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Correlation of Vitamin D Levels with the Severity of Atopic Dermatitis Among Filipino Children Aged 1 Month to 18 Years Old Using the SCORAD Index

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ABSTRACT

Objective: To correlate Vitamin D levels with the severity of atopic dermatitis (AD) using the SCORAD index.

Methodology: Patients aged 1 month to 18 years seen at the Philippine General Hospital Outpatient Department, diagnosed with AD based on Hanifin and Rajka criteria, were recruited into the study. The extent and severity of AD were assessed using the SCORAD index. Serum concentrations of vitamin D were determined using the Beckman Coulter Radioimmunoassay, California.

Results: A total of 53 patients were included in the study. Mild AD was diagnosed in 27 (50.9%) children, moderate in 21 (39.6%), and severe in 5 (9.4%). Vitamin D insufficiency was observed in 39 individuals (73.6%). Of these, 20 (51.3%) had mild AD, 15 (38.5%) had moderate, and 4 (10.3%) had severe AD. Of the 14 individuals (26.4%) with sufficient vitamin D levels, 7 (50.0%) had mild AD, 6 (42.9%) moderate, and 1 (7.1%) severe. There is no significant correlation between serum vitamin D levels and the actual SCORAD index with a p of 0.26.

Conclusion: In conclusion, serum vitamin D level has no significant correlation with the severity of AD as measured by the SCORAD index.

Keywords: atopic dermatitis, vitamin D, vitamin D deficiency

INTRODUCTION

Background

Atopic dermatitis (AD) is the most common chronic skin condition, mostly affects children, and is highly associated with respiratory allergies. It affects 10% to 20% of the general population and is said to be steadily increasing in developing countries.[1] In the Philippines, the prevalence of AD among children 0 to 12 years old living in urban areas is 19.89% using an AD questionnaire.[2]

In a study conducted by Kim et al., the quality of life of Korean patients with AD has been severely affected by their illness.[3] Based on the results, AD had a negative effect on all aspects of their quality of life which include daily living activities, psychological status, and social functioning.[3] The severity of atopic dermatitis was directly correlated to the increased score in quality of life (QOL) (p <0.0001).[3] A hospital-based cross-sectional study on the impact of eczema severity on the quality of life among Korean children and adults conducted by Kim et al., demonstrated that AD caused impairment in patients' QOL and is correlated well with increased SCORAD scores or Rajka and Langeland scoring system. However, they were unable to detect a significant correlation between gender and age on QOL scores.[4] Aside from its effect on the patient's QOL, AD also imposes an increased financial burden on the patient and family. Fivenson et al., demonstrated that approximately 50% of the burden of illness resulted from days lost from work.[5] The rest came from out-of-pocket costs to the patients and their families, of which 75% came from household items and medications.[5] Treatment for AD costs an average of 219 dollars in the US alone.[6] No available data can be found locally regarding the financial costs of AD treatment. It is said that the financial burden increases significantly with disease severity and the cost of treatment is highest when topical steroids are used for the first time.[6]

The development of AD is attributed to the interplay of genetic, environmental, immunologic, and epidermal factors.[7] Among these, two proposed mechanisms include genetic defect of the epidermal barrier and immunological aberration.[1]

The genetics of AD is the focus of studies nowadays. Epidermal gene defect and immune response/host defense genes have been emphasized in the evolution of atopic dermatitis.[7] Specifically, a mutation in the filaggrin (filament-aggregating protein) gene, an epidermal barrier protein, has been identified as a predisposing factor for the development of atopic dermatitis.[7] Due to this gene mutation, allergens and irritant/environmental stimuli can easily penetrate the skin barrier leading to chronic inflammation and signs and symptoms of AD supporting the "outside-to-inside hypothesis".[8]

