureus* culture and severity of SCORAD (Spearman  $r = 0.55$ ,  $P < 0.0001$ ). There was also a positive, though weaker, correlation between SCORAD and ethnicity with Māori /Polynesian children generally having more severe atopic dermatitis ( $r = 0.22$ ,  $P = 0.028$ ). Although a greater proportion of Māori or Pacific Island children were colonised by *S. aureus* than other ethnic groups this did not reach statistical significance (78% and 60%, respectively,  $P = 0.0842$ ). There was no significant correlation between either *S. aureus* prevalence or its density and age ( $r = 0.09$ ,  $P = 0.59$  and  $r = 0.12$ ,  $P = 0.23$ , respectively). There were no significant differences in sex or treatments (use of antibiotics, antiseptics, calcineurin inhibitors, emollients or corticosteroids) between *S. aureus*-positive and *S. aureus*-negative children. Only 12 *S. aureus*-positive children demonstrated antibiotic resistance, 10 to erythromycin and only two to flucloxacillin.

**Conclusions:** Three quarters of children with atopic dermatitis have at least one positive culture, of which the vast majority is *S. aureus*. The density of *S. aureus* colonisation correlates to severity of atopic dermatitis. Children who are *S. aureus* culture-positive had no significant demographic or clinical features different to children who were culture-negative. Only two children grew *S. aureus* resistant to flucloxacillin (2% resistance rate), which remains the ideal first line of treatment in our local population.

**Key words:** antibiotic resistance, atopic dermatitis, MRSA, paediatric, *Staphylococcus aureus*.

### INTRODUCTION

The skin of patients with atopic dermatitis can be persistently colonised with *S. aureus* on both lesional and non-involved skin.<sup>1</sup> *Staphylococcus aureus* colonisation

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density generally correlates with the severity of atopic dermatitis<sup>2</sup> as assessed by SCORAD (Scoring Atopic Dermatitis).<sup>5</sup> A previous study of New Zealand children noted Polynesian (Māori and Pacific Island) children demonstrated a high incidence and increased relative risk of limb skin infections with *S. aureus*.<sup>4</sup> The reasons for this were unknown but suggestions included household crowding, economic deprivation and other environmental and genetic factors.

In New Zealand there are marked geographic variations in methicillin-resistant *S. aureus* (MRSA) colonisation. Counties Manukau has the highest MRSA rate (486.7/100 000) with less than 50/100 000 for the Nelson Marlborough region. Our department is in the Waikato region with a MRSA rate of 252.7 per 100 000.<sup>5</sup> We were unable to locate any study which assessed the prevalence of *S. aureus* colonisation in New Zealand children with atopic dermatitis.

Our tertiary level department serves a large population (approximately 812 265 people (19.4% of New Zealand's total population) with a number of risk factors for both *S. aureus* and MRSA.<sup>6</sup> Within the Waikato District Health Board region there is a large proportion of children (approximately 30% of the population is 19 years or younger), urban underserved communities (78% live in urban areas and 45.7% live in high deprivation), and indigenous populations (35% identify as Māori or Pacific Island people).<sup>7</sup>

The dermatology department is staffed by three dermatologists who work closely together. Hence, there is a standardized, although non-formal, approach to the management of infected atopic dermatitis. Routine use of topical antibiotics (mupirocin and fusidic acid) has been discouraged for 15 years because of concerns regarding development of resistance, while bleach baths and antiseptic ointments (such as hydrogen peroxide based creams) have been encouraged as alternatives. If systemic antibiotics are required then flucloxacillin is the local oral antibiotic of choice, with amoxicillin/clavulanic acid the common alternative. Erythromycin is only used as a first-line agent in patients thought to be penicillin sensitive. Erythromycin is not used as a first- or second-line treatment of acne vulgaris. This conservative topical antibiotic stewardship predates a period where mupirocin could be obtained over the counter. A 2003 study in New Zealand showed a rapid increase in the mupirocin resistance rate (up to 24% in some regions) among *S. aureus* isolates.<sup>8</sup>

Our audit aimed to determine the prevalence of *S. aureus* carriage in paediatric atopic dermatitis patients in New Zealand and to assess the prevalence of antibiotic resistance to ensure that the local choice of flucloxacillin as a first-line single therapy agent remained appropriate.

