Medical Science

To Cite:
Wójcicki M, Kędzierska M, Biernacki M, Kowalska A. Vitamin D deficiency in childhood and the risk of developing atopic dermatitis- a review of current data. *Medical Science* 2026; 30: e18ms3771
doi: https://doi.org/10.54905/disssi.v30i167.e18ms3771

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Peer-Review History
Received: 03 September 2025
Reviewed & Revised: 16/September/2025 to 12/January/2026
Accepted: 21 January 2026
Published: 30 January 2026

Peer-review Method
External peer-review was done through double-blind method.

Medical Science
pISSN 2321–7359; eISSN 2321–7367

Vitamin D deficiency in childhood and the risk of developing atopic dermatitis- a review of current data

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ABSTRACT

Beyond its well-known role regarding bone health, Vitamin D is also important for the immune system and the skin's protective barrier. This review analyzes research from the past 15 years on the relationship between Vitamin D levels and atopic dermatitis (AD) in children. The studies suggest that Vitamin D supports the maintenance of the skin barrier by regulating proteins that seal skin cells together and by boosting antimicrobial peptides, such as cathelicidins. Research also shows that lower blood Vitamin D levels are linked to worse AD, notably in locations with little sunlight. Clinical trials indicate that Vitamin D supplements can reduce symptom severity, particularly in children with severe AD or low Vitamin D to begin with. While Vitamin D appears to be a safe and helpful add-on treatment, differences between study designs make it hard to recommend a single standard dose for all children.

Keywords: vitamin D deficiency, atopic dermatitis, atopic eczema, children and pediatric

1. INTRODUCTION

Vitamin D is not a single substance, but a group of fat-soluble compounds—mainly D2 and D3—that perform prohormonal functions in the body. These reserves are replenished in two ways: through dietary intake or through skin synthesis. Exposure to ultraviolet B (UVB) radiation triggers the cutaneous synthesis of vitamin D3 from a cholesterol precursor (Hossein-nezhad & Holick, 2013; Przechowski et al., 2025). Interestingly, skin cells called keratinocytes can also produce this active form locally, helping control how skin cells grow and mature (Bikle, 2011). Beyond its well-known function in preserving bone health, vitamin D is essential for immune function. It also acts as an immune regulator, regulating T cells to prevent an inflammatory overreaction. The upregulation of filaggrin is central with respect for the maintenance of barrier integrity and hydration (Bikle, 2011; Hattangdi-Haridas et al., 2019). This protection is indispensable for the one in five children dealing with the severe pruritus and xerosis associated with atopic dermatitis. Increasing attention is being paid to the co-occurrence of vitamin D deficiency in patients. Research shows that low levels of this substance are linked to skin problems, but whether taking supplements helps treat them is still unclear. This is because the results of published studies are often contradictory (Hattangdi-Haridas et al., 2019; Przechowski et al., 2025). The purpose of this study is to

examine the current evidence linking Vitamin D status to the onset and severity of atopic dermatitis in children.

2. REVIEW METHODS

Search Strategy

This review paper was prepared based on scientific literature searched in key databases, including PubMed. The search process utilized combinations of English keywords: vitamin D deficiency, atopic dermatitis, atopic eczema, children, and pediatric. The focus was primarily on publications from the last 15 years, published in English, to ensure a review of current data.

Inclusion and Exclusion Criteria

The review included review articles and meta-analyses that systematized knowledge on the immunological mechanisms of vitamin D and epidemiological data on the prevalence of deficiency. Publications from basic science research were also included to explain molecular mechanisms (e.g., effects on the epidermal barrier and antimicrobial peptides).

Case reports, editorial comments, and publications for which the full has been not available were excluded from the analysis. It is worth noting that studies indicated in the literature as having certain study design weaknesses (e.g., small sample size) were also included in the analysis, so they could be critically discussed in a dedicated section, in line with the paper's objective.

Study Selection and Data Extraction

The works selected for the next stage were subjected to a detailed full-text analysis based on the accepted inclusion criteria. Next, the authors responsible for individual parts of the work extracted and compiled the key data necessary to prepare the relevant subsections. A preliminary search of databases identified 286 records. After removing duplicates and screening titles and abstracts, 69 articles were selected for full-text evaluation. Based on inclusion and exclusion criteria, 14 publications were included in the final synthesis. The entire selection process is illustrated in the PRISMA chart (Figure 1).