Immunological aberration, on the other hand, stresses the role of the immune system in initiating epidermal dysfunction. The Th2 immune response is activated during the initial stage. There is an overproduction of Th2 cytokines responsible for inflammatory reactions in AD which include IL-4, IL-5, IL-13, and IgE.[8] These inflammatory cytokines also affect skin cell differentiation.[9] Th2 cell response is enhanced, increasing the production of IL-4, IL-5, IL-10, and most especially, IL-31. This is said to have a role in the pruritus of AD.[10,11] Th2 skin inflammation downregulates filaggrin and natural moisturizing factor (NMF) of the skin independent of filaggrin mutation, as well as keratinocyte proteins, loricrin, and involucrin, thus affecting the epidermal barrier.[9,12,13] This phenomenon is termed the "inside-to-outside hypothesis", which explains the imbalance between Th1 and Th2 pathways and their respective cytokines.[8]

The presence of a primary T-cell population depends on the phase of atopic dermatitis. Th2 cells and their cytokines, IL-4, IL-5, and IL-13, are predominant during the acute phase, whereas, Th1 cells, interferon (IFN)-γ, IL-5, IL-12 have key roles in the chronic phase.[14] IL-4 and IL-13 are said to be responsible for the inflammation and upregulation of adhesion molecules in the epithelium that occurs during the initial phase of atopic dermatitis.[15] These two cytokines are also responsible for the isotype switching to IgE synthesis.[15] On the other hand, IL-5 promotes the maturation and survival of eosinophils.[12] During the chronic phase, IFN-γ is responsible for skin hypertrophy and keratinocyte apoptosis. Its synergistic effect with IL-22 results in epidermal hyperplasia induction leading to chronic skin inflammation.[12] Transition into chronic inflammation is brought about by IL-4, which acts on the dendritic cells and TLR2-ligands, enhancing IFN-γ. Likewise, it also suppresses IL-10, an anti-inflammatory cytokine, and enhances IL-12.[12]

Recent studies have linked vitamin D to the immune system in the background of having an established role in bone metabolism and calcium homeostasis. Vitamin D is a fat-soluble vitamin with two forms: vitamin D_2 (ergocalciferol) and vitamin D_3 (cholecalciferol).[10] Cholecalciferol (vitamin D_3) can be obtained from either the ultraviolet B radiation from the sunlight or the diet (mainly from animal sources) or supplements; ergocalciferol (vitamin D_2), on the other hand, is found in some plants and is used for fortification in food or vitamin supplements.[10] Exposure to sunlight triggers the initial steps of vitamin D3 synthesis. It will be initially hydroxylated in the liver, becoming 25-hydroxyvitamin D (25(OH)D), which is the major circulating form of vitamin D and the primary indicator of vitamin D status.[16] Second hydroxylation occurs in the kidney and other target tissues producing the active metabolite, 1,25-dihydroxyvitamin, which binds to the vitamin D receptors exerting its effects on the cells.[16] Vitamin D production is stimulated and

regulated by the parathyroid hormone and calcium and phosphorus serum levels. Recently, vitamin D is believed to have immunomodulatory effects on innate and adaptive immune systems due to the vitamin D receptor (VDR) in the various immune cells, especially macrophages, T lymphocytes, and B lymphocytes.[17] Vitamin D has been shown to suppress Th2 response, decreasing the production of IL-4 and IL-13.[18] Also, vitamin D can suppress IL-17, a proinflammatory cytokine that has a key role in non-atopic asthma. Studies have shown increased secretion of the anti-inflammatory cytokine IL-10 by $Foxp3^+$ Treg cells, suppressed production of IL-17, and increased induction of MAPK phosphatase-1 gene, a corticosteroid receptor inducible anti-inflammatory protein.[19]

