

# Skin Colonization With Staphylococcus Aureus In Patients With Atopic Dermatitis

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## Abstract

**Objectives:** To investigate the presence of *S. aureus* in the skin of AD patients and compare with healthy control group.

**Patients/Methods:** Forty patients with AD were recruited in to our study. *S. aureus* skin colonization was determined in AD patients and controls, also skin distribution of *S. aureus* colonization was compared in three age groups of AD patients.

**Results:** *S. aureus* was found on the skin of 42.5% and 7.5% of AD patients and control group, respectively ( $p=0.0003$ ). The most common involved skin areas with *S. aureus* colonization were face (in  $\leq 2$  yrs old), flexor surfaces (in  $>2$  and  $\leq 12$  yrs old) and extremities (in  $>12$  yrs old).

**Conclusions:** The incidence of *S. aureus* on the skin of AD patients was considerably higher rather than controls. Further studies are needed to investigate the clearance of *S. aureus* from the skin of AD patients using anti-staphylococcal treatment.

The work was done at Department of Dermatology and Microbiology of Ghaem Hospital, Mashhad University of Medical Sciences, Mashhad, Iran.

## INTRODUCTION

Atopic dermatitis (AD) is a chronic relapsing condition of pruritus and eczematous lesions that affects 15-20% of the childhood population and 1-3% of adults worldwide with increasing prevalence in highly industrialized countries.<sup>1</sup> AD is associated with other atopic diseases and sixty percent of patients develop AD within the first year of life, 85% by age 5.<sup>2</sup> Early onset often indicates a more severe course. AD affects infants, children, and young adults predominantly. AD is the itch that, when scratched, erupts. Thus, scratching or rubbing itchy, atopic skin characterizes this eczema as being isomorphic. Its distribution is variable and age-related, with a distribution that corresponds to areas of the body that are accessible to scratching and rubbing.<sup>3</sup>

Yet, the nose is almost always spared and is referred to as the head-light sign. The diaper area is usually spared. The distribution of AD is almost exclusively isomorphic. The eczema is polymorphic, with acute (oozing, or crusted, eroded microvesicles on papular, erythematous plaques),

subacute (thicker, paler, somewhat scaly, erythematous, excoriated plaques), and chronic (lichenified, more scaly, hyperpigmented, excoriated, papular plaques) forms. It is not unusual for each stage of evolution to be present at the same time in an individual patient with AD. The dermatitis is more likely to be generalized during infancy and childhood, and more apt to be localized in older individuals. Localized AD has been erroneously labeled as dermatitis confined to specific areas, such as eyelid dermatitis, nipple dermatitis, palmar-plantar dermatitis, cheilitis, and pityriasis alba.<sup>4</sup>

Although the exact pathophysiologic mechanism is not yet known, a multifactorial pathogenesis, involving genetic, immunologic, and environmental mechanisms, has been proposed. Generally, decreased production of ceramides by keratinocytes in both normal and affected skin causes disruption in the barrier function of skin, resulting in increased permeability to environmental irritants and allergens, and transepidermal water loss. There also appears to be an immunologic derangement in the body's response to skin injury, manifested by an increased Th2 response in the acute lesions and IgE sensitization to various allergens. While genetic predisposition appears to be important, the change in incidence of disease by time, climate, and

immigration patterns suggests that environmental factors play an essential role.

*Staphylococcus aureus* (*S. aureus*) is the most important microorganism of the normal skin flora.<sup>5</sup> The bacterial skin flora of patients with atopic dermatitis is different from that in healthy people. In addition, such patients more often suffer from microbial infections such as impetigo, folliculitis, and furunculosis.<sup>6</sup> *S. aureus* infection is perceived not only as a secondary complication of AD, but also as a culprit in the worsening of this condition.