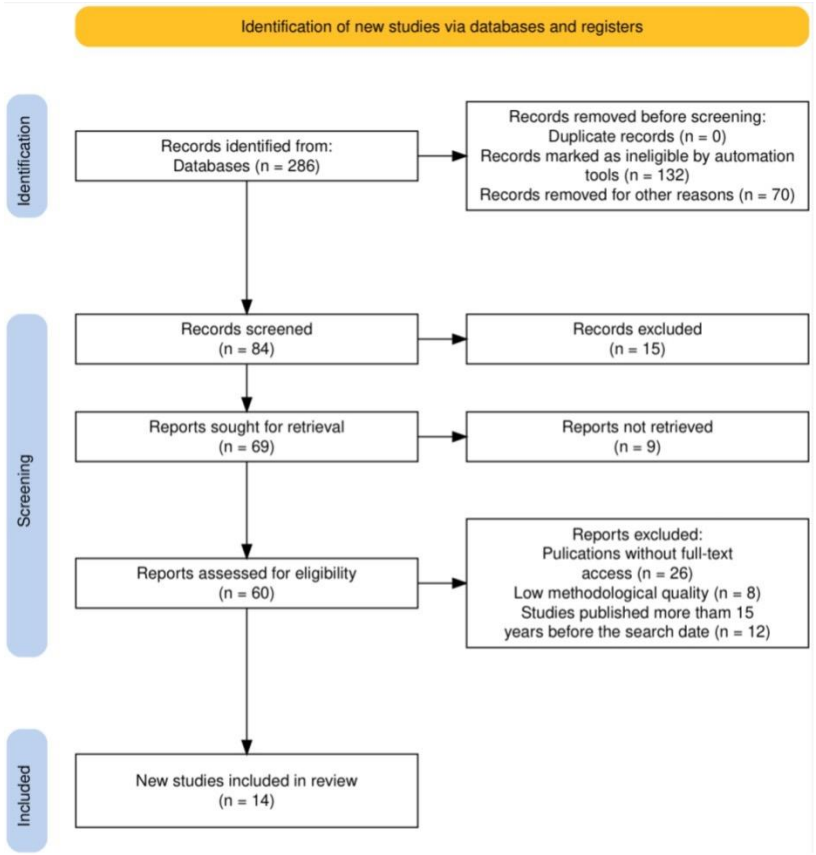

Figure 1: PRISMA Chart

3. RESULTS & DISCUSSION

Effects of Vitamin D on the skin barrier, immune response, and antimicrobial activity

Vitamin D affects immunological pathways that are important in the pathogenesis of atopic dermatitis (Yamamoto & Jørgensen, 2020). Since a weak skin barrier is a major cause of AD, vitamin D's role in sustaining skin health is very important. Recent research shows that taking supplements can help improve the skin barrier (Hidayati et al., 2023). This mechanism is confirmed at the molecular level – it has been shown that the VDR receptor signalling pathway is fundamental for upholding epithelial continuity, as it modulates tight junction proteins, including ZO-1, occludin, and claudin-1 (Yamamoto and Jørgensen, 2020). In vitamin D deficiency, the barrier function is weakened, making the host more susceptible to pathogen penetration and subsequent interaction with immune cells.

One of the fundamental defence mechanisms strongly associated with vitamin D is its ability to fight microorganisms (Golpour et al., 2019). Vitamin D stimulates the skin to produce antimicrobial peptides (AMPs), especially cathelicidins, and maintains their proper levels (Hidayati et al., 2023). These molecules, as one of the most important elements of the host defence system (HDP), are capable of combating a wide range of bacteria, including Gram-positive and Gram-negative strains. The method includes lysing the pathogen's cell membrane (Golpour et al., 2019). At the molecular level, vitamin D acts as a direct inducer of the transcription of genes encoding AMPs, including the cathelicidin (CAMP) gene (Yamamoto and Jørgensen, 2020). This connection is important to grasp atopic dermatitis (AD). As AD worsens, the skin produces fewer antimicrobial peptides (AMPs), while Staphylococcus aureus grows more readily on the skin. This can lead to lower vitamin D levels because reduced AMP production makes people with AD more likely to experience recurrent bacterial infections. Studies support this idea. For example, giving vitamin D3 to children with AD reduced the amount of S. aureus on their skin (Hidayati et al., 2023).

