A Systematic Review and Meta-analysis of Association between Serum Vitamin D and Atopic Dermatitis

Pichanee Chaweekulrat, M.D.*, Chaiyawat Suppasilp, M.D.*, Bhoom Suktitipat, M.D., Ph.D. *,**

**Department of Biochemistry, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, **Integrative Computational BioScience Center (ICBS), Mahidol University, Salaya, Phuttamonthon, Nakhon Pathom 73170, Thailand.*

ABSTRACT

Objective: The relationship between vitamin D and atopic dermatitis remains controversial. Here, we systematically reviewed and meta-analyzed the association between serum 25-hydroxy vitamin D concentration (25(OH)D) and atopic dermatitis (AD), AD severity, and the benefits of oral vitamin D supplementation.

Methods: A total of 15 observational studies and 5 RCTs from 12 countries were included in this review. The effects of vitamin D deficiency or vitamin D level on AD and standardized AD severity score were performed using a random-effects model on 3 aspects: 1) serum vitamin D and risk of AD, 2) serum vitamin D level and severity of AD, and 3) the benefits of oral vitamin D supplementation on AD severity.

Results: The analysis showed serum 25(OH)D deficiency marginally increased the risk of AD (OR = 1.55, 95%CI = 0.94 - 2.55, p = 0.084). Low serum 25(OH)D was correlated with greater AD severity (r = -0.29, 95%CI = -0.504 to -0.048, p = 0.020), and oral vitamin D supplementation helped reduced AD severity score by 0.963 standard deviation (95%CI = 0.23 to 1.70, p = 0.011).

Conclusion: The association between serum 25(OH)D deficiency and risk of AD was still controversial. However, our meta-analysis suggested that higher serum 25(OH)D is associated with lower severity of AD. Moreover, oral vitamin D supplementation also helps to reduce AD severity.

Keywords: Atopic dermatitis, vitamin D, systematic review, meta-analysis

Siriraj Med J 2015;67:219-226
E-journal: http://www.sirirajmedj.com

INTRODUCTION

Atopic dermatitis (AD) is a chronic inflammatory skin disease that has a wide range of clinical presentations including pruritic skin, erythema, xerosis, oozing and crusting. Since AD is a chronic disease, it has a highly negative impact on patients' quality of life.[1] AD occurs within the first year of life in 60 percent of the cases and within 5 years of age in almost 90% of the patients. The majority of patients have a remission before adulthood, but more than 10% of these patients continue to have persistent symptoms. The incidence of AD is increasing over time, especially in urban areas and developed countries.[2]

Vitamin D has been used as an alternative choice for AD treatment to reduce hyper-responsive T-cells.[3] A nutritional survey demonstrated that AD patients had lower vitamin D intake than

Correspondence to: Bhoom Suktitipat
E-mail: bhoom.suk@mahidol.ac.th
Received 12 March 2015
Revised 19 May 2015
Accepted 25 June 2015

a healthy group.[4] In addition, vitamin D was associated with immunologic mechanism in urticarial and AD.[5] Vitamin D supplement was shown to reduce the severity of AD.[6]

The association between vitamin D level and dermatitis risk or severity has remained controversial. Vitamin D deficiency was inversely correlated with the severity of AD in 37 patients,[7] and vitamin D supplement was shown to improve the clinical of winter related AD in Boston children.[6] However, some studies failed to show the correlation between vitamin D and AD or the benefits of vitamin D supplementation. For example, Chui et al., founded no correlation between serum 25(OH)D and AD severity, among 97 AD pediatric population.[8]

In this study, we performed meta-analysis and systematic reviews of available literatures to clarify associations between serum vitamin D and AD. We reviewed available publications in 3 aspects: 1) serum vitamin D and risk of AD, 2) serum vitamin D level and severity of AD, and 3) the benefits of oral vitamin D supplementation on AD severity.

MATERIALS AND METHODS

This meta-analysis and systematic review was done following PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analysis) recommendation[9] and MOOSE (Meta-analysis of Observational Studies in Epidemiology) statements.[10]

Search approach

Articles were searched from PUBMED, SCOPUS and Cochrane library databases from August 1952 until October 2014. The search was done using keywords "vitamin D AND (atopic dermatitis OR eczema)".

Eligible studies

Inclusion and exclusion criteria have been summarized in Table 1.