## MATERIALS AND METHODS

One hundred children (aged 18 years or younger) with atopic dermatitis who presented to our tertiary public hospital dermatology clinic from March 2007 to May 2008 for routine atopic dermatitis care were included irrespective of

clinical severity or treatment at presentation. The diagnosis of atopic dermatitis was made by the treating dermatologist using the criteria of Hanifin and Rajka.<sup>9</sup> Using a standardised questionnaire the patient demographics, number of people living in their home, and current and previous systemic and topical treatments were documented. Patients were examined and the severity of atopic dermatitis determined using SCORAD.

Two skin swabs were taken for culture and standard sensitivities; one from a standardised site, the left antecubital fossa, and one from lesional skin. Skin swabs were cultured onto Columbia blood, MacConkey and colistin nalidixic acid agar (Fort Richard Laboratories, Otahuhu, New Zealand). Plates were incubated for 48 h at 35°C and examined after 24 and 48 h. Isolates of *S. aureus* were identified from the Columbia blood agar by detection of coagulase activity using a latex test kit (BactiStaph, Oxoid NZ Ltd, Auckland, New Zealand). Antimicrobial susceptibility was determined by the Vitek2 system (bioMérieux, Marcy l'Etoile, France) using the AST-P545 card according to the manufacturers' instructions. Isolates were reported as susceptible, intermediate, or resistant to flucloxacillin and erythromycin according to Clinical and Laboratory Standards Institute (CLSI) guidelines.<sup>10</sup> The identification of flucloxacillin resistant *S. aureus* was confirmed by Rabbit plasma (coagulase plasma, Remel Inc., Lenexa, KS, USA). Isolates resistant to flucloxacillin were also confirmed to be MRSA by the agar disc diffusion method, using a 30 µg cefoxitin disc, according to CLSI guidelines.

Demographic and clinical data from children with *S. aureus* was analysed. *S. aureus* density was scored as follows: 0 = no *S. aureus*; 1 = slight; 2 = light; 3 = moderate; and 4 = heavy colonisation. Density was not provided by the laboratory for MRSA. Spearman's correlation was used to examine the relationship between *S. aureus* density and SCORAD. Fisher's exact test was used for contingency tests. All *P*-values are two-tailed.

As this was an observational audit of standard practice, local ethics committee approval was not needed.

## RESULTS

### Patient demographics, clinical assessment and treatment

Table 1 displays the general characteristics of the study population. Forty-five percent were children of Māori or Pacific Island heritage (Polynesian) versus the general

**Table 1** Demographics and SCORAD (Scoring Atopic Dermatitis)

| Characteristics        | <i>N</i>    |
|------------------------|-------------|
| Patients               | 100         |
| Male/Female            | 45/55       |
| Māori /Pacific Island  | 45          |
| European/Other         | 40/15       |
| Median age yrs (range) | 5 (0.25–18) |
| Mean SCORAD (range)    | 52 (12–100) |

**Table 2** Microbial isolates

| Isolate                                  | No. of children |
|------------------------------------------|-----------------|
| <i>Staphylococcus aureus</i>             | 68              |
| Haemolytic <i>Streptococcal</i> Group A  | 9               |
| Coliforms                                | 5               |
| Coagulase-negative <i>Staphylococcus</i> | 5               |
| <i>Streptococcus pneumoniae</i>          | 1               |
| <i>Bacillus cereus</i>                   | 1               |

hospital catchment population of 55% and 12% for all of New Zealand under the age of 15.<sup>11</sup> There was no significant correlation between SCORAD and age ( $r = 0.09$ ,  $P = 0.57$ ) or SCORAD and the number of people living in the home ( $r = -0.05$ ,  $P = 0.66$ ).

