Evaluation of 25-hydroxy vitamin D and specific immunoglobulin E to *Staphylococcus aureus* in patients with atopic dermatitis and their correlation with the disease severity
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**Background**

Atopic dermatitis (AD) is an inflammatory, chronically relapsing, noncontagious and pruritic skin disorder. Vitamin D has major effects on the innate and adaptive immunity, which make the association between vitamin D and allergic diseases a field of interest.

**Objective**

The aim of the study was to estimate the serum level of 25-hydroxy vitamin D [25(OH)D] concentration and specific immunoglobulin E (IgE) to *S. aureus* in patients with AD and their correlation with disease severity.

**Patients and methods**

Thirty patients were enrolled in this case–control study. Diagnosis of AD was made according to the UK Working Party diagnostic criteria for AD. Disease severity determination by SCORAD index and measurement of 25(OH)D and specific IgE to *S. aureus* in the sera of the patients were performed. Twenty age-matched and sex-matched apparently healthy individuals were also included in the study as controls.

**Results**

The mean value of 25(OH)D was significantly lower in the AD patients group compared with the control group, and 66.7% of the AD patients had insufficient or deficient vitamin D. In this study, an inverse correlation between serum concentrations of 25(OH)D and the severity of disease was found. The mean value of specific IgE to *S. aureus* was significantly increased in patients than in controls. There was a significant correlation between specific IgE to *S. aureus* and the severity of AD and an inverse correlation between serum 25(OH)D levels and IgE to *S. aureus*.

**Conclusion**

Vitamin D may be insufficient or deficient in a subset of AD children, especially those with moderate and severe disease; these patients were sensitive to *S. aureus*.

**Keywords:**

atopic dermatitis, SCORAD, *Staphylococcus aureus*, vitamin D

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**Introduction**

Atopic dermatitis (AD) represents a chronic and relapsing T-cell-mediated inflammatory skin disorder with immunoglobulin E (IgE)-mediated sensitization to allergens. AD most often affects infants and young children, but it may persist into adulthood or may first develop in adults as late-onset AD [1]. Several cofactors, such as an impaired skin barrier function, modifications of the immune system and a complex genetic background, direct the course of AD [2]. There is a growing body of evidence that vitamin D is an important regulator of cutaneous immunity [3]. Vitamin D increases innate immunity in skin to enable efficient antimicrobial defence at the epithelial surfaces [4]. The active form of vitamin D [1,25(OH)2D3] enhances expression of antimicrobial peptides such as defensins and cathelicidin in human skin, which prevent skin infections. In addition, vitamin D stimulates protein synthesis, such as filaggrin, which is necessary for stratum corneum barrier formation.

Therefore, vitamin D deficiency might exacerbate AD by disturbed epidermal barrier function and immunologic dysregulation, with consequent impaired defences against infections [5,6]. Vitamin D also affects B-lymphocyte functions and modulates the humoral immune response including secretion of IgE [7]. Persistent *Staphylococcus aureus* colonization is associated with higher total IgE levels, suggesting that IgE may contribute to an increased susceptibility to infection [8].

The aim of our study was to correlate vitamin D concentrations and specific IgE to *S. aureus* in patients who had AD with clinical severity of the disease.

**Patients and methods**

This case–control study was conducted on 30 patients with AD. Twenty age-matched and sex-matched healthy individuals were studied as the control group. The
studied patients were selected from the Outpatient Clinics of Dermatology Departments of Benha University Hospital and Quesna Hospital during the period from November 2012 to April 2013. Written informed consent was signed by a parent of each patient, which was approved by Ethics Committee of Human Research, Benha University.

Inclusion criteria were patients who had the criteria of AD. Exclusion criteria were patients who were taking vitamin supplements for at least 6 months and who received topical steroids or topical calcineurin inhibitors in the previous 4 weeks or any systemic corticosteroids or cyclosporin treatment in the previous 6 months.

All patients were subjected to the following: personal history taking including name, age and sex, the frequency of flare, associated itching, body regions affected, sleep disturbance by itching, personal history of any allergic diseases and family history of AD. AD was diagnosed by fulfilling the UK Working Party diagnostic criteria [9]. Disease severity was determined by the SCORAD index for AD developed by the European Task Force [10] on AD. Eczema was scored in each patient as mild (<25), moderate (25–50) or severe (>50).

