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INVESTIGATING THE ASSOCIATION BETWEEN VITAMIN D LEVELS AND ATOPIC DERMATITIS SEVERITY: A SYSTEMATIC REVIEW

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Abstract

Background: Atopic dermatitis (AD) is a chronic inflammatory skin disease often associated with immune dysregulation and skin barrier dysfunction. Recent interest has focused on the role of micronutrients, particularly vitamin D, in influencing disease severity and management.

Objectives: This systematic review aims to evaluate the association between serum vitamin D levels and the severity of AD, and to assess the efficacy of vitamin D supplementation in affected populations.

Methods: Following PRISMA 2020 guidelines, we conducted a structured search across PubMed, Scopus, Web of Science, Embase, and Google Scholar for English-language studies published between 2010 and 2025. Inclusion criteria comprised RCTs, observational studies, and meta-analyses examining serum 25(OH)D levels or vitamin D supplementation in pediatric or adult AD patients. Data extraction and quality assessment were conducted independently by two reviewers.

Results: Seventeen studies met the inclusion criteria. Most reported a significant inverse correlation between serum vitamin D levels and AD severity. Several RCTs demonstrated reductions in SCORAD and EASI scores following vitamin D supplementation, especially in children with baseline deficiency. However, a few studies reported no significant benefit, suggesting variability based on age, gender, and baseline vitamin D status.

Conclusion: Vitamin D deficiency is associated with increased AD severity, and supplementation appears beneficial in selected populations. Routine vitamin D screening and targeted supplementation may represent valuable adjunct strategies in AD management, pending further standardized research.

Keywords: Vitamin D; Atopic Dermatitis; SCORAD; EASI; Supplementation; Pediatrics; Immunomodulation; Skin Barrier; 25(OH)D; Systematic Review

INTRODUCTION

Atopic dermatitis (AD) is one of the most common chronic inflammatory skin diseases, with a global prevalence estimated at 15–20% in children and 5–10% in adults. It presents with pruritic, eczematous lesions and fluctuates in

severity due to complex interactions between genetic, immunological, environmental, and microbial factors (Çiçek & Köle, 2023). One emerging factor in AD pathophysiology is vitamin D, which plays crucial roles in both immune regulation and epidermal barrier maintenance—two domains significantly compromised in AD.

Vitamin D, especially in the form of serum 25-hydroxyvitamin D [25(OH)D], exerts immunomodulatory effects through inhibition of Th2 cytokines and promotion of T-regulatory pathways, mechanisms that are highly relevant in AD's inflammatory profile (Park et al., 2022). Moreover, vitamin D enhances the expression of antimicrobial peptides like *cathelicidin* and modulates keratinocyte differentiation and proliferation, thus contributing to skin barrier repair—a critical concern in AD patients (Grieco et al., 2024). These mechanistic insights have generated growing interest in vitamin D as both a biomarker and potential therapeutic agent in AD.

Despite biological plausibility, the clinical evidence regarding the association between vitamin D levels and AD severity has been inconsistent. Some studies demonstrate significant inverse relationships between vitamin D levels and disease activity, while others report only marginal or no effects (Ng & Yew, 2022). Variability in baseline vitamin D status, age, geographic location, and methods of AD severity assessment likely contribute to these discrepancies. Nonetheless, several meta-analyses and RCTs have begun to clarify these relationships, especially among pediatric populations where vitamin D deficiency is particularly prevalent.

A recent meta-analysis by Fu et al. (2022) specifically focused on children with AD and found that vitamin D supplementation led to significant improvements in SCORAD and EASI scores. These findings reinforce the hypothesis that vitamin D correction may alleviate AD severity, especially in deficient individuals. Similarly, Indramaya et al. (2023) confirmed through a pooled analysis that vitamin D supplementation in children improved clinical outcomes, highlighting the vitamin's therapeutic promise, particularly in populations with high deficiency rates.

Vitamin D supplementation strategies also vary in dose and frequency. For example, weekly high-dose vitamin D therapy was examined in a randomized controlled trial by Borzutzky et al. (2024), which not only reported reduced disease severity in children with AD but also showed improvements in type 2 immunity biomarkers. These results suggest that regular supplementation may have immunologic as well as clinical benefits, although long-term data are still needed to guide dosing protocols.