The microbial flora of AD patients shows striking differences in term of the presence of *S. aureus*. Of children with AD, 76-100% are colonized with *S. aureus*, as compared to 2-25% of healthy controls. In addition, *S. aureus* is the most common cause of secondarily infected eczematous lesions. The specific attributes of atopic skin may explain this high rate of colonization and infection. Recently, Ong et al showed that patients with AD demonstrate poor expression of the naturally occurring antimicrobial peptides, beta defensin 2 and cathelicidin, in the face of inflammation. This failure to produce endogenous antimicrobial peptides may increase the risk of bacterial, fungal and viral infections. In addition, the disrupted lipid layer of atopic skin results in low levels of sphingosine, thought to normally exert a potent antimicrobial effect on *S. aureus*. Finally, *S. aureus* contains adhesins, which readily bind to laminin and fibronectin that are exposed in the “sticky” keratinocytes of patients with AD and skin injury.

The deleterious effects of *S. aureus* in activating AD have led us to investigate the presence of *S. aureus* as a pathogen or “superantigen”<sup>7</sup> in the patients who suffer from AD.

The aim of this study was to determine the presence of *S. aureus* in the skin of AD patients and healthy control group.

### **MATERIALS & METHODS**

In this cross-sectional study, we recruited 40 patients (21 male and 19 female) in various age groups with atopic dermatitis (AD) attending the outpatient department of dermatology of the academic hospital (Ghaem Hospital, Mashhad University of Medical Sciences, Mashhad, Iran). Forty age and sex matched healthy volunteers without personal and familial history of AD or other skin or allergic diseases, served as control group. The study was approved by the Clinical Research Ethics Committee of the University and informed consent was obtained. AD was diagnosed

under supervision of dermatologist and based on Hanifin and Rajka criteria.<sup>8</sup>

Specimens for bacteriological examination were obtained by a sterile swab from the affected skin areas of AD patients and from their corresponding skin areas of control subjects, cultured in 5% Blood Agar plates (Oxoid, Hampshire, UK) and incubated for 24 h at 37 °c. Then, the specimens were cultured on Nutrient Broth (Himedia) and incubated in the same condition. The specimens were transferred from Nutrient Broth and cultured again in Blood Agar and incubated at the same temperature and period mentioned above. The plate was assessed for typical colonies of various bacterial or non-bacterial agents. Colonization was quantified by counting the number of colony forming units per cm<sup>2</sup> of the investigated skin surface. If the growth of *Staphylococcus* was observed, the confirmation tests including coagulase activity and Mannitol fermentation would be performed for identifying the various staphylococcus species. *S. aureus* is coagulase-positive and mannitol-positive, *S. saprophyticus* is coagulase-negative and usually mannitol-positive and *S. epidermis* is coagulase-negative and mannitol-negative.

### **STATISTICAL ANALYSIS**

Chi-square test and ANOVA test were carried by using computer program SPSS ver. 10. Value of  $P < 0.05$  was always considered to be significant.

### **RESULTS**

The study was conducted in 40 patients with atopic dermatitis in three age groups ( $\leq 2$  yrs old,  $> 2$  and  $\leq 12$  yrs old and  $> 12$  yrs old). The most common symptoms of disease seen in our patients were dryness accompanied with eczematous plaques (65%). There was personal or familial history of atopy in 72.5% of AD patients and allergic rhinitis was the most common atopic manifestation in these patients (47.5%). The atopic manifestations in AD patients were as follow: asthma in 3 (7.5%), allergic rhinitis in 10 (25%), urticaria in 5 (12.5%), asthma and allergic rhinitis in 6 (15%), asthma and urticaria in 2 (5%), rhinitis and urticaria in 2 (5%) and asthma, allergic rhinitis and urticaria in 1 (2.5%). The percents of bacterial and non bacterial agents isolated from the skin of AD patients and control subjects have been shown in table 1. The total number of positive cultures for staphylococcus were 38 (95%) and 11 (27.5%) in AD patients and controls, respectively ( $p < 0.0001$ ). There was a significant relationship in *S. aureus* skin colonization between AD patients and controls ( $p = 0.0003$ ). *S.*

saprophyticus was the most isolated agent in AD patients (47.5%), meanwhile bacillus was the most common one in the control subjects as well (62.5%).