Measurement of serum vitamin D level

All studies measured 25(OH)D as total serum vitamin D level (Table 2). In this study, vitamin D deficiency was defined as serum 25(OH)D concentration less than 20 ng/mL or 50 nmol/L.[11]

Selection and extraction of studies

Titles and abstracts of the articles were screened by two independent reviewers (PC and CW) for their eligibility. Full-text articles were obtained and reviewed for their acceptability. The data were extracted by first reviewer and the second reviewer checked for the accuracy of the extracted data using a pre-designed data extraction form.

TABLE 1. Articles inclusion and exclusion criteria.

Inclusion criteria	Exclusion criteria
Types of studies	Review articles, animal studies, case report
RCTs or observational studies	Studies that were not in English
Types of participants	Studies of vitamin D levels in pregnant woman or in the cord blood at the time of delivery
AD patients: diagnosed by doctors, questionnaires or medical records	Studies that used other routes of vitamin D supplements other than oral route
Types of exposure	
Observational studies: serum vitamin D level	
RCTs : oral vitamin D supplementation	
Types of outcome	
Observational studies : number of AD patients, severity of AD	
RCTs : severity of AD, serum vitamin D	

TABLE 2. Characteristics of studies in this review.

Study (year)	Type of study	25(OH)D detection method †	Mean age (years)	Population	Total N	Main Conclusion
Oren E (2008)	Case-control	N/A	43±15	USA	290	Vitamin D deficiency increases risk of AD in obese patients.
Vähävihu K (2008)	Case-control	RIA	36±12	Finland	23	Almost all AD Patients have vitamin D deficiency which can be effectively corrected by NB-UVB.
Vähävihu K (2010)	Case-control	RIA	40.5	Finland	33	Almost all AD Patients have vitamin D deficiency and heliotherapy can corrects both serum vitamin D deficiency and severity of AD.
El taieb MA (2013)	Case-control	CMA	6.3±2.8	Egypt	59	Vitamin D deficiency may be related to the severity of AD.
Noh S (2014)	Case-control	N/A	25.2±7.4	Korean	131	Serum 25(OH)D is significantly inversely associated with eczema area than with severity of AD.
Rose RF (2014)	Case-control	MS/MS	40	England	38	There are no relationship between serum vitamin D and severity of AD.
Wang SS. (2014)	Case-control	EIA	11.4±4	Hong Kong-Chinese	826	Vitamin D deficiency is associated with childhood AD.
Peroni DG (2011)	Cross-sectional	CIA	5.6	Italy	37	Vitamin D deficiency may be related to the severity of AD.
Akan A (2013)	Cross-sectional	CIA	2.8	Turkey	74	Vitamin D correlates with severity of AD in children with allergic sensitization.
Chui YE (2013)	Cross-sectional	LC-MS	3	USA	94	Serum 25(OH)D does not correlate with AD severity.
Heimbeck I (2013)	Cross-sectional	CIA	1-17	Germany	9,838	Serum 25(OH)D is inversely associated with AD.
Lee SA (2013)	Cross-sectional	LLE & SPE	9.92	Korean	157	Vitamin D deficiency correlates with the severity of AD associated with food sensitization.
Samochocki Z (2013)	Cross-sectional	ECIA	29.9±8.5	Poland	153	There are no association between serum 25(OH)D and AD severity but vitamin D supplementation may help improve AD symptoms.
Baek JH (2014)	Cross-sectional	CIA	0.67	Korean	168	Vitamin D deficiency associates with severe AD in infancy.
Cheng HM (2014)	Cross-sectional	N/A	44±15.1	Korean	15,212	Vitamin D deficiency increases likelihood of AD
Sidbury R (2008)	RCTs	N/A		USA	11	Vitamin D supplementation improves sign and symptoms of winter related AD.
Javanbakht MH (2011)	RCTs	RIA	25.9±2.2	Iran	45	Vitamin D supplementation significantly improves AD severity but there are no association between serum 25(OH) D and AD severity.
Amestejani M (2012)	RCTs	RIA	23.3±2.1	Iran	53	Vitamin D supplementation improves AD severity.
Hata TR (2013)	RCTs	N/A	31.5±10.6	USA	60	There are no association between serum 25(OH)D and AD severity and vitamin D supplementation does not improve clinical of AD.
Camargo CA Jr (2014)	RCTs	N/A	9	Mongolian	107	Vitamin D supplementation improves winter related AD among Mongolian children.