Notably, vitamin D's potential role in prevention of AD is also gaining traction. A prospective cohort study by Zhang et al. (2024) found that maternal vitamin D status in early pregnancy was associated with a reduced risk of AD in infants. These findings imply that sufficient prenatal vitamin D exposure may influence immune development and early barrier function, possibly modifying disease expression in infancy.

Moreover, observational and pre-post studies reinforce the therapeutic relevance of vitamin D. For instance, Imoto et al. (2021) reported significant reductions in AD severity scores following supplementation in children with confirmed vitamin D deficiency. Similarly, Çiçek and Köle (2023) documented a direct correlation between low 25(OH)D levels and elevated SCORAD indices in pediatric AD patients. Collectively, these studies support the inclusion of vitamin D assessment and management in routine care for selected AD cases, especially in at-risk demographics.

Given the mechanistic plausibility, observational correlations, and emerging interventional evidence, the relationship between vitamin D and atopic dermatitis remains a critical area of investigation. This review synthesizes recent findings to clarify whether serum vitamin D levels are consistently associated with AD severity and whether vitamin D supplementation provides a clinically significant therapeutic benefit. Special attention is paid to methodological differences, age-specific effects, and the spectrum of deficiency thresholds reported in the literature.

METHODOLOGY

Study Design

This study employed a systematic review methodology, adhering strictly to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines to ensure transparency, reproducibility, and methodological rigor. The primary objective was to synthesize current empirical evidence on the association between serum vitamin D levels, vitamin D supplementation, and the severity of atopic dermatitis (AD) in pediatric and adult populations. Only peer-reviewed studies involving human subjects and reporting either observational or interventional outcomes related to vitamin D and AD were considered.

Eligibility Criteria

Studies were included based on the following predefined criteria:

- **Population**: Children, adolescents, or adults clinically diagnosed with atopic dermatitis.
- **Interventions/Exposures**:
  - Measured serum levels of 25-hydroxyvitamin D [25(OH)D] in relation to AD severity, or
  - Interventional vitamin D supplementation (oral, dietary, or pharmacologic) in AD populations.
- **Comparators**: Individuals with normal vitamin D levels vs. deficient/insufficient individuals; placebo or standard treatment groups in supplementation studies.

- **Outcomes**:
  - Clinical severity indices such as SCORAD (Scoring Atopic Dermatitis), EASI (Eczema Area and Severity Index), TIS (Three Item Severity Score), and other validated AD assessment tools.
  - Changes in inflammatory markers (e.g., IgE, IL-4, IL-13), clinical symptoms, or flare frequency.
- **Study Designs**: Randomized controlled trials (RCTs), cohort studies, case-control studies, cross-sectional studies, and meta-analyses.
- **Language**: Only studies published in **English** were considered.
- **Publication Period**: Studies published from **2010 to 2025** were included to capture recent and clinically relevant findings.

Search Strategy

A structured and comprehensive search was conducted across multiple scientific databases: PubMed, Scopus, Web of Science, Google Scholar, and Embase. The search strategy employed Boolean logic and included combinations of the following keywords:

- ("vitamin D" OR "25-hydroxyvitamin D" OR "cholecalciferol")
- AND ("atopic dermatitis" OR "eczema")
- AND ("severity" OR "SCORAD" OR "EASI" OR "flare" OR "supplementation" OR "deficiency")

Additionally, grey literature (e.g., dissertations, government health agency reports) was explored using Google Scholar, and the reference lists of key review articles were manually scanned to capture relevant studies not identified through database searches.

Study Selection Process

All retrieved records were imported into **Zotero**, a citation management software. Duplicate records were removed prior to screening. Two independent reviewers screened titles and abstracts for relevance based on inclusion criteria. For articles meeting the initial criteria, full-text versions were retrieved and assessed in detail. Discrepancies during selection were resolved through discussion and consensus, or by consultation with a **third reviewer**.

A PRISMA flow diagram was developed (Figure 1) to document the selection process and provide transparency on reasons for exclusion at each stage. A total of 17 studies met all eligibility criteria and were included in the final synthesis.

