ABSTRACT

**Background:** Atopic dermatitis is a prevalent skin condition with a 10% lifetime prevalence, affecting 15%-20% of children and 1%-3% of adults globally. Atopic dermatitis is often multimorbid and more prone to allergic disorders. Vitamin D (VD) deficiency has been linked to an increase in allergy disorders and atopic dermatitis worldwide, suggesting that VD supplementation may play a role in the improvement of atopic dermatitis.

**The aim:** This study aims to determine the effectiveness of vitamin D supplementation in atopic dermatitis.

**Methods:** By comparing itself to the standards set by the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020, this study was able to show that it met all of the requirements. So, the experts were able to make sure that the study was as up-to-date as it was possible to be. For this search approach, publications that came out between 2014 and 2024 were taken into account. Several different online reference sources, like Pubmed, SAGEPUB, and ScienceDirect, were used to do this. It was decided not to take into account review pieces, works that had already been published, or works that were only half done.

**Results:** In the PubMed database, the results of our search brought up 60 articles, whereas the results of our search on SAGEPUB brought up 2017 articles, and our search on ScienceDirect brought up 2023 articles. In the end, we compiled 6 papers, 4 of which came from PubMed, one of which came from ScienceDirect, and one of which came from SagePub. We included six research that met the criteria.

**Conclusion:** In conclusion, administration of vitamin D supplement can improve atopic dermatitis. It is more advisable to give it for 3 months.

**Keywords:** Atopic dermatitis, vitamin D, outcomes
INTRODUCTION

One of the more prevalent skin conditions, atopic dermatitis, atopic eczema, or neurodermatitis, is an inflammatory skin disease with a 10% lifetime prevalence that is chronic, relapsing, and remitting.\(^1\)\(^2\) Globally, AD affects 15%–20% of children and 1%–3% of adults, according to estimates from the International Study of Asthma and Allergies in Childhood (ISAAC).\(^3\) In children under the age of 18, the prevalence of atopic dermatitis was 13% (2007-2008 National Survey of Children's Health [NSCH]), 7% (2012 NHIS and AD in America study) in adults over the age of 18, and 12% (2012 National Health Interview Survey [NHIS]).\(^4\)

Genetic, immunologic, and environmental factors that damage the epidermis are all part of the complex pathophysiology of atopic dermatitis. Atopy in the family history and mutations in the FLG gene are the two main risk factors that have been repeatedly linked to the development of atopic dermatitis.\(^2\)\(^5\) It is triggered by environmental and lifestyle variables and develops on the foundation of a hereditary propensity known as a diathesis.\(^1\) Individuals diagnosed with AD are often multimorbid (i.e., co-occurring multiple chronic conditions) and more prone to developing allergic disorders. Asthma and allergic rhinitis are linked to AD in infancy in numerous studies; 80% of patients eventually develop one or both of these conditions.\(^3\)

Sleep disturbances and skin soreness were ranked as the second most bothersome symptoms by about 10% of individuals. Nonetheless, blisters or bumps, red or irritated skin, pain, sleep disturbance, and open sores or leaking were more frequently reported as the most bothersome symptoms by persons with moderate and severe AD.\(^4\) As a result of immunological dysregulation brought on by FLG gene mutations and destruction of the epidermis, cutaneous infections are the most frequent consequence of atopic dermatitis.\(^1\)\(^2\) S. aureus is typically colonized on lesional skin in AD patients and, to a lesser extent, on nonlesional skin and nasal mucosa.\(^5\)

There is no conclusive laboratory test for atopic dermatitis; it is a clinical diagnosis alone. In the primary care context, atopic dermatitis is diagnosed and treated in about 80% of cases.\(^2\) Although topical corticosteroids (TCS) are effective in treating most patients with mild-to-moderate AD, there is still a need for topical agents due to safety concerns regarding TCS use for AD, particularly on sensitive skin like the face, and the black box warning for topical calcineurin inhibitors (TCI), which contradicts growing evidence from long-term studies disputing the theoretical risk of malignancy.\(^2\) Intake of zinc, vitamin E, and VD by pregnant mothers was linked to a lower incidence of wheezing disorders in infancy, but not of childhood-onset asthma or other atopic conditions in children, according to a prior study.\(^6\)

