Paediatrica Indonesiana

p-ISSN 0030-9311; e-ISSN 2338-476X; Vol.57, No.5(2017). p. 234-8; doi: http://dx.doi.org/10.14238/pi57.5.2017.234-8

Original Article

Serum 25-hydroxyvitamin-D level and atopic dermatitis severity in children

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Abstract

Background Vitamin D plays an important role in the immune system. It inhibits B-lymphocyte proliferation and modulates the humoral response to suppress IgE production. Studies on the relationship between serum 25-hydroxyvitamin-D level and the severity of atopic dermatitis in several countries have had varying results.

Objective To assess for a possible correlation between serum 25-hydroxyvitamin-D level and atopic dermatitis severity in children.

Methods A cross-sectional study was conducted in 26 children with atopic dermatitis from September to December 2015. We evaluated the severity of disease using the *Scoring of Atopic Dermatitis* (SCORAD) index and measured serum 25-hydroxyvitamin-D levels. Spearman's test was used to analyze for a correlation between serum 25-hydroxyvitamin-D level and the atopic dermatitis score in children with atopic dermatitis.

Results Mean SCORAD index was 32.0 (SD 14.99) , with a range of 10.9 to 71.4. Mean serum 25-hydroxyvitamin-D level was 41.1 (SD 24.81) ng/mL, with a range of 10-137 ng/mL. There was a moderate correlation between serum 25-hydroxyvitamin-D level and the SCORAD index (r=-0.591), with higher SCORAD index associated with lower serum 25-hydroxyvitamin-D level (P=0.01).

Conclusion There is a moderate correlation between serum 25-hydroxyvitamin-D level and the SCORAD index in children with atopic dermatitis. **[Paediatr Indones. 2017;57:234-8; doi: http://dx.doi.org/10.14238/pi57.5.2017.234-8]**.

Keywords: *atopic dermatitis; vitamin D; children*

Atopic dermatitis (AD) is the most prevalent skin disease in infants and children and is characterized by an inflammatory reaction on the skin in response to hereditary and environmental factors.[1] The incidence was estimated to be 15-30% in children, with 85% affected before the age of 5 years and 2-10% affected as adults. In genetically at-risk babies, the onset in 48-65% of cases was in the first 6 months of life, 57% before 4 months of life, and 75-80% within the 1st year, with male prevalence higher than female.[2] Atopic dermatitis has increased by 2- to 3-fold during the past 3 decades in industrialized countries.

The pathogenesis of AD is not completely understood, however, the disorder appears to result from a complex interaction between defects in skin

This study was presented at the *Pertemuan Ilmiah Tahunan Ilmu Kesehatan Anak VIII/PIT IKA VIII* (The 8th Child Health Annual Scientific Meeting), Makassar, South Sulawesi, September 17-21, 2016.

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barrier function, immune abnormalities, as well as environmental and infectious agents.[3] Hanifin and Rajka's criteria is the gold standard for diagnosing AD, defined as fulfilling 3 out of 4 major criteria or 3 out of 23 minor criteria.[4] The severity of disease can be evaluated by the SCORAD index. The SCORAD index consists of interpreting the severity of the disorder by 3 criteria: extent (the percentage of the skin surface affected according to the rule of nines), intensity (composed of erythema, edema/papules, effect of scratching, oozing/crust formation, lichenification, and dryness), and subjective symptoms (composed of pruritis and sleeplessness.[5]

Vitamin D is a hormone with multiple physiologic actions, the metabolites of which are stored in tissue and circulate in plasma.[6] Vitamin D has been shown to inhibit B-lymphocyte function and modulate the humoral immune response, resulting in diminished secretion of IgE.[7] Calcidiol or 25-hydroxyvitamin-D [25(OH)D] is the most common vitamin D metabolite in human serum, with a half-life of 3 weeks in serum so it is considered to be an acceptable proxy for vitamin D level in the body.[8]

Several studies reported a correlation between vitamin D and atopic dermatitis. A small study of 37 children with atopic dermatitis found a significant correlation between serum 25(OH)D level and severity score for atopic dermatitis.[9] A Chinese study in 2013 reported a significant correlation between atopic dermatitis and low serum level of 25(OH) D in children. Also, the total IgE was found to be higher in patients with low levels of 25(OH)D.[10,11] But a study in Milwaukee in 2013 reported that serum 25 hydroxyvitamin D did not correlate with atopic dermatitis severity, with lower serum 25(OH) D concentration in mild AD cases compared to moderate and severe AD cases.[12]

The differing study results spurred us on to assess for a correlation between serum 25-hydroxyvitamin-D level and SCORAD index in children with atopic dermatitis in Medan, North Sumatera, especially in the Helvetia health clinic (Puskesmas), a tropical environment with a mid-low socioeconomic population.