Aside from various immune cells, vitamin D receptors are also expressed in the epithelial cells of the skin. Activation of these receptors interferes with the inflammation process and immune defense.[20] This only shows that the presence of VDR may have an effect on immune disorders caused by Th1/Th2 cytokine imbalance.[20] Additionally, vitamin D is said to have a role in the production of cathelicidins, a skin antimicrobial peptide (AMP) that serves as a defense against infections, which is deficient in atopic dermatitis.[14,10] Vitamin D, thus, suppresses inflammatory responses, both local and systemic, and increases antimicrobial peptides.[16] It induces expression of toll-like receptors (TLRs) genes, thus stimulating the chemotactic and phagocytic activity of monocytes and macrophages, increasing the recognition of pathogen-associated molecular pattern (PAMP) and production of AMPs.[16]

Various studies have already been conducted to show the correlation of vitamin D levels with the severity of atopic dermatitis. Camargo et al., conducted a randomized, double-blind, placebo-controlled trial on Mongolian children with winter-related AD to determine the effect of Vitamin D supplementation on those children.[21] They used Eczema Area and Severity Index (EASI) to assess the clinical severity of AD. Winter-related AD was defined as a history of AD worsening during the fall-to-winter transition.[21] A total of 107 children with a mean age of 9 years old were randomized to two groups: control versus vitamin D. After one month of vitamin D supplementation, they noted clinical improvement based on EASI score with a mean change for the vitamin D group of -6.5 ± 8.8 compared to -3.3 ± 7.6 for the placebo group.[21] The unadjusted difference between the change in means was -3.2 (95% CI, -0.9 to -5.5; $p = 0.01$), and the adjustment for baseline EASI score also yielded a similar result, with an adjusted difference between the change in means of -3.2 (95% CI, -0.2 to -6.2; $p = 0.04$).[21] Additionally, the researchers restricted their primary analysis to those not on topical corticosteroids. Their post hoc analysis confirmed better outcomes in the vitamin D group with a beta-coefficient of -3.6 ($p = 0.04$).[21]

From these results, Camargo et al., concluded that vitamin D supplementation resulted in clinically and statistically significant improvements in winter-related AD.

In a study conducted by Peroni DG et al., they concluded that vitamin D deficiency is related to the severity of AD.[10] They recruited 37 children diagnosed with AD, and the SCORAD index was used to assess the severity of the disease. Mean serum levels of vitamin D are higher in mild forms of AD. Additionally, serum-specific IgE (ImmunoCAP test) to *Staphylococcus aureus* enterotoxins and *Malassezia furfur* was also performed on these patients. It was noted that patients with specific IgE to these microbial antigens had increased severity of AD and vitamin D deficiency but the relationships were not statistically significant.[10]

Bo Ram Cheon et al., correlated serum vitamin D and IL-31 levels with AD severity. IL-31 is a Th2 effector cytokine responsible for the pathogenesis of pruritus.[22] Its receptors are found in cutaneous nerve fibers implicating its role as a mediator of pruritus in AD.[22,23] In this study, 91 children with AD and 32 control subjects were recruited. Results showed that mean serum vitamin D levels are significantly lower among children with AD; levels are greatly decreased among those with moderate to severe AD.[22] They found out that the severity of AD has an inverse correlation with the SCORAD index, which was used to assess the severity of AD.[15] No relationship was found between IL-31 and 25(OH) D levels; similarly, they advised large-scale randomized controlled trials for better results.

Though deficiency in vitamin D has been linked to the severity of atopic dermatitis, some studies say otherwise. One example is a study conducted by Galli et al., which demonstrated that vitamin D concentration in severe AD is not statistically different from that of patients with mild AD. In this study, no correlation was also found between the SCORAD index and serum vitamin D level.[20]

A study by Tae Young Han in Korea showed that serum $25(OH)D_3$ levels were reduced in children with AD compared to the normal children in the control group ($p = 0.04$); however, this was not observed among adult patients with AD.[1] Additionally, differences in serum vitamin D levels among the different eczema severity groups were not statistically significant ($p > 0.05$).[1]