Measurement of the serum level of 25-hydroxy vitamin D
A single measurement of vitamin D measured as 25-hydroxy vitamin D [25(OH)D] in serum was obtained from all patients and controls using 25(OH) vitamin D direct ELISA kit (Immundiagnostik AG, Bensheim, Germany; Australian patents). Vitamin D status definitions according to Holick [11] were: satisfactory (or sufficient), at least 30–40 ng/ml (75–100 nmol/l); insufficient, 20–30 ng/ml (50–75 nmol/l) and deficient, less than 20ng/ml (<50nmol/l).

Measurement of the serum level of specific immunoglobulin E to Staphylococcus aureus
A single measurement of the serum level of specific IgE to S. aureus was obtained from all patients and controls using RIDASCREEN Spezifisches IgE kits (R-Biopharm AG, Darmstadt, Germany). The IgE concentrations were determined by enzyme allergo-sorbent test (EAST) according to the manufacturer’s instruction. Concentration of IgE was determined in classes from 0 to 6 on the basis of the reference sera concentrations: class 0 had IgE less than 0.35 IU/ml (none-found); class 1 had IgE 0.35–0.69 IU/ml (low); class 2 had IgE 0.7–3.49 IU/ml (increased); class 3 had IgE 3.5–17.49 IU/ml (significantly increased); class 4 had IgE 17.50–49.99 IU/ml (high); class 5 had IgE 50.00–99.99 IU/ml (very high) and class 6 had IgE of at least 100.00 IU/ml (extremely high).

Statistical analysis
The clinical and laboratory data were tabulated, coded and then analysed using Excel program for figures and SPSS (Program Statistical Package for Social Science version 16; SPSS Inc., Chicago, Illinois, USA). Description of the data was expressed in the form of mean ± SD for quantitative data and frequency and percentage for qualitative data. The analysis of the data was performed to test statistically significant difference between groups. For quantitative data, the Student *t*-test was used to compare between two groups. *P* value less than 0.05 was considered statistically significant.

Results
Descriptive data
This study was conducted on 30 patients with AD (12 female patients and 18 male patients) whose age ranged from 1 to 14 years with mean age 5.29 ± 3.55 years and on 20 controls (nine female individuals and 11 male individuals) whose age ranged from 1 to 14 years with mean age 5.40 ± 3.73 years. The clinical criteria of the patients are shown in Table 1.

Laboratory data
The mean value of 25(OH)D was significantly lower in the AD patients group compared with the control group (Table 2). The serum level of 25(OH)D was deficient in six (20%) patients, insufficient in 14 (46.7%) patients and sufficient in 10 (33.3%) patients (Fig. 1).

There was no significant relationship between either sex, personal history of atopic diseases or family history of atopic diseases and serum levels of 25(OH)D among the patients group (Table 3). In addition, there was no significant correlation between serum 25(OH)D levels and the age of the patients (*r* = 0.157, *P* = 0.41).

There was a statistically high significant difference in the mean value of 25(OH)D serum level according to the severity of AD assessed by SCORAD (Table 4).

<table>
<thead>
<tr>
<th>Variables</th>
<th>N (%)</th>
<th>(N=30)</th>
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</thead>
<tbody>
<tr>
<td>Severity of atopic dermatitis</td>
<td></td>
<td></td>
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<tr>
<td>Mild</td>
<td>12 (40.0)</td>
<td></td>
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<tr>
<td>Moderate</td>
<td>14 (46.7)</td>
<td></td>
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<tr>
<td>Severe</td>
<td>4 (13.3)</td>
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<tr>
<td>Personal history of atopic diseases</td>
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<td></td>
</tr>
<tr>
<td>No</td>
<td>21 (70.0)</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>9 (30.0)</td>
<td></td>
</tr>
<tr>
<td>Associated topic diseases</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bronchial asthma</td>
<td>8 (26.7)</td>
<td></td>
</tr>
<tr>
<td>Allergic conjunctivitis</td>
<td>1 (3.3)</td>
<td></td>
</tr>
<tr>
<td>Family history of atopic diseases</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>14 (46.7)</td>
<td></td>
</tr>
<tr>
<td>Bronchial asthma</td>
<td>2 (6.7)</td>
<td></td>
</tr>
<tr>
<td>AD</td>
<td>10 (33.3)</td>
<td></td>
</tr>
<tr>
<td>Both</td>
<td>4 (13.3)</td>
<td></td>
</tr>
</tbody>
</table>

AD, atopic dermatitis.

| Table 2. Comparison of the studied groups regarding 25-hydroxy vitamin D serum levels and specific immunoglobulin E to Staphylococcus aureus |
|-----------------|-----------------|-----------------|-----------------|
| Variables | Patients (N=30) | Controls (N=20) | t | *P* |
| 25(OH)D serum level (nmol/l) | 60.89 ± 27.28 | 89.79 ± 8.07 | 4.59 | <0.001* |
| Specific IgE to S. aureus (IU/ml) | 2.072 ± 0.29 | 0.192 ± 0.042 | 28.7 | <0.001* |

25(OH)D, 25-hydroxy vitamin D; IgE, immunoglobulin E.