Methods

This cross-sectional study was conducted on 26 children aged ≤ 5 years with atopic dermatitis who visited the Helvetia health clinic (*Puskesmas*) in Medan, North Sumatera, from September to December 2015. Diagnosis of AD was estabished by Hanifin and Rajka's criteria.[4] We evaluated the severity of disease using the SCORAD index. Serum 25-hydroxyvitamin-D level was obtained from laboratory by using *@Alegria* machine. The Sample of blood is taken from vena mediana cubiti about 1.5 mL.

The SCORAD index was developed by the *European Task Force on Atopic Dermatitis* (ETFAD).[13] To measure the extent of AD, the rule of nines is applied on a front/back drawing of the patient's inflammatory lesions, and graded on a scale of 0-100. The intensity criterion of the SCORAD index consists of six items: erythema, edema/papules, excoriation, lichenification, oozing/crusting, and dryness. Each item can be graded on scale of 0-3. (0=no, 1=mild, 2=moderate, 3=severe). The subjective criterion includes daily pruritus and sleeplessness, was graded on a visual analogue scale of 1-10, with a maximum subjective score of 20. All items should be filled out on the standardized SCORAD evaluation form. The SCORAD index formula is A/5 + 7B/2 + C, with A defined as extent (0-100), B defined as intensity (0-18), and C defined as subjective symptoms (0-20). Total SCORAD index < 25 was defined as mild, 25-50 was defined as moderate, and >50 was defined as severe.[5]

Data distribution was evaluated using Shapiro-Wilk's test. Spearman's test was used to analyze for a correlation between serum 25-hydroxyvitamin-D level and SCORAD index in children with atopic dermatitis. Results with P values < 0.05 were considered to be statistically significant, with 95%confidence intervals (CI).

Results

The characteristics of subjects are shown in **Table 1**. The characteristics consisted of sex, age, birth order in family, body weight, body hight, nutrition, family history of atopy and the SCORAD index. We found

that atopic dermatitis in male more prevalence than female, and children with atopic dermatitis in the < 1 year old group was bigger than the 1-5 year old group. Regarding birth order, the first and the second children were more likely to have atopic dermatitis. Most subject had normoweigth. We also found children with AD more prevalence in atopic of one of parent than both. The most prevalence SCORAD index of the children was moderate.

Table 2 shows the mean (SD) SCORAD index and serum 25-hydroxyvitamin-D levels, as well as range of values in children with atopic dermatitis. Mean of the SCORAD Index was 32 (SD 14.99), with the lowest score of 10.9 and the higher score was 71.4. Mean of the serum 25-hydroxyvitamin-D level was 41.06 (SD 24.81) ng/mL, with the lowest level of 10 ng/mL and the higher level of 137 ng/mL.

There was a moderate, negative correlation between serum 25-hydroxyvitamin-D level and the SCORAD index (P=0.01), with higher SCORAD index associated with lower serum 25-hydroxyvitamin-D level (r = - 0.591) (**Figure 1**).

Table 1. Characteristics of subjects

Characteristics	N=26
Gender, n	
Male	16
Female	10
Age, n	
< 1 year	11
1-5 years	15
Birth order in the family, n	
1st	10
2nd	10
3rd	5
4th	1
Mean body weight (SD), kg	10.4 (4.85)
Mean body height (SD), cm	78.0 (19.03)
Nutrition, n	
Overweight	2
Normoweight	22
Moderate malnutrition	1
Severe malnutrition	1
Family history of atopy, n	
None	9
Father only	1
Mother only	8
Mother and father	3
Siblings	11
SCORAD index, n	
Mild	10
Moderate	13
Severe	3
Mean SCORAD index (SD)	32.0 (14.99)