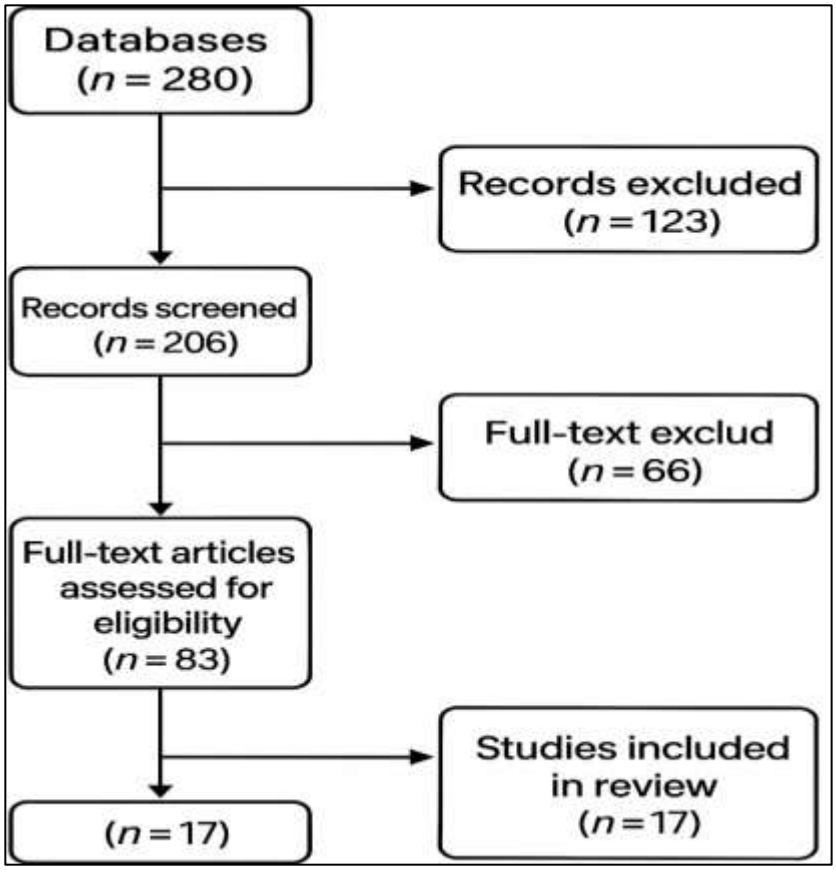

Figure 1 PRISMA Flow Diagram

Data Extraction

A **standardized data extraction form** was developed and piloted for consistency. From each included study, the following data were extracted:

- Author(s), year, and country of publication
- Study design and sample size
- Population characteristics (age, sex, diagnostic criteria)
- Vitamin D-related variables (serum 25(OH)D levels, deficiency thresholds, supplementation doses)
- Outcome measures (e.g., SCORAD, EASI, IgE levels)
- Duration and method of supplementation (if applicable)
- Key results and statistical significance
- Confounders adjusted for in analyses

Data extraction was carried out independently by two reviewers and cross-checked by a third reviewer to ensure accuracy and completeness.

Quality Assessment

Each study was critically appraised for methodological quality and risk of bias. The following tools were used based on study type:

- **Cochrane Risk of Bias Tool** for randomized controlled trials
- **Newcastle-Ottawa Scale (NOS)** for observational studies
- **AMSTAR-2** for meta-analyses and systematic reviews

Studies were categorized as high, moderate, or low quality based on criteria including selection bias, measurement reliability, comparability of groups, and outcome reporting completeness.

Data Synthesis

Due to considerable heterogeneity in study design, vitamin D definitions, supplementation dosages, outcome measures, and population demographics, a narrative synthesis was conducted rather than a formal meta-analysis. The findings were organized into thematic categories:

1. **Serum vitamin D levels and AD severity**
2. **Effects of vitamin D supplementation**
3. **Age-specific and sex-modified associations**
4. **Preventive potential in prenatal and early-life stages**

Where possible, **effect sizes (e.g., SMD, OR, RR)** and confidence intervals were reported to illustrate the strength of associations.