*P*<0.05 is considered statistically significant.
The mean values of specific IgE to *S. aureus* was significantly higher in AD patients than in controls (Table 2). The percentage of *S. aureus*-specific IgE serum level among the patients group was not found in 30%, low in 50%, increased in 10%, significantly increased in 3.3% and high in 6.7% (Fig. 2).

There was a high significant difference in the mean value of 25(OH)D and specific IgE to *S. aureus* serum level according to the severity of AD assessed by the SCORAD index (Table 5). There was a significant inverse correlation between serum level of 25(OH)D and serum level of *S. aureus*-specific IgE (*r*= −0.455, *P*= 0.011) (Fig. 3).

### Discussion

In the present study, it was found that the mean value of 25(OH)D was significantly lower in the AD patients group compared with the control group. This is in agreement with the study by other authors [12–15], who linked vitamin D deficiency to prevalence of AD and other allergic diseases. In addition, we found that 66.7% of the AD patients had insufficient or deficient vitamin D; this is in accordance with the results of other studies [13–15] but with different percentages ranging from 61 to 82.5%. This variation in the percentages of patients with insufficient or deficient vitamin D may be due to the great variation in the clinical severity of AD in each study. In contrast, Ito *et al.* [16] showed that there was no association between serum vitamin D status and the prevalence of allergic diseases (asthma, rhinoconjunctivitis and eczema). This may be because they evaluated vitamin D status in the whole group not in each disease.
individually. In the present study, an inverse correlation was found between serum concentrations of 25(OH)D and the disease severity as evaluated by the SCORAD index. This is consistent with the studies by Ayman et al. [13] and Shim et al. [17], who found that the mean serum levels of vitamin D were significantly higher in patients with mild disease as compared with those with moderate or severe AD. This indicates that vitamin D may have different immunomodulating effects on the different inflammatory profiles of AD patients with and without allergen sensitization [15].

The current study showed no significant correlation between serum 25(OH)D levels and the age of the patients. However, Chiu et al. [14] found significantly lower serum 25(OH)D concentrations to be associated with an age of 3 years or above. Lack of significant correlation between serum 25(OH)D levels and age of the patients in the present study may be due to limited number of patients in a wide age range (1–14 years).

In the present study, the mean value of specific IgE to S. aureus was higher in AD patients than in controls. There was a significant correlation between specific IgE to S. aureus and the severity of AD. This is in agreement with the study by Ong et al. [18], who showed that the percentages of allergic sensitization to staphylococcal superantigens in mild and moderate AD were 38 and 63%, respectively. These remarks confirm previous beliefs that the prevalence of allergic sensitization to staphylococcal superantigens increases with the severity of AD [19].

In addition, there was a significant negative correlation between vitamin D and specific IgE to S. aureus in the present study. These data are compatible with those of Peroni et al. [20] who reported an increased prevalence of patients who were sensitive to S. aureus in children with insufficient levels of 25(OH)D. This is because of the preventive effect of vitamin D on skin colonization by bacteria. Heine et al. [21] reported that previously stimulated B cells showed markedly lower interleukin-4-mediated production of IgE after the administration of vitamin D. Hartmann et al. [7] supported this finding, revealing that vitamin D receptor antagonists led to suppressed IgE production by cultured human B cells in an allergy mouse model. Oral administration of vitamin D3 induce production of cathelicidin in atopic individual, which improves SCORAD index with a decrease in mean index for lichenification and pruritus [22].

Conclusion
There is a potential role of vitamin D deficiency in the pathogenesis and exacerbation of AD; it could be explained on the basis of the molecular effects of vitamin D in the skin, which affect the three domains of AD pathogenesis including immune system, antimicrobial defence mechanism and epidermal barrier integrity.

Acknowledgements

Conflicts of interest
There are no conflicts of interest.

References