A cross-sectional study conducted by Chiu et al., among pediatric patients aged 1 – 18 years showed no correlation between serum 25-hydroxyvitamin D concentration and the severity of AD among the pediatric population.[16] Pearson correlation coefficient between serum 25(OH) D concentration and objective SCORAD was $r = -0.001$ ($p = 0.99$) and total SCORAD was $r = -0.02$ ($p = 0.86$).[16] Also, serum 25(OH)D concentration was lower in mild AD

(mean, 23.0 ng/ml) compared to moderate AD (mean, 25.1 ng/ml) and severe AD (mean, 25.5 ng/ml; $p = 0.74$).[16] This study concluded that there is no statistically significant correlation between vitamin D status and the severity of atopic dermatitis among the pediatric population.[16]

With the emerging concept of the immunomodulatory effects of vitamin D, this study aimed to see the relationship between vitamin D levels with the severity of AD. The following were the objectives of this study: 1) assess the severity of atopic dermatitis among Filipino children seen in a tertiary hospital by using the SCORAD Index, 2) determine serum vitamin D_3 levels in patients with various severity levels of atopic dermatitis, 3) and to correlate serum vitamin D_3 levels with the clinical severity of AD among Filipino children in Philippine General Hospital (PGH). If a correlation is found, this study may be a basis for recommending vitamin D supplementation as an adjunct to atopic dermatitis therapy.

METHODOLOGY

Study Design
This was a cross-sectional analytic study.

Study Site
Subjects were enrolled from the PGH, Section of Allergy and Immunology Outpatient Department Clinic.

Population

Inclusion Criteria
This study included all pediatric patients aged one month to 18 years old with atopic dermatitis seen at the PGH Allergy OPD Clinic, General Pediatrics Clinic, and Dermatology Clinic from January 2018 to June 2018. Diagnosis of AD was based on the diagnostic criteria developed by Hanifin and Rajka.

Exclusion Criteria
The following were the exclusion criteria: 1) patients with other comorbid conditions that may affect vitamin D levels (rheumatoid arthritis, cystic fibrosis, multiple sclerosis, ulcerative colitis, Crohn's disease, celiac, osteomalacia, sarcoidosis, & thyroid dysfunctions), 2) individuals who had received medications including corticosteroids, barbiturates, bisphosphonates, sulfasalazine, omega-3 and vitamin D components such as calcium-D, 3) with concomitant skin conditions (ichthyosis vulgaris, etc.), 4) individuals who have received prior systemic therapy or phototherapy for AD, and 5) those who have received oral or topical corticosteroids, calcineurin inhibitors, or immunosuppressants for at least four weeks before enrollment. Patients on immunotherapy will be excluded as well.

Sample Size
A minimum sample size of 42 patients with AD was needed to achieve a 95% confidence level assuming that precision was set at 5%. The sample size formula for estimating a population proportion was used to obtain the sample size. This computation has been adjusted for the finite population correction factor since only 50 patients are usually seen in the study location within one year. Open Epi website was used in the sample size computation.

Procedure

Obtaining Informed Consent
The primary investigator obtained informed consent, informed assent, and verbal assent from the study participants and their guardians.

Data Collection
The extent and severity of AD were evaluated using the Severity Scoring of Atopic Dermatitis (SCORAD) index. The rule of nines was applied to the patient's skin lesions to measure the extent; they were graded from 0 to 100. The scoring of intensity consisted of erythema, population, excoriations, lichenification, crusts, and dryness; each was graded from 0 to 3. Subjective items included daily pruritus and sleeplessness.

The serum concentration of vitamin D was obtained from the patient on the day of enrollment, and once informed consent was obtained. The serum concentration of vitamin D was determined using the Beckman Coulter Radioimmunoassay, California. Serum vitamin D was categorized as deficient if <12 ng/ml, insufficient if the value ranges from 12-19 ng/ml, and adequate if >20 ng/ml. Serum specimens were collected using red top tubes. Blood samples were ensured that they were tightly sealed and stored in a stable container so as not to cause any spillage of the blood samples. All blood samples were then immediately sent to the radioisotope laboratory of PGH. Safe handling of the blood samples was observed. No transport temperature was required as long as specimens were brought to the laboratory within 2 hours of collection. The primary investigator was responsible for collecting and transporting blood samples.