Vitamin D (VD) deficient epidemics have coincided with an increase in allergy disorders worldwide in Westernized countries, which lends credence to the theory that VD may have a role in the development of allergies. Dietary factors and sun exposure are the primary determinants of VD levels, making them a significant modifiable factor in the prevention of allergies.\(^6\) Peroni et al. demonstrated an inverse relationship between the severity of AD and serum levels of the circulating form of vitamin D, known as 25-hydroxyvitamin D.\(^7\)\(^8\) The previous study observed a substantial improvement in the active group after 60 days, independent of the initial severity of AD, in a double-blind RCT where 60 AD patients aged ≥14 years were randomized to receive either 1,600 IU/day of VD or placebo. This implies that VD supplementation may improve AD. However, these findings were not confirmed in other studies.\(^6\)\(^7\) The purpose of this study is to investigate the effectiveness of vitamin D supplementation in atopic dermatitis.

METHODS

PROTOCOL

By following the rules provided by Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020, the author of this study made certain that it was up to par with the requirements. This is done to ensure that the conclusions drawn from the inquiry are accurate.

CRITERIA FOR ELIGIBILITY

For the purpose of this systematic review, we compare and contrast the effectiveness of vitamin D supplementation in atopic dermatitis. It is possible to accomplish this by researching or investigating EASI score, SCORAD score, and the side effects of vitamin D supplementation. As the primary purpose of this piece of writing, demonstrating the relevance of the difficulties that have been identified will take place throughout its entirety.

For researchers to take part in the study, they needed to fulfill the following requirements: 1) The paper needs to be written in English, and it needs to investigate the effectiveness of vitamin D supplementation in atopic dermatitis. For the manuscript to be considered for publication, it needs to meet both of these requirements. 2) The studied papers include several that were published after 2014, but before the period that this systematic review deems to be relevant. Examples of studies that are not permitted include editorials, submissions that do not have a DOI, review articles that have already been published, and entries that are essentially identical to journal papers that have already been published.
SEARCH STRATEGY
We used "atopic dermatitis"; "vitamin D"; and “outcomes” as keywords. The search for studies to be included in the systematic review was carried out in July, 04th 2024 using the PubMed, SAGEPUB, and ScienceDirect databases by inputting the words: (("dermatitis, atopic"[MeSH Terms] OR ("dermatitis"[All Fields] AND "atopic"[All Fields])) OR "atopic dermatitis"[All Fields] OR ("atopic"[All Fields] AND "dermatitis"[All Fields]) AND ("vitamin d"[MeSH Terms] OR "vitamin d"[All Fields] OR "ergocalciferols"[MeSH Terms] OR "ergocalciferols"[All Fields]) AND ("outcome"[All Fields] OR "outcomes"[All Fields]) AND ((y_10[Filter]) AND (english[Filter])) with interposition of Boolean operators ‘AND’ and ‘OR’ used in searching the literature.

DATA RETRIEVAL
After reading the abstract and the title of each study, the writers examined to determine whether or not the study satisfied the inclusion criteria. The writers then decided which previous research they wanted to utilize as sources for their article and selected those studies. After looking at several different research, which all seemed to point to the same trend, this conclusion was drawn. All submissions need to be written in English and can't be seen anywhere else.

**Figure 1. Prisma Flow Diagram**

Only those papers that were able to satisfy all of the inclusion criteria were taken into consideration for the systematic review. This reduces the number of results to only those that are pertinent to the search. We do not take into consideration the conclusions of any study that does not satisfy our requirements. After this, the findings of the research will be analysed in great detail. The following pieces of information were uncovered as a result of the inquiry that was carried out for the purpose of this study: names, authors, publication dates, location, study activities, and parameters.

QUALITY ASSESSMENT AND DATA SYNTHESIS
Each author did their own study on the research that was included in the publication's title and abstract before deciding on which publications to explore further. The next step will be to evaluate all of the articles that are suitable for inclusion in the review because they match the criteria set forth for that purpose in the review. After that, we'll determine which articles
to include in the review depending on the findings that we've uncovered. This criteria is utilized in the process of selecting papers for further assessment to simplify the process as much as feasible when selecting papers to evaluate. Which earlier investigations were carried out, and what elements of those studies made it appropriate to include them in the review, are being discussed here.