During the six weeks prior to presentation the most commonly used oral antibiotics were penicillin derivatives: flucloxacillin (35 children); amoxicillin (4); and amoxicillin/clavulonic acid (4). Only one child had used erythromycin and one child doxycycline. It was unclear which antibiotic had been prescribed in three children. There was no significant correlation between ethnicity and steroid or emollient use but there was a higher proportion of Māori or Pacific Island children (60%) who had used oral or topical antibiotics in the preceding six weeks ( $P = 0.0439$ ) versus other ethnicities (38%).

### *Staphylococcus aureus* colonisation

Seventy-two children had at least one positive culture from the lesional or standardised site. Table 2 shows the colonizing bacterium, with *S. aureus* the predominant isolate from 68 children (67 from lesional skin, 35 from the standardised site of the left antecubital fossa).

There was a positive correlation between the density of *S. aureus* culture and severity of SCORAD (Spearman  $r = 0.55$ ,  $P < 0.0001$ , Fig. 1). There was also a positive, though weaker, correlation between SCORAD and ethnicity with Māori/Pacific Island children generally having more severe atopic dermatitis ( $r = 0.22$ ,  $P = 0.028$ , Fig. 2). Although a greater proportion of Māori or Pacific Island children were colonised by *S. aureus* than other ethnic groups, this did not reach statistical significance ((78% and 60% respectively)  $P = 0.0842$ ). There was no significant correlation between either *S. aureus* prevalence or density and age ( $r = 0.09$ ,  $P = 0.59$  and  $r = 0.12$ ,  $P = 0.23$ , respectively). There were no significant differences in sex or treatments (use of topical or oral antibiotics, antiseptics, calcineurin inhibitors, emollients or corticosteroids) between *S. aureus*-positive and *S. aureus*-negative children.

### *Staphylococcus aureus* antibiotic resistance

In 68 children in whom *S. aureus* was isolated, antibiotic resistance was demonstrated in 12 cases, 10 to erythromycin (15% of culture-positive children, 10% of the overall group), and two (both were female and Māori/Pacific

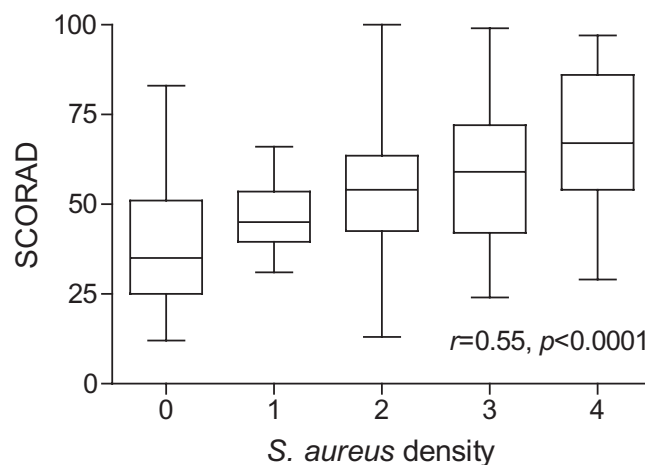


**Figure 1** Relationship between *Staphylococcus aureus* density and SCORAD. (0 = no *S. aureus*; 1 = slight; 2 = light; 3 = moderate; and 4 = heavy colonisation).

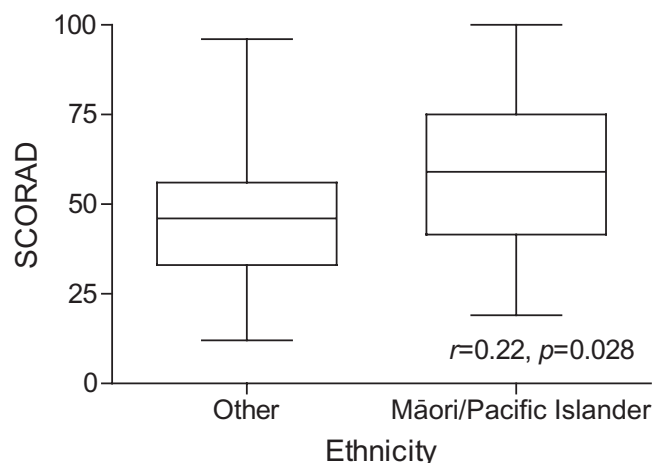


**Figure 2** Relationship between SCORAD and ethnicity.

Islanders) to flucloxacillin (3% of culture-positive children, 2% of the overall group). No organisms demonstrated resistance to both antibiotics.