Other studies also show that vitamin D can help prevent these infections. Its effects on the immune system go beyond the skin barrier or AMPs – it also helps the body's overall immune defence (Hidayati et al., 2023; Golpour et al., 2019). The overarching goal of this action is to generally extinguish excessive inflammatory responses and promote an anti-inflammatory environment (Yamamoto and Jørgensen, 2020). Vitamin D precisely regulates lymphocyte populations: on the one hand, it supports the formation of regulatory T cells (Tregs), and on the other, it blocks the differentiation of pro-inflammatory Th1 and Th17 lines. At the same time, it affects B lymphocytes, weakening their development and functions (Yamamoto and Jørgensen, 2020). The clinical manifestations include limited proliferation of these cells and, importantly, decreased immunoglobulin E (IgE) production (Hidayati et al., 2023). The overall modulating effect is complemented by the inhibition of cytokine production (including both the Th1 profile, such as IL-2, IL-12, IFN-γ, and Th2, such as IL-4, IL-5) (Golpour et al., 2019) and a reduction in the level of monocyte activation (Yamamoto and Jørgensen, 2020).

The incidence of atopic dermatitis and 25(OH)D levels

Clinical data regarding the association between 25(OH)D levels and the spread of atopic dermatitis (AD) are numerous, although not always entirely consistent. The majority of observational studies indicate a clear association between the two. A meta-analysis of 11 observational studies revealed that patients with AD had statistically significantly lower 25(OH)D concentrations- 14 nmol/L lower on average- compared to healthy controls. A sub-analysis limited to children (from 9 studies) confirmed this finding, showing a difference of 16 nmol/L (Hattangdi-Haridas, 2019). Another meta-analysis focused on children up to 18 years old also found that kids with AD had significantly lower blood levels of 25(OH)D than healthy controls. Additionally, an analysis of 9 studies including 1,096 patients and 765 healthy children showed that the risk of 25(OH)D deficiency (less than 20 ng/mL) was more than twice as high (OR = 2.17) in children with AD compared to healthy children (Fu, 2022). A prospective case-control study also found that children with AD had lower 25(OH)D levels at ages 2 and 4 years than healthy children, although no difference was seen at 6 months (Shen et al., 2024). An extensive Japanese cohort study (JECS) found no evidence to support the hypothesis that lower vitamin D levels in early childhood increase the odds of developing AD. In this study, neither vitamin D deficiency nor insufficiency was found to increase the risk of AD in children (Yang et al., 2021).

The Association Between Season and Geographical Latitude and the Risk of Morbidity

Clinical data point out an association between ambient factors affecting vitamin D synthesis and the risk of Atopic Dermatitis. A higher prevalence of AD is observed in higher northern latitudes and during the winter months. This phenomenon is directly linked to vitamin D levels. It has been noted that AD aggravation in winter occurs mainly in higher-latitude countries, where serum 25(OH)D tends to be particularly low during this season (Hattangdi-Haridas, 2019). A review of studies also indicates that the incidence of AD increases in countries with high urbanization rates or in high-latitude regions during winter (Fu, 2022).

Meta-analyses provide evidence for a correlation between low vitamin D levels and intensification of AD symptoms, as measured by the SCORAD and EASI scales. A meta-analysis of 9 pediatric studies (totalling 224 patients with mild AD and 196 with severe AD) revealed that serum 25(OH)D levels in patients with mild AD were considerably higher (mean difference of 9.23) than in those with severe AD. This suggests that a decrease in vitamin D levels may be associated with AD exacerbation (Fu, 2022).

Important data also stem from meta-analyses of interventional studies evaluating the influence of vitamin D supplementation on SCORAD and EASI scores:

Meta-analysis (Hattangdi-Haridas, 2019):

- An analysis of RCTs (randomized controlled trials) demonstrated a highly statistically significant reduction in the SCORAD index by 11 points in patients receiving vitamin D.
- An analysis of repeated-measures studies (in which the patient served as their own control) showed an even greater reduction in SCORAD, averaging 21 points.
- The authors noted that the reduction they observed (11–21 points) exceeds the Minimal Clinically Important Difference (MCID) for SCORAD, which is 9 points. This shows that the results are clinically important.