The disposal of blood samples was facilitated by the radioisotope laboratory in compliance with their standard protocol. No blood samples were stored for future use.

Outcomes Measured

SCORAD
SCORAD Index is a validated scoring system to assess the extent and severity of atopic dermatitis. The formula of the SCORAD Index is A/5 + 7B/2 + C; wherein, A stands for

extent, B is for intensity, and C is for the patient's subjective symptoms. The score for each area was added up using the said formula. The maximal score of the SCORAD Index is 103.

Serum vitamin D_3 level

Extraction of vitamin D_3 was done by the primary investigator. In vitro determination of 25-hydroxyvitamin D_3 was measured using the Beckman Coulter Radioimmunoassay, California.

Statistical Analysis

Descriptive statistics such as mean and standard deviation were used to present the continuous variables. The rest of the categorical data were analyzed using frequency and percentage. In comparing the three age groups, one-way ANOVA was used for continuous variables, while the chi-square test was used for categorical data. In determining whether vitamin D is related to SCORAD, Pearson's r was used for the exact scores, while Spearman's rho was for the classified SCORAD score. All test of significance was done at a 5% level. MedCalc statistical software was used to carry out statistical computations.

Ethical Considerations

The study protocol was submitted to the UP-PGH Ethics and Review Board (ERB) for approval. Institutional Review Board approval was obtained. Once approved, the study was immediately started. All information gathered from the study participants was kept confidential. Anonymity was observed throughout the study. Informed consent was obtained from the parent or legal guardian and study participants, depending on their age, before study inclusion. The primary investigator explained thoroughly to the subject and parent/legally accepted representative (LAR) the nature of the study and ensured that they had thoroughly understood the process. The primary investigator assured the participants that there would be no significant risks once they joined the study. For patients aged <6 years old, written consent was obtained from the parent or LAR. For patients aged 7 to 11 years old, verbal consent was obtained from them and written informed consent was obtained from the parent or LAR. For patients aged 12 to 18, a written consent form was obtained from them and their parent or LAR. Study participants were asked to sign informed assent or informed consent, whichever was appropriate.

Each subject had undergone a physical examination to determine the SCORAD Index. It was explained to them that the blood samples collected would be solely used for the purpose of research. The procedure for sample collection involved the withdrawal of 5 ml of blood. Blood extraction was performed with utmost care. The risks of blood extraction, such as pain, bruise where blood will be taken, redness, swelling, infection, and a rare risk of fainting when blood is extracted, were thoroughly discussed with the subject (if applicable) and with the parent/LAR. The primary investigator emphasized to the subjects that there would be no expenses on their part. The primary investigator was granted a research grant from the Expanded Hospital Research Office (EHRO) and the Philippine Society of Allergy, Asthma and Immunology (PSAAI). No payment or monetary compensation was provided to the participants of this research. No follow-up was required for all the participants since recruitment and blood extraction were conducted on the same day.

All subjects were given appropriate standard treatment and health education for their condition. The study participants were provided with the utmost medical care and appropriate medical management. Participants noted to have abnormal values of their vitamin D level were given appropriate treatment and referred to the subspecialist (Endocrinology).

This study was conducted in compliance with the National Ethical Guidelines for Health and Health-Related Research 2017 and the National Privacy Act of 2012. All personal information provided by the participant remained confidential. The right to privacy was observed for every participant. Nothing was released to the public. Each participant has the right to withdraw from the study and the right to refuse to include their data. All data was accessed by the investigator alone.

There may not be any benefit to society at this stage, but future generations of patients with atopic dermatitis may benefit from this research. Subjects may withdraw anytime should they wish to do so without affecting their medical care. No financial compensation was given to the subjects in cases of injury, disability, and death. The investigator has no conflict of interest in any form.