## DISCUSSION

As predicted from similar studies in other countries<sup>12,15</sup> *S. aureus* is the most predominant bacteria colonising children with atopic dermatitis, with the density of the colonisation correlating with SCORAD. Although not statistically significant, there was a trend toward a higher percentage of Māori/Pacific Island children colonised with *S. aureus* than other ethnic groups. These children also tended toward more people living in the home, although this also did not reach statistical significance. This could indicate overcrowding (although the number of bedrooms per person per household was not recorded), which is a risk factor for transmission of *S. aureus*. A study from Singapore studied

the prevalence and molecular characteristics of *S. aureus* isolates colonising patients with atopic dermatitis and their close contacts.<sup>14</sup> They noted 45% of close contacts were colonised with largely the same *S. aureus* type, which suggests people in the home may be a reservoir. This was a similar finding to a 2008 study which found 48% of the parents of children colonised with *S. aureus* were also carriers.<sup>15</sup> The high percentage in parent and child of identical pulsed field gel electrophoresis and enterotoxin patterns and antibiotic resistance profiles indicated intrafamilial transmission.

Because of the association of *S. aureus* colonisation with severity of atopic dermatitis, some practitioners advocate anti-staphylococcal treatment. Commonly used measures include antibiotics as well as antiseptics such as the chronic use of dilute bleach baths with intermittent application of mupirocin ointment. In accordance with our department's first-line choice we are pleased to note that flucloxacillin is the antibiotic most commonly prescribed largely by general practitioners. A 2009 randomised placebo controlled study confirmed the efficacy of antiseptics in decreasing the clinical severity of atopic dermatitis.<sup>16</sup> However, within our study population there was no difference in the use of antiseptics (generally bleach baths) between patients colonised with *S. aureus* and not. This supports the 2009 Cochrane review on interventions to reduce *S. aureus* in atopic dermatitis which found no clear evidence for oral antibiotics, antibacterial soaps, antibacterial bath additives, topical antibiotics or antiseptics, in terms of short term atopic dermatitis control.<sup>17</sup>

Because of the large percentage of children with atopic dermatitis colonised with *S. aureus* there is a concern that they might represent a large reservoir of MRSA. Certainly two recent international studies found the MRSA rate in children with atopic dermatitis was 18% and 16%, respectively.<sup>18,19</sup> We are pleasantly surprised and reassured that only two children in our study were colonised with MRSA and, because the study cultures were taken from lesional skin as well as a standardised site, we feel this low incidence of MRSA is a true reflection of MRSA colonisation. Although both children with MRSA were Māori /Pacific Island and female, no other conclusions can be drawn because of the small number.

The reason for our low MRSA rate despite a high *S. aureus* colonisation rate remains unclear. A study from Philadelphia noted that 16% of 54 children with atopic dermatitis had MRSA, with previous hospitalisation independently associated with increased risk, as well as having used topical calcineurin inhibitors in conjunction with topical steroids.<sup>12</sup> In our study only two children had used a topical calcineurin inhibitor, neither of whom showed antibiotic resistance. No record was made regarding recent hospitalisation.

This audit confirms that the prevalence of *S. aureus* carriage in paediatric atopic dermatitis patients in New Zealand is high, but fortunately resistance to antibiotics is low and the local choice of flucloxacillin as a first-line single therapy agent remains appropriate in this setting. If our local laboratory reported increasing MRSA within the

general community then this policy may need to be re-evaluated. In individual patients, a repeat review of *S. aureus* colonisation and antibiotic susceptibility would be advisable if signs of infection persist after standard therapy.

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