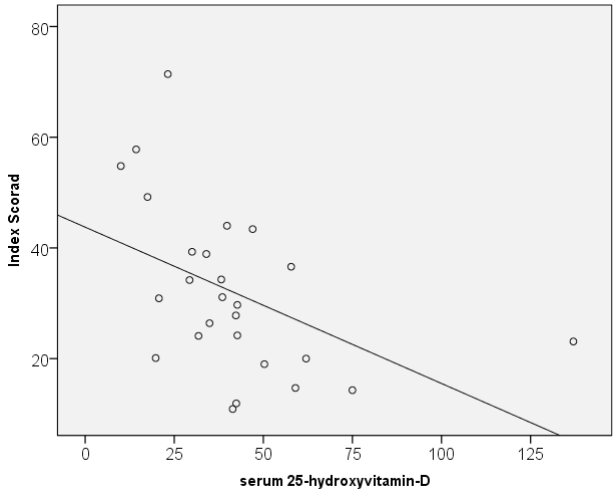

Figure 1. Scatterplot correlation between 25-hydroxyvitamin-D level and SCORAD index

Table 2. Subjects' mean SCORAD index and 25-hydroxyvitamin-D level

	Mean (SD)	Min	Max	95%CI	P value
SCORAD Index	32.0 (14.99)	10.9	71.4	25.95 to 38.06	0.248
25-hydroxyvitamin-D serum, ng/mL	41.6 (24.81)	10	137	31.58 to 51.62	<0.001

Discussion

Atopic dermatitis is a skin disease characterized by an inflammatory reaction on the skin, often due to hereditary and environmental factors.[1] The prevalence of atopic dermatitis in children is 75-80% appearing at first life of age.[2] We found children with AD in the < 1-year-old group was higher than in the 1 to 5-year-old group. The higher prevalence of AD in the first life of age is caused by the failure of immune deviation that should normally select for Th1 cell in immune response skewed to Th2 in post nataly in atopic children.[14]

Atopy is more prevalence in male than female before puberty. There is a reversal of this sex ratio during puberty with girls having more asma and atopy throughout there productive years. Hormonal changes have been implicated in the reversal of sex ratio. Estrogen is understood to have a biphasic dose-response, with higher levels promoting Th2 responses and at lower levels, a Th1 response. Progesterone has been shown to stimulate interleukin-4 production and promote the development of human Th2 cells.15 In this study we found the male to female AD ratio was 1.6:1.

Regarding birth order, the first and the second children were more likely to have atopic dermatitis. In 1989, David Strachan introduced the "hygiene hypothesis," postulating that infection protects against atopy. So reduced exposure to infections during childhood results in aberrant immune responses to innocuous antigens later in life. This hypothesis was based upon Strachan's observations that infants with higher numbers of siblings were at decreased risk for developing allergies.[16,17] In this study we found the first and the second children had more atopic dermatitis.

Familial atopy has been reported to be related to the occurrence of allergic disease manifestation and the severity of AD. A Netherlands study in 1996 reported that of one parent had atopy, the risk of allergic disease in children was 20-40%. If both parents had allergies, then the children had a 60-80% risk. If a sibling had allergic disease, then a child had a risk of 20-30%. And if the family had no history of atopy, then the child's risk of allergic disease was only 10%.[18] Our study found children with AD more prevalence in atopic one of parents than both parents, as seen in **Table 1**. We also found that both atopic parents have all their children with atopic dermatitis. Nine of our subjects had no history of atopy in the family.

It is important to determine the severity of AD in order to evaluate disease improvement during and after therapy. The ETFAD developed the SCORAD index to create a consensus on assessment methods for AD.[5] An Italian study found that lower 25(OH) D level was correlated with higher SCORAD index.[9] Vitamin D plays a crucial role in skin barrier function, where vitamin D3 stimulates the production of cathelicidin.[12] Cathelicidin in macrophages triggers the Th2 response, by reducing dendritic cells maturation and migration, which, in turn, leads to B cells reducing IgE production. Vitamin D also acts as an anti-inflammatory agent; 1,25(OH)D inhibits maturation of dendritic cells and production of cytokines IL-12 and IL-23.[5,8] Cathelicidin is deficient in AD. The pathogenesis of AD involves a complex interplay of epidermal barrier dysfunction and dysregulated immune response, and vitamin D is involved in both processes.[12]

Previous studies have shown that vitamin D can be given as a protective therapy to reduce the severity of AD.[10,19,20] The *American Academy of Pediatrics* (AAP) recommends giving 400 IU of vitamin D as a supplement to newborns to prevent vitamin D deficiency.[5]

In conclusion, there is a moderate correlation between serum 25-hydroxyvitamin-D level and SCORAD index in children with atopic dermatitis.

Conflict of Interest

None declared.

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