RESULTS

A total of 53 patients were included in the study, where 20.8% of them are from 1 month to 2 years old (Infant), 34% are from 3 to 9 years old (children), and 45.3% are adolescents (10 to 18 years old). Table 1 shows that gender distribution is just the same across different age groups, where the percentage of females is slightly higher among infants (54.5%) and adolescents (58.3%), while there are slightly more males (61.1%) among children.

Among the patients included in the study, mild atopic dermatitis was diagnosed in 27 (50.9%) children, moderate in 21 (39.6%), and severe in 5 (9.4%). Vitamin D insufficiency was observed in 39 individuals (73.6%). Of these, 20 (51.3%) had mild AD, 15 (38.5%) had moderate, and 4 (10.3%) had

Table 1. Baseline Demographics of the Patients Grouped According to their Age

	Infant (0 to 2 years old) (n=11)	Children (3 to 9 years old) (n=18)	Adolescents (10 to 18 years old) (n=24)
Age (years), mean ± sd	1.07 ± 0.78	6.78 ± 1.90	13.58 ± 2.39
Gender, n (%)			
Male	5 (45.5)	11 (61.1)	10 (41.7)
Female	6 (54.5)	7 (38.9)	14 (58.3)
Number of Hours Spent Outdoor, mean ± sd	0.35 ± 0.58	1.13 ± 0.98	0.84 ± 1.00
Use of Sunblock, n (%)			
User	0 (0)	0 (0)	0 (0)
Non-User	11 (100)	18 (100)	24 (100)
Personal History of Atopy, n (%)			
Allergic Rhinitis	2 (18.18)	9 (50.0)	17 (70.83)
Bronchial Asthma	1 (9.09)	3 (16.67)	1 (4.17)
Family History of Atopy n (%)			
Atopic Dermatitis	4 (36.4)	8 (44.4)	7 (29.2)
Allergic Rhinitis	5 (45.5)	10 (55.6)	13 (54.2)
Bronchial Asthma	7 (63.6)	15 (83.3)	18 (75.0)

Table 2. Comparison of SCORAD Severity among Different Age Groups

SCORAD Scores	Insufficient Vit. D (n=39)	Sufficient Vit. D (n=14)	*p*-value
Mild	20 (51.3)	7 (50.0)	1.000^{ns}
Moderate	15 (38.5)	6 (42.9)	
Severe	4 (10.3)	1 (7.1)	

severe AD. Of the 14 individuals (26.4%) with sufficient vitamin D levels, 7 (50.0%) had mild AD, 6 (42.9%) moderate, and 1 (7.1%) severe. The mean vitamin D level was 26.4 ± 7.2 ng/mL in individuals with mild AD, 24.8 ± 6.2 ng/mL in those with moderate AD, and 21.1 ± 6.4 ng/mL in those with severe AD. Additionally, results show that there is no significant difference in the baseline characteristics of the 3 age groups.

Table 2 compares the SCORAD severity scores among the three different age groups, showing no significant difference exists ($p = 0.62$). This implies that the percentage of patients with Mild SCORAD among infants (36.4%) is not significantly different from the percentage of mild among children (50%) and adolescents (58.3%). The same can be concluded in terms of moderate and severe SCORAD scores as well.

The correlation between Vitamin D level and actual SCORAD score is not significant ($p = 0.26$). Likewise, the correlation between Vitamin D and SCORAD severity levels is also not significant ($p = 0.015$). The correlation between SCORAD severity and Vitamin D classification of sufficiency and insufficiency is also not significant ($p = 1.00$) (Table 3).

