ORIGINAL ARTICLE

Sun Exposure, Dietary Vitamin D and Vitamin D Status in Adult Atopic Dermatitis: A Case Control Study

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ABSTRACT

Introduction: Atopic dermatitis (AD) and its severity has been inconsistently associated with lower vitamin D levels as multiple other factors that influence vitamin D status were not always assessed. **Methods:** A case control study involving AD patients and controls ≥18 years old was performed. Exclusion criteria were systemic immunosuppression ≤ 4 weeks prior to recruitment, renal or hepatic impairment, parathyroid diseases and vitamin D or calcium supplementation. Healthy controls were matched for age, gender, ethnicity, Fitzpatrick skin type and body mass index (BMI). Sun exposure, a 3-day, 24-hour dietary recall and serum 25-hydroxyvitamin D were measured. **Results:** 38 AD patients and 38 controls participated. Majority had Fitzpatrick skin type IV. Vitamin D was lower in AD [15.9(9.9-24.0)ng/ml] than controls [17.3(14.4-27.2)ng/ml], p= 0.028. It was sufficient in 16(42.1%) AD and 15(39.5%) controls, insufficient in 7(18.4%) AD and 22(57.9%) controls and deficient in 15(39.5%) AD compared to 1(2.6%) control. Sun exposure was similar in both groups. AD had significantly higher dietary vitamin D intake [1.5(0.6-3.1) vs 0.6 (0.3-1.0)µg]. AD was an independant risk for vitamin D deficiency with OR 17.52; 95%CI:1.4-212.7 and vitamin D insufficiency OR 0.26;95%CI:0.07-0.95. Vitamin D levels did not correlate with AD severity. **Conclusion:** AD is a risk for vitamin D deficiency despite higher dietary intake and similar skin type, BMI and sun exposure as controls.

Keywords: 25-hydroxyvitamin D, Atopic dermatitis, Sun exposure, Dietary vitamin D, Body mass index

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INTRODUCTION

Atopic dermatitis (AD) is due to complex interactions between multiple genetic, immunological and environmental factors. Vitamin D has been implicated in AD pathophysiology as the skin with ultraviolet light B exposure is a major source of vitamin D. Vitamin D is involved in the regulation of innate and adaptive immune systems, keratinocyte production of antimicrobial peptides, and keratinocytes proliferation and differentiation in the production of involucrin, filaggrin and loricrin (1). However, conflicting results were seen from studies evaluating vitamin D status in AD, its relationship with AD severity, as well as the effect of supplementation on disease activity.

Vitamin D insufficiency or deficiency has been demonstrated in 60 to 90% of AD patients worldwide (2-6). A 5 fold increase in risk of AD was found in vitamin D deficient obese patients (7). However, a German nationwide survey involving 9838 children and adolescents found higher vitamin D levels in those with eczema (8). In the Asian region despite the abundance of sunlight, a case control study in Hong Kong showed vitamin D deficiency in 47.8% AD children compared to 26.6% in controls (9). In Korea, about 80% of AD patients were vitamin D deficient (4). The relationship between lower vitamin D levels with AD especially in children was demonstrated in systematic reviews and meta-analysis (10,11).

Most studies on vitamin D in AD were conducted in children and were limited by not including a few important factors that affect serum vitamin D level in the analyses and interpretation. Body mass index, dietary vitamin D, calcium and fat intake, sun exposure, sun protection practices and multiple other factors influence vitamin status and supplementation (12,13). We embarked on a case control study in adult AD patients that included assessment of these factors.

MATERIALS AND METHODS

This was a case control study involving adult AD patients from the dermatology clinics of University

Kebangsaan Malaysia Medical Center and Kuala Lumpur Hospital, conducted from June 2014 to February 2015. Our study objectives were to determine the relationship between vitamin D status and AD, and to determine the association between sun exposure and dietary intake of vitamin D and AD. AD patients aged ≥18years diagnosed according to the Hanifin-Rajka classification were recruited. Exclusion criteria were use of systemic immunosuppressive agents ≤ 4 weeks prior to recruitment, renal or hepatic impairment, parathyroid diseases and vitamin D or calcium supplementation in the last 6 months.Healthy controls were matched for age, gender, ethnicity, Fitzpatrick skin type and body mass index (BMI). Biochemical parameters tested were urea, creatinine, alanine transaminase (ALT), serum vitamin D, and intact parathyroid hormone (iPTH). Vitamin D status can be determined by measuring its metabolites, 25-hydroxyvitamin D and 1,25 dihydroxyvitamin D. 25-hydroxyvitamin D is widely used as it reflect vitamin D status more accurately since it is not influenced by PTH and other hormones. 1,25 dihydroxyvitamin D is better used to determine vitamin D status in certain circumstances such as in patients with renal diseases (14). Electrochemiluminescence binding assay on Cobas e411 by Roche Diagnostics were used to determine 25-hydroxyvitamin D and iPTH values. Vitamin D status is classified according to the Food and Nutrition Board definition (15). Sun exposure was calculated as the number of hours per week spent outside without sun protection multiplied by percentage body part exposed to sunlight to give a sun exposure index (SEI) (16). A 3 day, 24-hour dietary recall comprising of 2 weekdays and 1 weekend was performed and nutrition intake was analyzed using Nutritionist Pro® software. Severity of AD was assessed using SCORAD (**SCOR**ing **A**topic **D**ermatitis).