† RIA = radioimmunoassay, CIA = chemiluminescent immunoassay, CMA = chemiluminescent microparticle immunoassay, MS = mass spectrometry, EIA = enzyme immunoassay, LC-MS = Liquid chromatography–mass spectrometry, LLE = liquid-liquid extraction, SPE = solid phase extraction, ECA = electrochemiluminescent immunoassay

Quality of studies

Grading of Recommendations, Assessment, Development and Evaluations (GRADE) system was used to analyze the quality of evidence.[12]

Statistical analysis

We analyzed all data in 3 topics: 1) serum vitamin D level and risk of AD, 2) correlation between serum vitamin D level and severity of AD, and 3) benefit of oral vitamin D supplementation on AD severity. Studies were included in the meta-analysis if they had available data on diagnosis, exposure, and similar outcome measurements. Effect sizes, such as odds ratio (OR), correlation coefficient (r) and standardized mean difference (SMD) were recorded as outcomes. To examine the heterogeneity, we used Cochran's Q statistic and the I^2 statistic. Random effect model was used if heterogeneities was present. For all results, a two-sided p-value ≤0.05 was considered as statistical significance, and ≤0.10 was considered marginally significant. All analyses were performed using the software package Medcalc® v.14.8.1.

Publication bias

Evidence of publication bias was explored using a visual-base method through funnel plots.

RESULTS

Database search with keywords "vitamin D AND (atopic dermatitis OR eczema)" revealed 203 publications (Fig 1). After screening the titles and abstracts, the full text of 20 articles that met the inclusion criteria were retrieved and reviewed in detail. Among these 20 articles, 5 were randomized controlled trials, and 15 were case-control or cross-sectional studies.[6-8,13-29]

Studies characteristics

Characteristics of these 20 studies have been shown in Table 2, involving 27,409 participants from 12 countries. There were 13,492 woman and 13,864 men. The mean age was 20.39±5.4 year-old (range from 0.3 to 73). Among the six studies that gave oral vitamin D supplements, only one study used vitamin D2 (ergocalciferol) as supplements6, while 5 other studies used vitamin D3 (cholecalciferol).[13,14,16,17,28] Evidence provided by most studies were graded "Low" according to GRADE except for the studies by Javanbakht et al. and Amestejani et al.[20,23]

Serum vitamin D and atopic dermatitis

AD is one of several inflammatory diseases associated with vitamin D deficiency.[30] Deficiency of serum vitamin D is defined by most experts as 25 (OH)D < 20 ng/Ml.[11] The combined results from 10 studies that reported vitamin D levels in 1,418 AD patients found 74.9% of all AD patients with vitamin D deficiency (Table 3).

From the included 4 case-control studies, there were more vitamin D deficient patients (80.35%) among AD patients than in the control (65.45%).[14,20,23,24] We found that patients with vitamin D deficiency were 1.54 times more likely to have AD (95%CI: 0.94 to 2.55, p = 0.084). However, the association was marginally significant (Fig 2A).

Given that most of these studies were small and vitamin D deficiency only has a small effect on the risk of AD, a larger study might be needed to investigate the association. Serum vitamin D might have to be lower than 12 ng/mL to increase the risk of AD.[23,22] However, discrepancies in the results can still be seen.[26]

Correlation between serum vitamin D and severity of atopic dermatitis

To grade severity of AD, various scoring systems were used among these studies, for example, SCORing Atopic Dermatitis (SCORAD), Nottingham Eczema Severity scores (NESS), Rajka and Langerland's scoring system, and Eczema Area and Severity Index (EASI). SCORAD was the most common scoring system among the 20 included articles reported in 92% of the patients (11,167 out of 12,079). Hence, we chose to perform the meta-analysis of studies that used SCORAD system.