RESULT
In the PubMed database, the results of our search brought up 60 articles, whereas the results of our search on SAGEPUB brought up 2017 articles, and our search on ScienceDirect brought up 2023 articles. In the end, we compiled 6 papers, 4 of which came from PubMed, one of which came from ScienceDirect, and one of which came from SagePub. We included six research that met the criteria.

Table 1. The literature included in this study

<table>
<thead>
<tr>
<th>Author</th>
<th>Origin</th>
<th>Method</th>
<th>Sample Size</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aldaghi, 2022⁹</td>
<td>Iran</td>
<td>RCT</td>
<td>81 participants</td>
<td>The results of this study imply that the administration of multistrain synbiotics and vitamin D3 supplements as supplemental therapy in addition to standard treatments may be useful in lessening the severity of AD in newborns.</td>
</tr>
<tr>
<td>Camargo, 2014¹⁰</td>
<td>USA</td>
<td>RCT</td>
<td>107 children</td>
<td>The findings showed that in youngsters from Mongolia, a population prone to wintertime vitamin D insufficiency, vitamin D treatment alleviated winter-related AD.</td>
</tr>
<tr>
<td>Imoto, 2021¹¹</td>
<td>Brazil</td>
<td>Prospective pre-post interventional study</td>
<td>152 participants</td>
<td>From this study, we concluded that to lessen the severity of atopic dermatitis, vitamin D supplementation may be helpful.</td>
</tr>
<tr>
<td>Lara-Corrales, 2019¹²</td>
<td>Canada</td>
<td>Cross-sectional study &amp; RCT</td>
<td>77 participants</td>
<td>The results suggested that vitamin D (VD) supplementation did not considerably lessen the severity of the disease, despite a correlation between VD levels and the severity of atopic dermatitis.</td>
</tr>
</tbody>
</table>
The findings suggested in cases of severe atopic dermatitis, vitamin D supplementation may be a useful adjuvant therapy that enhances clinical results.

The findings showed that the severity of atopic dermatitis was found to be inversely correlated with baseline serum vitamin D levels. A decrease in SCORAD indicated that vitamin D administration had the greatest beneficial effect in cases of severe AD.

CLINICAL IMPROVEMENT

In this systematic review, we compared the changes in SCORAD or EASI score. Four articles showed that the EASI and SCORAD scores decreased after three months of taking vitamin D supplementation.\textsuperscript{11-14} Following three months of oral \textit{VD}, the SCORAD index decreased (19.4 before vs 12.3 after supplementation, \(p = 0.001\)) and the vitamin levels were found to be considerably higher (35.9ng/mL) than baseline (23.7ng/mL; \(p = 0.001\)). Following \textit{VD} supplementation, SCORAD categorised DA. In 96 individuals, or 82.7\%, there was a change in severity category as AD improved.\textsuperscript{11} Lara-Corrales, et. al (2019) showed that there was a mean (SD) SCORAD drop of 15.35 (9.71) and 15.13 (8.97), respectively (\(P = 0.7\)).\textsuperscript{12} In addition, Mansour, et al. (2020) showed that by the time the study ended, the vitamin D group's mean percentage change from baseline in the EASI score (56.44\%) was considerably higher than that of the placebo group (42.09\%) (\(P = 0.039\)). Interestingly, compared to 7.1\% of patients in the placebo group, around 38.6\% of supplemented patients attained EASI 75.\textsuperscript{13}

After two months of taking vitamin D supplementation, Aldaghi, et al. (2022)\textsuperscript{9} showed that the mean SCORAD score was significantly lower in the vitamin D3 groups (\(P = 0.001\)) when compared to the control group, according to the multivariable regression analysis. After one month of taking vitamin D supplementation, Camargo, et al. (2014)\textsuperscript{10} showed that the EASI score improved clinically and statistically significantly when vitamin D supplementation was used as compared with placebo; the mean change for vitamin D was 5 26.5 (SD 8.8) as opposed to 23.3 (SD 7.6) for the placebo; the unadjusted difference between the mean changes was 23.2 (95\% CI 20.9 to 25.5; \(P = 5.01\)). Raj, et al. (2022)\textsuperscript{14} showed that a reduction in SCORAD indicated that vitamin D administration had the greatest beneficial effect in cases of severe AD.