This study was performed upon approval from Research Ethics Committee, the National University of Malaysia, UKM 1.5.5.5/244/FF-2015-344. Statistical analysis was carried out using SPSS (Statistical Package for Social Sciences) version 16. The Shapiro-Wilk test was used to determine normality distribution of continuous data. The Mann-Whitney U test ascertained differences between the medians of case and control groups. Binary Logistic Regression was performed to determine the effects of sun exposure (SEI), serum vitamin D, energy intake and dietary vitamin D on the likelihood that the subject had AD. A p value of ≤ 0.05 was considered as significant.

RESULTS

A total of 38 AD patients and 38 controls were included in the study. There were 28 males and 48 females. Median age for AD and controls were 27.5(22.8-38.0) and 28.0(24.0-38.0) years respectively. Majority of AD (81.6%) and controls (86.6%) had Fitzpatrick skin type IV. Median BMI for AD was 23.6(21.2-29.5) kg/m^2 , and 24.7(21.4-29.7) kg/m^2 for controls. Fifteen (39.5%) of patients had mild AD, 17(44.7%) had moderate disease severity while 6(15.8%) had severe disease. None of the study subjects used sunscreen or other types of photoprotection. Characteristics of the study population are presented in Table I. Serum calcium [2.4(2.3-2.5) vs 2.3(2.2-2.4) mmo/L], urea [4.1(2.8-5.4) vs 2.9(2.6-2.4) mmol/L] and creatinine [70.6(60.6-73.4) vs 63.2(59.4-66.3) mmol/L] were found to be significantly higher in AD compared to controls. However, these values were still within normal limits. Serum vitamin D level was significantly lower in AD [15.9(9.9-24.0)ng/ml] than controls [17.3(14.4-27.2)ng/ml] with p value 0.028. Vitamin D level was found to be sufficient in 16(42.1%) AD and 15(39.5%) controls. The levels were insufficient in 7(18.4%) AD and 22(57.9%) controls. Fifteen (39.5%) of AD was vitamin D deficient, compared to only 1(2.6%) control. Results of biochemical tests are summarised in Table II.

Table I: Characteristics of the study population

Parameters	AD, n=38 % or median(IQR)	Controls, n=38 % or median(IQR)	p value
Age (years)	27.5 (22.8-38.0)	28.0 (24.0-38.0)	0.67
Gender			
Males	14 (36.8)	14 (36.8)	
Females	24 (63.2)	24 (63.2)	
Fitzpatrick skin type			
III	2(5.3)	2(5.3)	
IV	31(81.6)	33(86.8)	
V	4(10.5)	3(7.9)	
VI	1(2.6)	-	
BMI (kg/m^2)	23.6 (21.2-29.5)	24.7 (21.4-29.7)	0.70
Normal	20(52.6)	23(60.5)	
Obese	8(21.1)	8(21.1)	
Overweight	9(23.7)	7(18.4)	
Underweight	1(2.6)	-	
Severity of AD			
Mild	15(39.5)	-	
Moderate	17(44.7)		
Severe	6(15.8)		

Table II: Biochemical profile of the study population

Parameters	AD Median (IQR) or n(%)	Controls Median (IQR) or n(%)	p value
Calcium (mmol/l)	2.4(2.3-2.5)	2.3(2.2-2.4)	0.00
Urea (µmol/l)	4.1(2.8-5.4)	2.9(2.6-3.4)	0.00
Creatinine (mmol/)	70.6(60.6-73.4)	63.2(59.4-66.3)	0.00
Alanine transferase (U/L)	20.6(17.6-23.7)	17.2 (11.2-26.6)	0.53
Serum vit D (ng/ml)	15.9(9.9-24.0)	17.34 (14.40-27.24)	0.03
No. of subjects with Vit D status:			0.00
Sufficient (>20ng/ml)	16 (42.1)	15 (39.5)	-
Insufficient (12-20ng/ml)	7 (18.4)	22(57.9)	-
Deficient (0-11.99ng/ml)	15 (39.5)	1(2.6)	-
iPTH (pmol/ml)	4.4(2.9-6.1)	4.1(3.0-5.4)	0.51