**Figure 1**

Table 1: Percents of bacterial and non bacterial agents isolated from the skin of AD patients and control group

	AD Patients, n (%)	Controls, n (%)	P value
Staphylococcus saprophyticus	19 (47.5%)	7 (17.5%)	p=0.004*
Staphylococcus aureus	17 (42.5%)	3 (7.5%)	p=0.0003*
Staphylococcus epidermidis	2 (5%)	1 (2.5%)	p=0.5
Bacillus	2 (5%)	25 (62.5%)	p<0.0001*
Coli bacillus	-	4 (10%)	P=0.11

\* Significant P value

The demographic and characteristics of AD patients in three age groups are shown in table 2. The age group of  $\leq 2$  yrs old was the most included group in our study (40%). The most common involved skin areas in the age group of  $\leq 2$  yrs old were face (87.5%), extensor surfaces (50.6%) and head (25%). In the age group of  $>2$  and  $\leq 12$  yrs old, they were flexor surfaces (54.5%), face (45.4%), extensor surfaces (27.2%) and head (9.09%). In the last age group of  $>12$  yrs old, they were hand or foot (69.2%), flexor surfaces (46.15%) and extensor surfaces (7.7%).

**Figure 2**

Table 2: The demographic and characteristics of AD patients in three age groups

	AD patients		
	$\leq 2$ y old, n (%)	$>2$ and $\leq 12$ y old, n (%)	$>12$ y old, n (%)
No	16 (4.%)	11 (27.5%)	13 (32.5%)
Age (years; mean $\pm$ SD)	1.11 $\pm$ .64	6.45 $\pm$ 3.---	38.46 $\pm$ 13.51
Sex	12M, 4F	4M, 7F	5 M, 8F
Involved skin area			
Face	7 (43.75%)	1 (9.9%)	-
Head	-	-	-
Extensor surfaces	2 (12.5%)	1 (9.9%)	1 (7.7%)
Flexor surfaces	-	5 (45.45%)	3 (23.8%)
Head & Face	-	1 (9.9%)	-
Face & extensor surfaces	3 (18.75%)	2 (18.19%)	-
Face & flexor surfaces	-	1 (9.9%)	-
Head & face & extensor surfaces	4 (25%)	-	-
Foot	-	-	3 (23.8%)
Hand	-	-	3 (23.8%)
Flexor surfaces & foot or hand	-	-	3 (23.8%)

The demographic and characteristics of AD patients with S aureus skin colonization are shown in table 3. S aureus was more common in females than males (58.8% vs. 41.2%, respectively) and it was most seen in the age group of  $>12$  yrs old. Dryness accompanied with eczematous plaques was the most common symptom in the AD patients with S aureus colonization. Personal or familial history of atopy was present in 64.7% of these patients and the majority of

atopic diseases were attributed to allergic rhinitis (54.54%). The most common involved skin area (which S aureus was isolated) in the age group of  $\leq 2$  yrs old were face (100%), extensor surfaces (50%) and head (25%). In the age group of  $>2$  and  $\leq 12$  yrs old, they were flexor surfaces (66.6%), face (50%) and head or extensor surfaces (16.6%). In the age group of  $>12$  yrs old, they were hand or foot (71.43%) and flexor surfaces (57.14%).

**Figure 3**

Table 3: The demographic and characteristics of AD patients with acetaphylococcus aureus skin colonization.

	$\leq 2$ y old, n (%)	$>2$ and $\leq 12$ y old, n (%)	$>12$ y old, n (%)
No	4 (23.5%)	6 (35.33%)	7 (41.17%)
Sex	3M, 1F	2M, 4F	2M, 5F
Involved skin area			
Face	2 (5.%)	-	-
Head	-	-	-
Extensor surfaces	-	-	-
Flexor surfaces	-	3 (5.%)	2 (28.57%)
Head & Face	-	1 (16.66%)	-
Face & extensor surfaces	1 (25%)	1 (16.66%)	-
Face & flexor surfaces	-	1 (16.66%)	-
Head & face & extensor surfaces	1 (25%)	-	-
Extensor & flexor surfaces	-	-	-
Foot	-	-	1 (14.29%)
Hand	-	-	-
Foot & hand	-	-	2 (28.57%)
Flexor surfaces & foot or hand	-	-	2 (28.57%)