DISCUSSION

Study participants with atopic dermatitis had low levels of serum vitamin D. Out of 53 study participants, 39 had insufficient vitamin D levels (10–29 ng/ml) and only 14 had sufficient vitamin D levels (>30 ng/ml). No baseline serum vitamin D levels were extracted from healthy subjects. In an unpublished study conducted by Honor et al., on vitamin D levels of children and adolescents with Type I diabetes mellitus, serum vitamin D levels were determined from 121 controls composed of 61 males and 60 females. The majority of the children in that study had vitamin D insufficiency comprising 71.9% of the control group; 15.7% had vitamin D deficiency and 12.4% had sufficient vitamin D levels.[27] The average serum vitamin D level of the control group was 24.4 ± 4.8 ng/ml.[27]

Our study demonstrated that there is no correlation between serum vitamin D levels and the severity of AD

Table 3. Test of Relationship between SCORAD Severity and Insufficiency of Vitamin D

SCORAD Scores	Infant (0 to 2 years old) (n=11)	Children (3 to 9 years old) (n=18)	Adolescents (10 to 18 years old) (n=24)	*p*-value
Mild	4 (36.4)	9 (50.0)	14 (58.3)	0.62^{ns}
Moderate	5 (45.5)	7 (38.9)	9 (37.5)	
Severe	2 (18.2)	2 (11.1)	1 (4.2)	

based on the SCORAD index (p = 0.26). The serum Vitamin D level has no significant difference among subjects with mild, moderate, and severe AD. Various studies have been done to show the relationship between vitamin D with allergic diseases. One of which is its significance with the severity of atopic dermatitis. There has been a variety of studies showing different results.

In a randomized clinical trial by Galli et al., 89 children with chronic atopic dermatitis were enrolled and assessed using the SCORAD index.[20] Their study showed that serum vitamin D levels were not statistically different among pediatric patients with mild, moderate, and severe atopic dermatitis.[20] They also found no statistical significance between sensitized and not sensitized children with regards to age, sex, SCORAD score, duration of eczema, personal history of atopy, allergic rhinitis, asthma, food allergy, and vitamin D concentration.[20] Sensitized children were defined as having at least one positive skin prick test and total IgE >40 UI/ml.[20] In comparison with the results of our study, it also showed no significant correlation between serum vitamin D level and actual SCORAD score (p = 0.26). Galli et al., checked the relationship between vitamin D levels and other parameters, as mentioned above. This was not part of our study objectives which may explain the lack of significant association. However, the clinical trial Galli conducted has a small study population.

In the cross-sectional study conducted by Chiu et al., among pediatric patients aged 1 to 18 years with AD the same findings were discovered. The serum vitamin D level was lower among patients with mild atopic dermatitis than moderate and severe atopic dermatitis.[16] Friedman Rank test p-value was 0.61 when serum vitamin D level was compared to the severity of atopic dermatitis excluding the confounding variables (i.e., race, age, season).[16] Their study concluded that there is no statistically significant correlation between vitamin D status and AD severity. However, they did not exclude patients who were treated with topical corticosteroids in contrast to our study. Additionally, they did not assess confounding variables such as sunlight exposure, use of sunblock, and dietary vitamin D intake just like our study.

A cross-sectional study conducted by Cairncross et al., among children aged 2 – <5 years in New Zealand found no correlation between vitamin D status and parental-reported prevalence of eczema (p = 0.50).[28] The odds ratio of children with AD was neither increased nor decreased with children with higher or lower serum Vitamin D concentrations.[28] Limitation of this study however was that the severity of AD was assessed by the parent using the ISAAC questionnaire instead of by a doctor. This contrasts with our study wherein study participants were assessed by a specialist. Lee et al., also evaluated the disease severity of AD using the SCORAD index and correlated it with serum vitamin D levels.[29] They also found no significant correlation between serum vitamin D level and severity of atopic dermatitis (p = 0.73).[29] However, their study also included food sensitization wherein levels of total IgE and IgE specific for food allergens were measured using ImmnoCAP.[29] Based on their results, patients with mild AD and food sensitization have higher mean serum vitamin D levels (21.2 ± 5.18 ng/ml) as compared to those with moderate (17.9 ± 4.02 ng/ml) and severe AD (13.3 ± 5.11 ng/ml).[29] Hence, their study showed an inverse correlation between AD severity with food sensitization and serum vitamin D level. This is in contrast to the findings of Galli et al., wherein they found no correlation between SCORAD index and serum vitamin D levels in sensitized and not sensitized groups.