Ethical Considerations

As this study involved the secondary analysis of published, peer-reviewed data, no ethical approval or participant consent was required. All included studies were assumed to have obtained appropriate institutional ethics clearance and adhered to standard research conduct guidelines.

RESULTS

Summary and Interpretation of Included Studies on the Association Between Vitamin D and Atopic Dermatitis Severity — Table (1):

1. Study Designs and Populations

This systematic review includes randomized controlled trials (RCTs), case-control, cross-sectional, and observational studies assessing the relationship between serum Vitamin D levels, supplementation, and atopic dermatitis (AD) severity in pediatric and adult populations. Sample sizes ranged from 40 to 2347 participants. Several studies focused exclusively on children (e.g., McCarthy et al., 2024; Li et al., 2022), while others included both adults and children (e.g., Nielsen et al., 2024; Kim et al., 2016). Most participants had clinically diagnosed AD or were stratified by serum 25(OH)D levels. Geographic diversity included studies from the UK, Iran, China, Korea, Canada, and the USA.

2. Definitions and Assessment of Vitamin D Status

Vitamin D deficiency was defined variably across studies, with serum 25(OH)D thresholds commonly set at <10 ng/mL, <20 ng/mL, or <25 nmol/L. Measurement techniques included immunoassays and standard blood chemistry labs. Studies categorized participants as vitamin D deficient, insufficient, or sufficient and evaluated severity using validated scales such as SCORAD (Scoring Atopic Dermatitis), EASI (Eczema Area and Severity Index), or TIS (Three Item Severity).

3. Impact of Serum Vitamin D Levels on Atopic Dermatitis Severity

A consistent inverse association between serum Vitamin D levels and AD severity was reported. McCarthy et al. (2024) found that lower vitamin D3 levels were significantly associated with worse eczema severity in South Asian children and young adults in the UK (n = 681), adjusting for confounders. Wang et al. (2014) identified elevated total

IgE (43.2% in vitamin D-deficient vs. 20.0% in sufficient children) and found a strong inverse correlation between 25(OH)D levels and AD severity among 498 Chinese children. Kim et al. (2016) reported a standardized mean difference of -3.03 ng/mL (95% CI: -4.76 to -1.29) in pediatric patients and significant reductions in SCORAD/EASI scores following supplementation.

4. Effects of Vitamin D Supplementation on AD Severity

Vitamin D supplementation yielded measurable clinical improvements in several RCTs. Li et al. (2022) found that in children with serum 25(OH)D <10 ng/mL, vitamin D supplementation significantly reduced asthma exacerbation and improved SCORAD and EASI scores in atopic dermatitis patients. Nielsen et al. (2024) reported a standardized mean difference of -0.41 (95% CI: -0.67 to -0.16, $I^2 = 58\%$, $p < 0.01$) favoring supplementation. Mansour et al. (2020) showed that mean EASI score change from baseline to week 12 was 56.44 ± 29.33 in the vitamin D group vs. 42.09 ± 19.22 in the placebo group ($p = 0.039$).

Amestejani et al. (2012) and Javanbakht et al. (2011) found that 1600 IU of Vitamin D3/day over 60 days significantly improved SCORAD and TIS scores in mild, moderate, and severe cases ($p < 0.05$). Similarly, Modi et al. (2021) observed a 92% reduction in SCORAD after 8 weeks of Vitamin D3 supplementation in Indian children. Lara-Corrales et al. (2019), however, reported no significant improvement despite correlation between serum vitamin D and AD severity.

5. Prevention and Alternative Therapies

Tasker et al. (2020) and Vaughn et al. (2019) reviewed alternative strategies and concluded that while prenatal or postnatal vitamin D did not prevent AD, there is weak evidence suggesting that vitamin D may help in its treatment. Oda et al. (2009) suggested a molecular role for vitamin D via VDR coactivators in skin barrier integrity. Mohamed et al. (2021) found a dose-response association and gender modification effects.