The relationship between serum vitamin D level and SCORAD had been reported in 7 studies, involving 597 subjects.[11,12,22,26,28,34,36] The meta-analysis result from these 7 studies showed

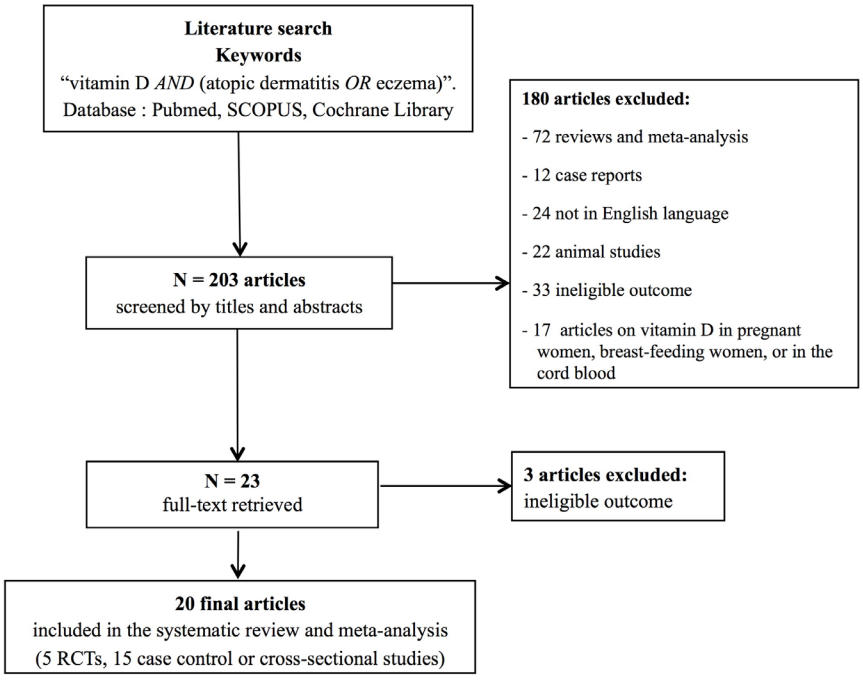

Fig 1. Flow chart of literature review

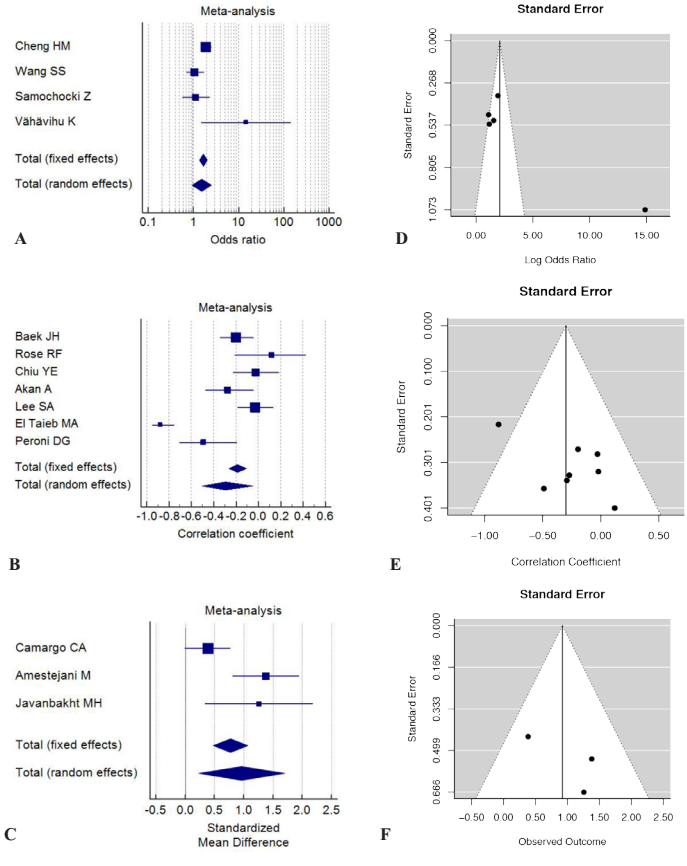

Fig 2. Meta-analysis results: A) Association of vitamin D deficiency and risk of atopic dermatitis; B) Correlation between serum vitamin D and atopic dermatitis severity (SCORAD); C) Vitamin D supplementation and atopic dermatitis; D) funnel plot of association results between vitamin D deficiency and atopic dermatitis; E) funnel plot of reported correlation between serum vitamin D and severity; F) funnel plot of reported benefits of vitamin D supplement on AD.

TABLE 3. Numbers of atopic dermatitis patients and controls with serum level of vitamin D.