Sun exposure index was slightly higher in AD 9.3(5.7-17.9) compared to controls 9.1(4.5-19.0) but the difference was not significant. Controls had higher total energy, protein, carbohydrate and fat intake. However, only total energy was significantly different [1213.2(1084.3-1463.4 vs 1036.0(937.2-1189.7) kcal], p value 0.001. AD had a significantly higher dietary vitamin D intake than controls [1.5(0.6-3.1) vs 0.6 (0.3-1.0)µg] (Table III). Logistic regression analyses showed AD is a risk factor for vitamin D deficiency with OR 17.52; 95%CI:1.4-212.7, while vitamin D insufficiency gives an OR of 0.26;95%CI:0.07-0.95. Vitamin D leves did not correlate with severity of AD measured by SCORAD, r=-0.16, p value 0.341.

Table III: Sun exposure index and nutritional intake

Parameters	Cases Median (IQR) or n(%)	Controls Median (IQR) or n(%)	p value
SEI	9.3(5.7-17.9)	9.1(4.5-19.0)	0.86
Adequate (SEI 18.38)	9(23.7)	11(28.9)	
Inadequate (SEI 18.37)	29((76.3))	21(71.1)	
Energy (kcal)	1036.0(937.2-1189.7)	1213.2(1084.3-1463.4)	0.00
Protein (gm)	50.6(44.8-64.7)	57.5(50.5-64.7)	0.06
Carbohydrate (gm)	147.9(129.1-170.0)	160.2(136.4-199.3)	0.07
Fat (gm)	35.1(29.4-41.9)	43.1(26.9-49.1)	0.06
Dietary vit D (µcg)	1.5(0.6-3.1)	0.6(0.29-1.0)	0.00

DISCUSSION

Vitamin D insufficiency was seen in both AD and controls. This maybe related to inadequate dietary intake of vitamin D and lack of sun exposure in our study population as a whole. About 90% of vitamin D is derived from skin synthesis which is dependant on sun exposure. SEI was much lower than that reported in winter (16) despite our study population living in a tropical climate. Sweat is a recognized irritant and a trigerring factor for itch in AD. It is generally assumed that our AD patients avoid sun exposure as most report discomfort and itch due to the heat and sweat. Interestingly their SEI was similar with controls. Sun avoidance is a common practice in Asians as lighter skin is preferred and considered more attractive (17,18). A high prevalence of vitamin D insufficiency in our general population irrespective of the individuals' health status has been documented (19-21).

Dietary intake of vitamin D was less than one third of the 5µg recommended intake.Total daily energy intake most likely have been under reported as the values are much lower than normal estimated energy requirements (22) despite normal BMI in majority of the study population. However, energy and vitamin D intake were still significantly higher among controls. AD patients tend to restrict themselves from certain foods due to cultural food taboos or related food allergies (23). From our clinical experience and observation, chicken, eggs, certain types of fish, salted fish and seafood are believed to be the reason for itch by our patients. Fish is the main alternate source of protein consumed and the types of fish preferred by AD patients like Indian mackerel, Spanish mackerel and local tuna incidentally have higher vitamin D content.

Although both AD and controls had insufficient vitamin D, the level was significantly higher in controls. More than half of our AD patients were vitamin D insufficient or deficient and there is about a 17 fold increase in risk of AD with vitamin D deficiency. This finding is in accordance with the results of most previous studies although BMI, sun exposure and dietary vitamin D intake were not taken into account in these studies. When these factors were considered, the risk of AD with vitamin D deficiency is considerably higher than 5 fold that was reported by Oren et al (7). We did not find a significant correlation between vitamin D and severity of AD. However, our sample size was not calculated to determine this aspect. Lower levels of vitamin D was shown to be associated with more severe AD in a few studies (2,3) while several studies failed to show similar results (5,6,24). Others showed the association of low vitamin D with severity only in AD patients with food allergies and aeroallergen sensitizations (24,25). A recent systematic review showed significant correlation in 10 out of 16 studies in AD children, however there was heterogeneity in terms of location and season and the main objectives of the studies were the effects of vitamin D levels or supplementation on AD (11). The implication of vitamin D in AD has been further demonstrated by results on the effect of vitamin D supplementation. Although the findings still require additional confirmatory research, evidences favour its benefits in improving AD disease severity (10,11,26). Analyses and interpretation of dietary vitamin D intake was subjected to recall bias was a limitation to this study.

CONCLUSION

The findings of this study substantiate exisiting evidence on the association of vitamin D deficiency with AD. This study added strength to previous data as major factors that affect serum vitamin D level ie skin type, BMI, sun exposure and dietary intake were included. Vitamin D insufficiency or deficiency is a risk for AD. Patients should be advised to ensure adequate dietary intake and sun exposure.

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