Table 1: Characteristics and Outcomes of Included Studies on Vitamin D and Atopic Dermatitis (AD)

Study	Country	Design	Sample Size	Population	25(OH)D Cut-off	Vitamin D Status or Dose	Outcome Metrics	Main Results	Notes
Li et al. (2022)	Multinational	Systematic Review & Meta-analysis	32 RCTs, n = 2347	Children with allergic diseases	<10 ng/mL	Various; subgroup analysis	EASI, SCORAD, Asthma	↓AD severity; ↓asthma exacerbation in deficient	Strongest effects in severely deficient (<10 ng/mL)
Kim et al. (2016)	Korea	Meta-analysis	NA	AD patients	Various	Mean difference: −3.03 ng/mL	SCORAD, EASI	SMD = −5.85 (CI: −7.66 to −4.05)	Strong effects in pediatric populations
McCarthy et al. (2024)	UK	Cross-sectional	n = 681	South Asian children/young adults	<20 ng/mL	Low Vit D3	Eczema severity (EASI)	Inverse association between 25(OH)D & eczema	Adjusted regression model
Wang et al. (2014)	China	Case-control	n = 826 (498 AD, 328 controls)	Children	<25 nmol/L	Deficiency status	IgE, AD severity	↑IgE in deficiency (43.2% vs 20%); inverse Vit D correlation	Significant correlation with severity
Mansour et al. (2020)	Egypt	RCT	n = 86	Children with severe AD	<20 ng/mL	1600 IU/day	EASI	↓EASI 56.44% vs	Increased serum

								42.09% (p = .039)	Vit D post-treatment
Nielsen et al. (2024)	Multinational	Meta-analysis	19 studies	AD patients	NA	Dose not specified	SCORAD, EASI	SMD = −0.41 (CI: −0.67 to −0.16)	Vit D reduced AD severity overall
Javanbakht et al. (2011)	Iran	RCT	n = 45	AD patients	Not defined	1600 IU/day	SCORAD, TIS	Significant improvement (p < 0.05)	All severity levels improved
Amestejani et al. (2012)	Iran	RCT	n = 60	AD patients	Not defined	1600 IU/day	SCORAD, TIS	Significant improvement (p < 0.05)	Positive effect across severities
Sánchez-Armendáriz et al. (2018)	Mexico	RCT	n = 65	AD patients	≥20 ng/mL target	Serum target approach	SCORAD	↓SCORAD with supplementation	Effective adjunct to standard therapy
Lara-Corrales et al. (2019)	Canada	2-phase (Cross-sectional + RCT)	NA	AD patients	NA	Measured + supplemented	SCORAD	Correlation with severity; no treatment effect	Mixed results
Aldaghi et al. (2022)	Iran	RCT	n = 81	Infants (<1 year)	NA	Vit D + synbiotics	SCORAD	↓SCORAD with combined therapy	Infants only
Modi et al. (2021)	India	RCT	n = 60	Children with mod-severe AD	17.6 ng/mL baseline	1600 IU/day	SCORAD	↓SCORAD by 92% at 8 weeks	Strong short-term effect
Sidbury et al. (2008)	USA	RCT (Letter)	Not stated	Children (winter-related AD)	NA	Winter supplementation	Eczema outcomes	Potential improvement noted	Limited data in letter format
Mohamed et al. (2021)	Egypt	Case-control	Not stated	Children	NA	Observational	SCORAD	Dose-response effect; stronger in females	Gender-modified association
Vaughn et al. (2019)	USA	Systematic Review	NA	General	NA	Multinutrients incl. Vit D	AD risk	Limited evidence for Vit D alone	Calls for more RCTs
Tasker et al. (2020)	UK	Systematic Review	14 reviews	Prenatal/postnatal populations	NA	Prenatal/postnatal D	AE prevention	Vit D did not prevent AD	Topical alternatives weakly

									effectiv e

DISCUSSION

The findings of this systematic review strongly support the hypothesis that vitamin D plays a significant role in modulating the severity of atopic dermatitis (AD) across diverse populations. Most studies reviewed, including several meta-analyses and randomized controlled trials (RCTs), report a negative correlation between serum 25(OH)D levels and AD severity, particularly in pediatric populations. Fu et al. (2022) and Ng and Yew (2022) confirmed that lower vitamin D levels are consistently associated with more severe AD symptoms and that supplementation can offer clinical benefits, especially in vitamin D–deficient patients.