Study	Case		Control		Total
	>20 ng/mL	<20 ng/mL	>20 ng/mL	<20 ng/mL	
Cheng HM (2014)	86	306	5187	9663	15,212
Wang SS (2014)	56	442	40	288	826
El Taieb MA (2013)	30	29	N/A	N/A	59
Samochocki Z (2013)	54	41	35	23	153
Lee SA (2013)	31	126	N/A	N/A	157
Chiu YE (2013)	57	37	N/A	N/A	94
Javanbakht MH (2011)	6	39	N/A	N/A	45
Peroni DG (2011)	29	8	N/A	N/A	37
Vähävihu K (2010)	1	17	7	8	33
Vähävihu K (2008)	6	17	N/A	N/A	23
Total	356	1,062	5,269	9,982	16,639

N/A: Normal control data were not available from these studies

a significant correlation between low serum vitamin D level and more severe AD as measured by SCORAD system (r = -0.292, 95%CI: -0.504 to -0.0484, p = 0.020) (Fig 2B).

Akan et al., (2013) and Lee et al., (2013) did not find statistically significant relationships between vitamin D level and AD severity in overall population. However, in a subgroup analysis among the patients with allergic sensitization, vitamin D level was statistically significantly correlated with AD severity.[22, 28]

Oral vitamin D supplementation and atopic dermatitis severity

The benefit of oral vitamin D in reducing atopic dermatitis severity was investigated in 5 RCTs,[6,13,16,17,28] and 1 cross-sectional study.[21] Most of these studies used different types of severity score, dosage, and duration of oral vitamin D supplementation. Most studies, except the study by Sidbury et al.[6], supplemented vitamin D_3[13,16,17,28]. Although the sample sizes included in these studies were small, most studies suggested some benefits from vitamin D supplementation.

We estimated the effects of vitamin D supplements as a standardized mean difference to account for the different scoring system using available data from three studies, which reported the mean severity score before and after receiving vitamin D supplements.[13,16,28] These three studies included 99 AD patients and 88 controls. Overall, vitamin D supplementation significantly reduced AD severity score by 0.96SD compared to the no-supplement group (SMD = 0.963, 95%CI: 0.226 to 1.700, p = 0.011) (Fig 2C).

Publication bias

We have explored the publication biases using a funnel-plot of the three main results reviewed in our study. We did not see any evidence suggesting the report of overly positive association or correlation between Vitamin D and AD (Fig 2D, 2E, 2F). Results from larger studies clustered near the overall mean and the correlations reported were more toward the null. Given a small number of available publications, the evidence for publication biases was rather limited.

DISCUSSION

The prevalence of vitamin D deficiency is high in many areas around the world so it has currently become a global healthcare problem. The definition of vitamin D deficiency is commonly defined as <20 ng/mL.[11] From National Health and Nutrition Examination Survey (NHANES) 2005-2006, 41.6% of the participants aged 20 or older had serum vitamin D level under 20 ng/mL.[31] Although the Thai population should have sufficient sunlight exposure, the prevalence of vitamin D deficiency was around 6% overall, but more than 14% in Bangkok.[32]

We explored three major relationships between vitamin D and AD. However, there are several challenges for this review. First, only a small number of articles were included in this systematic review and meta-analysis, the majority of which were observational studies. Second, these studies were heterogeneous with wide age-range of participants and study designs. Even the RCTs reviewed in this study used different doses and durations of vitamin D supplementation and different scoring system for AD severity, which complicated the meta-analyses of the combined benefits of vitamin D. A large RCT that addresses these issues could help to validate our conclusions. In most studies, the prevalence of vitamin D deficiency was higher in AD patients than in normal controls. However, we did not find a statistically significant association between vitamin D deficiency and AD. The estimated effects of vitamin D deficiency, combined among these studies, modestly increased the risk of AD.

The lack of association might be due to a small effect of vitamin D deficiency on the risk of AD or variation in effects of vitamin D across different age groups among these populations. Most studies were conducted in temperate countries zone or middle-eastern countries, which received insufficient sunlight exposure. Therefore, these results showed low average baseline serum vitamin D level.[33-36] The requirement of vitamin D for immune system to function properly might be lower than 20 ng/mL, so a lower cut-off for vitamin D deficiency of <12 ng/mL, was found associated with an increased risk of AD.[23] Although vitamin D deficiency did not significantly increase the risk of AD, lower serum vitamin D level was correlated with more severe clinical manifestation of AD. Oral vitamin D supplement increased serum vitamin D level, and helped in reducing AD severity.