SIDE EFFECTS

There were no side effects of oral vitamin D observed during the treatment period.\textsuperscript{11,12}

DISCUSSION

Atopic dermatitis (AD) is a chronic, multifactorial, and relapsing inflammatory skin condition presenting with pruritus as the cardinal finding in conjunction with erythema, edema, xerosis, erosions/excoriations, oozing, crusting, and lichenification.\textsuperscript{15} Research confined to the United States demonstrated that children under the age of five had the highest incidence of AD.\textsuperscript{16} AD is one of the most prevalent chronic illnesses worldwide, with an estimated incidence of about 230 million. Additionally, AD is becoming more commonplace throughout most of the world, including a sizable portion of Asia. The general prevalence for children between the ages of 6 and 7 in the Asia-Pacific area was 10.1\% (10.2\% males, 10.0\% girls); however, the rates for children between the ages of 13 and 14 are significantly lower at 5.3\% (4.7\% boys, 5.9\% girls), in contrast to the global average. In the Asia-Pacific region, 1.2\% of 6–7-year-olds and 0.7\% of 13–14-year-olds were found to have severe AD, indicating that 12\% of AD patients had the condition. When combined, mild to severe...
AD affects the majority of pediatric children (~88%) in the Asia-Pacific area. In a different study, 60% of children with AD continued to adulthood.

The etiology is multifaceted. Atopic dermatitis has a complex etiology that includes immunological dysregulation, primarily through the Th2 cytokine inflammatory pathway, and compromised epidermal barrier function. Barrier malfunction and inflammation interact intricately, with one causing and/or aggravating the other and vice versa, continuing the vicious cycle of chronic inflammation and damage. Genetics, environmental variables, S. aureus colonization or infection, and neurogenic inflammation are other factors that contribute to the development of atopic dermatitis. The FLG gene, which is found on chromosome 1q2, produces the FLG protein, a significant structural protein found in the stratum corneum (SC). Pro-FLG polymers undergo proteolytic cleavage and dephosphorylation to yield FLG monomers, which are linked to keratin filament aggregation and SC formation. The production of pyrrolidine carboxylic acid and urocyclic acid, byproducts of FLG breakdown, adds to the acidic pH of skin and SC hydration. It is commonly recognized that FLG null mutations raise the risk of AD and compromise the function of the epidermal barrier.

The history of the patient as well as clinical indicators, such as the shape and distribution of skin lesions, are used to make the diagnosis of AD. Major and minor diagnostic criteria for AD were put forth by Hanifin and Rajka in 1980. A diagnosis of AD requires meeting three of the four major criteria and three of the twenty-three minor criteria. The first stage in choosing a treatment is assessing the severity of the ailment, which is also useful for tracking the effectiveness of the treatment. For the purpose of assessing severity, many tools have been created. The SCORing AD (SCORAD) index and the Eczema Area and Severity Index (EASI) are examples of validated measurements. Both consider clinical indicators and the region of involvement; in addition, SCORAD incorporates a subjective sleep and pruritus assessment. Using these scales, conditions are classified as mild, moderate, or severe. It may take much too time for ordinary clinical practice to employ SCORAD and EASI, which are mostly used in clinical studies. Both the Patient-Oriented SCORAD (PO-SCORAD) index and the Patient-Oriented Eczema Measure (POEM) are validated, patient-reported measures that are easier to apply and require less time, although they may be less accurate. When deciding which instruments to regularly employ in the clinic, clinicians will need to weigh the benefits and drawbacks of each one.

The current treatment for AD symptoms includes calcineurin inhibitors, emollients, and nonspecific anti-inflammatory topical corticosteroids. In more severe cases, systemic immunosuppressants such as azathioprine, cyclosporine, and prednisolone are used. In later stages of clinical trials, broad-acting inhibitors of signal transduction kinase (phosphodiesterase 4 and Janus kinase) and specific monoclonal antibodies (biologics) that block T-helper cell (Th)2/Th 22/Th17-related cytokines are now being developed. There is a significant unmet clinical need, particularly in younger children, for disease treatment that is better focused to the etiology of AD while still being economical, safe, and effective. Regrettably, many of the current symptomatic AD medications are linked to unfavorable side effects. Our systematic review suggested vitamin D supplementation in AD showed no adverse effects.