## DISCUSSION

Our results revealed that 95% of AD patients had positive cultures for staphylococcus whereas it was only 27.5% in the healthy control group. Results of previous studies confirmed our results regarding increased staphylococcal skin colonization of affected and normal skin in patients with AD compared with controls., We found that the predominant staphylococcus isolated from our AD patients was S saprophyticus (47.5%) which is not in the agreement with other studies that the predominant bacterial agent was S aureus <sup>10,11</sup> S saprophyticus is sometimes found on the human skin as a part of the normal flora. After S saprophyticus, S aureus was the most common bacterial agent isolated from our AD patients' skin lesions (42.5%), although higher incidence of skin colonization with S aureus observed in the other studies, it was 100% <sup>12,13</sup>, more than 90% <sup>14,15</sup>, 86% <sup>16</sup>, 74% <sup>17</sup>, 69.7% <sup>18</sup>, 60.48% <sup>10</sup>, 50% <sup>19</sup> and 48.5% <sup>20</sup>. This variability may be related to the differences in sampling techniques, changes of the hygienic status of patients as well as the choice of sampling area of skin lesions (at locations that were difficult to reach by patients).

The growth of coagulase-negative staphylococcus (S. saprophyticus and S. epidermis) was also found in 52.5% of

AD patients vs. 20% of healthy controls in this study, whereas it was found in 22.37% of AD patients in another study.<sup>10</sup> So much lower percent (14.2%) of growth of coagulase-negative staphylococcus was found in the study which was done on Chinese children<sup>20</sup> that could be due to choice of special sampling areas (flexural and lesional areas). In our study, *S. aureus* colonization was detected on the facial skin of 100% of AD patients in the age group of  $\leq 2$  yrs old, however it was found on facial skin (cheek and nose) of 90% and 70% of infants with atopic dermatitis, respectively.<sup>21</sup>

Many studies showed a heavy colonization of AD with *S. aureus*. This phenomenon suggests that *S. aureus* in AD lesions influences the disease processes of AD.<sup>22,23</sup> Nevertheless, in our study, isolates of *S. aureus* was only found in approximately half of the specimens which in part implies direct pathogen invasion may not be the sole factor in mediating AD.

It has reported that the density of *S. aureus* on inflamed AD lesions without clinical superinfection can reach up to  $10^7$  colony-forming units per  $\text{cm}^2$  on lesional skin. Although the majority of patients with AD are colonized by *S. aureus*, its presence does not necessarily indicate that it acts as a pathogen; antibiotic treatment is indicated only when there is evidence of overt clinical infection or a superantigen effect is suspected.<sup>24</sup> Impetiginization is noted when there is a purulent oozing and crusting of the eczematous skin, and a superantigen reaction should be suspected when a generalized, serous-oozing, exquisitely pruritic, flare-up of the eczema is noted. Though not all studies agree, the importance of *S. aureus* is supported by the observation that these AD patients without obvious signs of a superinfection show a reduction in the severity of their skin disease when treated with a combination of antistaphylococcal antibiotics and topical corticosteroids.<sup>25</sup> Studies suggest that one strategy by which *S. aureus* exacerbates or maintains skin inflammation in AD is by secreting a group of toxins known to act as superantigens, which stimulate marked activation of T-cells and macrophages.<sup>26</sup>

Based upon our observations we postulate that there are three potential risk factors for staphylococcal skin colonization in the AD patients: increasing in age (adults); female sex; and presence of eczematous plaques.

Regarding to higher incidence of *S. aureus* skin colonization in AD patients rather than healthy control group (42.5% vs. 7.5%), we would recommend to use anti-staphylococcal

drugs for treatment of AD patients with eczematous plaques, especially if they have clinical signs of infection. Further studies are needed to evaluate if efforts to eliminate *S. aureus* and other Staphylococcal species are associated with clinical improvement of AD.

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