Meta-analysis (Fu, 2022):

- An analysis of RCTs also showed a significant reduction in SCORAD by 11.02 points following vitamin D supplementation.
- In self-controlled studies (pre- and post-treatment), the SCORAD score decreased by 18.8 points.
- A separate analysis of 3 RCTs evaluating the EASI index demonstrated that after vitamin D treatment, the EASI score was significantly lower (by 3.72 points) than in the placebo group.
- Both meta-analyses show that supplementation with doses ranging from 1000 to 1600 IU daily for 1 to 3 months leads to clinically relevant improvements and reductions in AD symptom severity (Hattangdi-Haridas, 2019; Fu, 2022).

Vitamin D supplementation

Vitamin D supplementation appears to confer measurable clinical benefits in children with atopic dermatitis (AD). This conclusion is supported by several recent studies, including comprehensive systematic reviews and meta-analyses (Fu et al., 2022; Hidayati et al., 2023; Li et al., 2022). A meta-analysis of 22 studies (Fu et al., 2022) and a meta-analysis of 10 RCTs (Li et al., 2022) showed that vitamin D supplementation resulted in statistically significant improvements and reductions in AD symptoms, as measured by the SCORAD and EASI scales, compared with placebo control groups. Certain differences in the study results are well illustrated by the meta-analysis by Hidayati et al., (2023). Although these authors demonstrated an overall improvement in patients' condition (SMD = -0.93) after vitamin D supplementation, their analysis did not confirm a statistically significant advantage over placebo (RR 1.46; 95% CI: 0.72 to 2.97) when a specific indicator, i.e., the percentage of recoveries, was taken into account. On the other hand, an RCT clinical trial focusing exclusively on patients (aged 5–16 years) with severe AD showed clear benefits. Patients receiving 1600 IU of vitamin D3 daily for 12 weeks, as an adjunct to standard topical therapy (1% hydrocortisone), had significantly lower final EASI scores ($p = 0.035$) and a significantly greater percentage improvement (56.44% vs. 42.09%; $p = 0.039$) compared to the placebo group (Mansour et al., 2020).

Factors determining efficacy

The key factor modulating the intervention's efficacy appears to be the baseline 25(OH)D level. Investigations show that children with AD generally have lower 25(OH)D concentrations than their healthy peers, and patients with severe AD have significantly lower levels than patients with mild AD (Fu et al., 2022). This is reflected in a subgroup analysis (Li et al., 2022), which showed that supplementation resulted in significant clinical improvement in children with baseline 25(OH)D levels below 30 ng/mL (SMD = -0.40), but was not effective in patients whose baseline levels exceeded 30 ng/mL. Furthermore, in a study by Mansour et al. (2020), a strong correlation was observed between the extent of increase in serum 25(OH)D concentration and the percentage improvement on the EASI scale (Spearman's rho, $r = 0.6$). When it comes to dosage, intervention duration, and patient age, the data are less clear. All of the reviews analyzed emphasize that the high methodological heterogeneity of the included studies (different doses, durations, and administration regimens) makes it impossible to formulate definitive recommendations (Hidayati et al., 2023; Fu et al., 2022; Li et al., 2022). The optimal dose and duration of treatment remain open. Hidayati et al., (2023) conclude outright that it is not yet possible to

establish such recommendations. This is consistent with the subgroup analysis by Li et al., (2022), which found no significant difference in treatment efficacy between doses <2000 IU/day and≥2000 IU/day.

Safety and recommended doses

Vitamin D supplementation in the studies analyzed was generally considered safe (Li et al., 2022). In the study by Mansour et al., (2020), using a dose of 1600 IU/day, the maximum 25(OH)D level achieved was 50 ng/mL, which was considered a safe concentration and did not cause toxicity. Nevertheless, the authors (Hidayati et al., 2023) note that not all studies reported final concentrations. These authors note that 25(OH)D levels should be monitored regularly to avoid side effects such as hypercalcemia. Unfortunately, because current studies vary so much in their methods, we cannot yet recommend a single standard dose for children with AD (Hidayati et al., 2023; Li et al., 2022).