CONCLUSION

From these evidences, vitamin D seems to be beneficial in AD patients and oral vitamin D can be one of the complementary choices for AD treatment. Our analyses highlight the relationship and the benefit of vitamin D to AD and could be interesting for advancing in AD treatment.

REFERENCES

1. Amaral CS, March Mde F, Sant'Anna CC. Quality of life in children and teenagers with atopic dermatitis. An Bras Dermatol. 2012 Sep-Oct;87(5):717-23.
2. Shaw TE, Currie GP, Koudelka CW, Simpson EL. Eczema prevalence in the United States: data from the 2003 National Survey of Children's Health. The Journal of investigative dermatology. 2011 Jan;131(1):67-73.
3 Silverberg JI. Atopic dermatitis: an evidence-based treatment update. Am J Clin Dermatol. 2014 Jul;15(3):149-64.
4 Solvoll K, Soyland E, Sandstad B, Drevon CA. Dietary habits among patients with atopic dermatitis. Eur J Clin Nutr. 2000 Feb;54(2):93-7.
5. Benson AA, Toh JA, Vernon N, Jariwala SP. The role of vitamin D in the immunopathogenesis of allergic skin diseases. Allergy. 2012 Mar;67(3):296-301.
6. Sidbury R, Sullivan AF, Thadhani RI, Camargo CA, Jr. Randomized controlled trial of vitamin D supplementation for winter-related atopic dermatitis in Boston: a pilot study. Br J Dermatol. 2008 Jul;159(1):245-7.
7. Peroni DG, Piacentini GL, Cametti E, Chinellato I, Boner AL. Correlation between serum 25-hydroxyvitamin D levels and severity of atopic dermatitis in children. Br J Dermatol. 2011 May;164(5):1078-82.
8. Chiu YE, Havens PL, Siegel DH, Ali O, Wang T, Holland KE, et al. Serum 25-hydroxyvitamin D concentration does not correlate with atopic dermatitis severity. J Am Acad Dermatol. 2013 Jul;69(1):40-6.
9. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Annals of internal medicine. 2009 Aug 18;151(4):264-9.
10. Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. JAMA. 2000 Apr 19;283(15):2008-12.
11. Holick MF. Vitamin D deficiency. N Engl J Med. 2007 Jul 19;357(3):266-81.
12. Guyatt G, Oxman AD, Akl EA, Kunz R, Vist G, Brozek J, et al. GRADE guidelines: 1. Introduction-GRADE evidence profiles and summary of findings tables. Journal of clinical epidemiology. 2011 Apr;64(4):383-94.
13. Javanbakht MH, Keshavarz SA, Djalali M, Siassi F, Eshraghian MR, Firooz A, et al. Randomized controlled trial using vitamins E and D supplementation in atopic dermatitis. J Dermatolog Treat. 2011 Jun;22(3):144-50.
14. Samochocki Z, Bogaczewicz J, Jeziorkowska R, Sysa-Jedrzejowska A, Glinska O, Karczmarewicz E, et al. Vitamin D effects in atopic dermatitis. J Am Acad Dermatol. 2013 Aug;69(2):238-44.
15. Lee SA, Hong S, Kim HJ, Lee SH, Yum HY. Correlation between serum vitamin d level and the severity of atopic dermatitis associated with food sensitization. Allergy Asthma Immunol Res. 2013 Jul;5(4):207-10.
16. Amestejani M, Salehi BS, Vasigh M, Sobhkhiz A, Karami M, Alinia H, et al. Vitamin D supplementation in the treatment of atopic dermatitis: a clinical trial study. J Drugs Dermatol. 2012 Mar;11(3):327-30.