Vitamin D (VD) has not yet been completely understood in relation to inflammatory cutaneous disorders. Numerous explanations, such as immunomodulation, decreased cell division, and enhanced epidermal barrier performance, have been suggested. Supplementing with vitamin D has been shown to significantly reduce symptoms associated with AD in two RCTs. The skin is the primary site of lipid soluble vitamin VD synthesis. UV light can be used to manufacture VD, an active secosteroid hormone, in the skin, or it can be absorbed through food. Rich in vitamin D are cod liver oil, eggs, tuna, salmon, and cow liver. Though VD may potentially be involved in the pathophysiology of cancer, autoimmune diseases, and cardiovascular disease, its function is primarily linked to calcium and phosphate homeostasis.

There is consensus that vitamin D intake of 400 IU per day can prevent nutritional rickets in infants and children. A few signs have surfaced suggesting that vitamin D administration may have some extra-skeletal benefits, particularly in individuals with severe vitamin D insufficiency (e.g., lower risk of developing type 2 diabetes, decreased infection rates, increased lung function, and decreased risk of cancer or overall mortality). Vitamin D2 did not show any statistically significant protective benefits on overall mortality (1.02, 0.96 to 1.08), whereas vitamin D3 appeared to reduce total mortality (risk ratio 0.94, 95% confidence interval 0.91 to 0.98) according to a 2014 Cochrane analysis. Nonetheless, heterogeneity between vitamin D2 and D3 was not found in the Cochrane review. As such, the evidence supporting the claim that vitamin D3 decreased all-cause mortality should be interpreted with caution (0.95, 0.91 to 1.00, P = 0.07). The increased risk of vitamin D deficiency in AD patients and their need for ongoing monitoring and vitamin D treatment were also validated by this research. Evidence suggests that the exacerbation of AD may be linked to a decline in vitamin D levels and deficiency, as the serum 25 (OH) D level of severe AD patients was considerably lower than that of moderate AD patients. Our systematic review suggested that vitamin D can improve AD. This finding was confirmed with previous study.

Vitamin D is recognised to be closely related to skin function, where it plays a part in normal keratinocyte formation, wound healing, and skin protein production, in addition to its roles in immune system function and calcium homeostasis. Because vitamin D has receptors on macrophages, dendritic cells, B cells, and T cells, it is also known to have immunomodulatory effects. It’s also thought that vitamin D inhibits type 1 helper T cells and encourages the transition to type 2 helper T cells. Furthermore, vitamin D suppresses dendritic cell development, differentiation, and activity while stimulating T regulatory cells.
It is possible that VD could influence the number of infections and the severity of AD through biological mechanisms. It is well established that VD affects both innate and adaptive immune reactions. Given its physiological function in maintaining healthy skin and the established correlations between reduced 25(OH)D concentrations and elevated IgE, decreased serum cathelicidin, and enhanced allergy sensitization, it is plausible that VD has a role in regulating the severity of AD. Furthermore, research on the disruption of the VDR has revealed decreased levels of barrier proteins such as involucrin, profilaggrin, and loricin. Increased levels of 25(OH)D cause keratinocytes from AD patients, psoriasis sufferers, and people with normal skin to overexpress functional human cathelicidin (hCAP18). A recent study provided evidence in favour of the aforesaid mechanisms by demonstrating that decreased serum 25(OH)D levels were associated with increased IgE levels, increased pathogenicity, and increased S. aureus colonisation. Methicillin-resistant S. aureus (MRSA) skin lesions have been observed to be substantially more common in those with VD deficiency. While Samochocki et al. observed no incidence of infection in their adult supplemented sample, another study found a reduction in S. aureus colonisation in a paediatric population receiving VD supplementation.25,30,31

While Galli et al. used 2000 IUs of VD3 for 12 weeks, Sidbury et al. used 1000 IUs of VD2 for 4 weeks, and neither group observed a discernible improvement in the severity of AD. Additionally, there was a range of 4 to 12.86 weeks during which the treatment showed benefits. The current literature's heterogeneity poses a challenge to comprehending the actual effects of vitamin D supplementation in youngsters. This emphasises the necessity of conducting a sizable prospective RCT using various VD dosages and durations in order to determine the best supplementation schedule.26 Four of identified studies showed significant improvement in AD after 3 months of vitamin D supplementation.

CONCLUSION
In conclusion, administration of vitamin D supplement can improve atopid dermatitis. It is more advisable to give it for 3 months.

REFERENCES