To offer a thorough synthesis of the current evidence, the key findings from the analyzed meta-analyses and clinical trials are summarized below. Table 1 outlines associations between serum 25(OH)D levels and Atopic Dermatitis severity, summarizes the outcomes of supplementation interventions, and notes the methodological diversity across the reviewed studies.

Table 1. Summary of key studies and meta-analyses regarding Vitamin D and Atopic Dermatitis (AD) discussed in the review.

Study (Author, Year)	Study Type	Key Findings and Observations
Hattangdi-Haridas et al., (2019)	Meta-analysis	• AD patients have significantly lower 25(OH)D levels compared to healthy controls (approx. 14–16 nmol/L lower) . • Supplementation led to a clinically significant reduction in SCORAD (11 points in RCTs, 21 points in repeated-measures studies).
Fu et al., (2022)	Meta-analysis	• Vitamin D deficiency (<20 ng/mL) is associated with a higher risk of AD (OR = 2.17) . • Patients with severe AD have lower vitamin D levels than those with mild AD . • Supplementation significantly reduced SCORAD (by ~11 points) and EASI scores.
Hidayati et al., (2023)	Systematic Review & Meta-analysis	• Confirmed overall symptom improvement (SMD = -0.93) but noted no statistically significant difference in recovery rates compared to placebo . • Highlighted that establishing a standard dose is currently impossible due to study heterogeneity.
Li et al., (2022)	Systematic Review & Meta-analysis	• Efficacy of supplementation depends on baseline levels: significant improvement observed only in children with baseline 25(OH)D <30 ng/mL. • Confirmed safety of supplementation, even with high loading doses.
Mansour et al., (2020)	RCT	• Investigated 1600 IU/day in children with severe AD. • Showed significant improvement in EASI score and percentage improvement compared to placebo. • Strong correlation found between the increase in serum 25(OH)D and clinical improvement.
Yang et al., (2021)	Cohort Study	• Found no evidence that vitamin D deficiency or insufficiency in early childhood increases the risk of developing AD, contrasting with other findings.

4. CONCLUSION

Vitamin D is integral to the management of atopic dermatitis, acting mainly through strengthening tight junctions and regulating the immune response. By suppressing IgE and promoting an anti-inflammatory environment, supplementation has been shown to improve clinical outcomes in children- especially those with severe symptoms and baseline IgE deficiency. While the intervention is safe, the wide variability in study protocols currently makes it difficult to establish a single, optimal dosing strategy.

List of abbreviations:

AD- Atopic Dermatitis

25(OH)D- 25-hydroxyvitamin D (Calcidiol)
UVB- Ultraviolet B
VDR - Vitamin D Receptor
AMPs - Antimicrobial Peptides
HDP-Host Defense System
CAMP- Cathelicidin Antimicrobial Peptide Gene
RCTs- Randomised Controlled Trials
SCORAD- Scoring Atopic Dermatitis (Scale)
EASI- Eczema Area and Severity Index (Scale)
MCID- Minimal Clinically Important Difference
Tregs-Regulatory T cells
IgE- Immunoglobulin E
S. aureus- Staphylococcus aureus
IL- Interleukin
IFN-γ - Interferon-gamma
JECS- Japan Environment and Children's Study
SMD - Standardized Mean Difference
OR- Odds Ratio
CI -Confidence Interval
RR- Relative Risk

Acknowledgments
The authors have no acknowledgments to disclose.

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Visualization: Agnieszka Kowalska, Milena Kędzierska.
All authors have read and agreed with the published version of the manuscript.

Informed consent
Not applicable.

Ethical approval
Not applicable. This article does not contain any studies with human participants or animals performed by any of the authors.

Funding
This research did not receive any external funding like specific grant from funding agencies in the public, commercial, or nonprofit sectors.

Conflict of interest
The authors declare that they have no conflicts of interest, competing financial interests or personal relationships that could have influenced the work reported in this paper.

Data and materials availability

All data associated with this study will be available based on reasonable request to the Corresponding Author.

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