17. Hata TR, Audish D, Kotol P, Coda A, Kabigting F, Miller J, et al. A randomized controlled double-blind investigation of the effects of vitamin D dietary supplementation in subjects with atopic dermatitis. J Eur Acad Dermatol Venereol. 2014 Jun;28(6):781-9.
18. Noh S, Park CO, Bae JM, Lee J, Shin JU, Hong CS, et al. Lower vitamin D status is closely correlated with eczema of the head and neck. J Allergy Clin Immunol. 2014 Jun;133 (6):1767-70.e6.
19. El Taieb MA, Fayed HM, Aly SS, Ibrahim AK. Assessment of serum 25-hydroxyvitamin d levels in children with atopic dermatitis: correlation with SCORAD index. Dermatitis. 2013 Nov-Dec;24(6):296-301.
20. Wang SS, Hon KL, Kong AP, Pong HN, Wong GW, Leung TF. Vitamin D deficiency is associated with diagnosis and severity of childhood atopic dermatitis. Pediatr Allergy Immunol. 2014 Feb;25(1):30-5.
21. Akan A, Azkur D, Ginis T, Toyran M, Kaya A, Vezir E, et al. Vitamin D level in children is correlated with severity of atopic dermatitis but only in patients with allergic sensitizations. Pediatr Dermatol. 2013 May-Jun;30(3):359-63.
22. Oren E, Banerji A, Camargo CA, Jr. Vitamin D and atopic disorders in an obese population screened for vitamin D deficiency. J Allergy Clin Immunol. 2008 Feb;121(2): 533-4.
23. Cheng HM, Kim S, Park GH, Chang SE, Bang S, Won CH, et al. Low vitamin D levels are associated with atopic dermatitis, but not allergic rhinitis, asthma, or IgE sensitization, in the adult Korean population. J Allergy Clin Immunol. 2014 Apr;133(4):1048-55.
24. Vahavihu K, Ala-Houhala M, Peric M, Karisola P, Kautiainen H, Hasan T, et al. Narrowband ultraviolet B treatment improves vitamin D balance and alters antimicrobial peptide expression in skin lesions of psoriasis and atopic dermatitis. Br J Dermatol. 2010 Aug;163(2):321-8.
25. Vahavihu K, Ylianttila L, Salmelin R, Lamberg-Allardt C, Viljakainen H, Tuohimaa P, et al. Heliotherapy improves vitamin D balance and atopic dermatitis. Br J Dermatol. 2008 Jun;158(6):1323-8.
26. Heimbeck I, Wjst M, Apfelbacher CJ. Low vitamin D serum level is inversely associated with eczema in children and adolescents in Germany. Allergy. 2013 Jul;68(7): 906-10.
27. Rebecca F. Rose CW, Thomas Oliphant, Fiona Browne, David Turner and Victoria Goulden. Serum 25-hydroxyvitamin D levels in patients with atopic eczema and the influence of narrowband ultraviolet B phototherapy. photodermatol photoimmunol photomed. 2014;30(5).
28. Camargo CA, Jr., Ganmaa D, Sidbury R, Erdenedelger K, Radnaakhand N, Khandsuren B. Randomized trial of vitamin D supplementation for winter-related atopic dermatitis in children. J Allergy Clin Immunol. 2014 Oct;134(4): 831-5.
29. Baek JH, Shin YH, Chung IH, Kim HJ, Yoo EG, Yoon JW, et al. The link between serum vitamin D level, sensitization to food allergens, and the severity of atopic dermatitis in infancy. J Pediatr. 2014 Oct;165(4):849-54.
30. Bikle D. Nonclassic actions of vitamin D. J Clin Endocrinol Metab. 2009 Jan;94(1):26-34.
31. Forrest KY, Stuhldreher WL. Prevalence and correlates of vitamin D deficiency in US adults. Nutr Res. 2011 Jan;31 (1):48-54.
32. Chailurkit LO, Aekplakorn W, Ongphiphadhanakul B. Regional variation and determinants of vitamin D status in sunshine-abundant Thailand. BMC Public Health. 2011; 11:853.
34. Hashemipour S, Larijani B, Adibi H, Javadi E, Sedaghat M, Pajouhi M, et al. Vitamin D deficiency and causative factors in the population of Tehran. BMC Public Health. 2004 Aug 25;4:38.
35. Alagol F, Shihadeh Y, Boztepe H, Tanakol R, Yarman S, Azizlerli H, et al. Sunlight exposure and vitamin D deficiency in Turkish women. J Endocrinol Invest. 2000 Mar;23 (3):173-7.
36. McKenna MJ. Differences in vitamin D status between countries in young adults and the elderly. Am J Med. 1992 Jul;93(1):69-77.