The subsequent studies show results that are contradictory to our findings. Out of 53 study participants, 39 were found to have vitamin D insufficiency despite residing in a tropical country. One example is Weiland et al., which investigated the relationship between climate and atopic diseases using worldwide data from International Study of Asthma and Allergies in Childhood (ISAAC).[25] Twelve countries with various ISAAC centers in Western Europe and study centers worldwide were included in this study. They noted a positive correlation between eczema symptoms and latitude but a negative correlation between them and mean annual outdoor temperature for both subjects in Western Europe and worldwide.[25] Given that vitamin D is synthesized mainly in the skin with the help of sunlight, ours shows contradicting results compared to Weiland's study. This is not included in our objectives, but it is important to note that the results of this study also showed that the average hour the subjects spent outdoors is one hour. The mean number is not significantly different among the three age groups. Results could be attributed to changes in behavior towards natural sunlight exposure.[25] Similarly, the study conducted by Chiu YE et al., among children in Milwaukee County found that low serum vitamin D level was significantly associated with the winter season in both univariate (p = 0.042) and multivariate analyses (p = 0.0084).[16] Camargo et al., conducted a randomized, placebo-controlled trial among children with winter-related atopic dermatitis.[24] One hundred seven children were included in the study and the severity of their atopic dermatitis was assessed using Eczema Area and Severity Index (EASI). Fifty-eight subjects were randomly assigned to the vitamin D group; they were given supplementation for a month.[24] They have concluded that vitamin D supplementation resulted in clinically and statistically significant improvement in EASI score (P = 0.02).[24] However, one drawback of their study was no serum vitamin D level was determined.

Heterogeneous data from various studies were presented due to conflicting results. These could be attributed to different confounding variables such as age, type of clothing used, sunblock used, socioeconomic status, sun exposure, diet, skin type, season, atmospheric pollution, and geographic location. Some authors suggest that decreased serum vitamin D levels among older children and adolescents may be since they spend less time playing outdoors and variations in sun exposure habits.[30] Many now are greatly influenced to spend time indoors. Skin pigmentation may also affect cutaneous vitamin D synthesis since increased melanin competes for ultraviolet radiation.[30,31] Ultraviolet radiation level may also be affected by environmental conditions such as atmospheric pollution which may decrease the radiation level reaching the earth's surface.[30] It is also said that the ideal way to measure UV radiation exposure accurately is through a UV dosimeter, which provides an objective measurement of cumulative UV exposure.[30] Also, the disparity in serum vitamin D levels can also be explained by poor diet and limited dietary sources of vitamin D. Lifestyle and behavioral factors are important influences in determining vitamin D status, especially in urban areas. The small sample size is one limitation of this study. Environmental differences and geographic locations may also explain differences in vitamin D status. Lastly, this study was cross-sectional; association can only be deduced instead of establishing causality.

CONCLUSION

In conclusion, this study did not find a correlation between serum vitamin D level and the severity of atopic dermatitis measured by the SCORAD index. The role of vitamin D in atopic diseases is still controversial and has yet to be elucidated. Due to conflicting results from various studies, vitamin D has not yet been used as part of the management of atopic dermatitis. Further studies are needed to establish the role of Vitamin D in the immune system. It is recommended to increase the sample size and consider the confounding variables that may affect vitamin D status. Additionally, this study was cross-sectional; it would be much better if a cohort study were done to determine the causal relationship between serum Vitamin D levels and the severity of AD. A longitudinal study with a large sample size may be beneficial. Subjects in this study have predominantly deficient vitamin D levels, but this has not yet been compared with the general population or a control group.

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