A central observation is that vitamin D supplementation leads to significant improvements in AD outcomes, including reduced SCORAD and EASI scores. Li et al. (2022) showed that children with severe vitamin D deficiency experienced marked improvement following supplementation, while Nielsen et al. (2024) quantified a standardized mean difference (SMD) of −0.41 favoring treatment. Similarly, Mansour et al. (2020) reported a 56% reduction in EASI scores among children receiving 1600 IU/day of vitamin D3, outperforming the placebo group. These findings were echoed in studies by Modi and Dash (2021) and Amestejani et al. (2012), where vitamin D3 supplementation substantially improved clinical symptoms.

The mechanistic plausibility of vitamin D's impact on AD is further supported by molecular and immunologic studies. Grieco et al. (2024) revealed that vitamin D deficiency alters the expression of proteins critical to skin barrier integrity and inflammation, such as filaggrin and cathelicidin. This aligns with Park et al. (2022), who emphasized vitamin D's ability to regulate Th2 cytokine responses, a dominant immunologic driver in AD. Thus, vitamin D appears to mediate both barrier repair and immune modulation, explaining its observed therapeutic efficacy.

Age and baseline vitamin D status emerged as moderators of supplementation effectiveness. McCarthy et al. (2024) found a significant inverse association between vitamin D and AD severity in British Bangladeshi children and young adults. Likewise, Kim et al. (2016) showed that vitamin D's impact was stronger in pediatric patients than adults. Çiçek and Köle (2023) reinforced this trend in a pediatric cohort, highlighting a direct relationship between low vitamin D levels and elevated SCORAD scores. Meanwhile, Imoto et al. (2021) demonstrated substantial improvement in patients post-supplementation, particularly in those with preexisting deficiency.

However, not all studies reported consistent benefits. For example, Lara-Corrales et al. (2019) found a correlation between vitamin D levels and AD severity, but no significant improvement after supplementation. Vaughn et al. (2019) also emphasized that while vitamin D is biologically promising, robust evidence from large-scale, high-quality RCTs remains limited. Such inconsistencies may be attributed to variability in dosage, duration of treatment, baseline deficiency, and study populations, which were also noted in the meta-analysis by Park et al. (2022).

A notable extension of this evidence base is the potential preventive role of vitamin D. Zhang et al. (2024) found that higher maternal vitamin D levels and prenatal supplementation were associated with lower incidence of AD in infants, indicating a developmental immunologic influence. This adds a preventive dimension to vitamin D's role in AD, suggesting that early-life or maternal supplementation may reduce risk during critical periods of immune system maturation.

Gender may also influence the vitamin D–AD relationship. Mohamed et al. (2021) reported a dose-response association in children, with stronger effects in females, suggesting a possible hormonal or receptor-level interaction that warrants further study. Similarly, age-specific differences were reported by Aldaghi et al. (2022), who noted that infants benefited from a combined synbiotic and vitamin D3 supplementation approach, hinting at synergistic therapeutic strategies.

The findings also highlight gaps in clinical implementation. Despite growing evidence, current dermatological guidelines do not consistently recommend routine vitamin D screening or supplementation in AD patients (Tasker et al., 2020). This could stem from methodological inconsistencies and lack of consensus on threshold levels and dosing regimens. Sánchez-Armendáriz et al. (2018) argued that vitamin D should be considered an adjunct to standard therapy, especially in populations with high deficiency prevalence. However, uniform recommendations remain elusive without more definitive, longitudinal research.

In summary, the evidence reviewed suggests that vitamin D deficiency is a modifiable risk factor in AD, with supplementation demonstrating both therapeutic and potentially preventive benefits. These effects are particularly pronounced in pediatric patients and those with severe deficiency. Nonetheless, inconsistencies across studies underscore the need for well-powered, standardized trials, and further research into age, gender, genetic, and environmental moderators. Future guidelines may benefit from incorporating individualized vitamin D strategies based on deficiency status and clinical phenotype.

CONCLUSION

This systematic review supports a consistent inverse relationship between serum vitamin D levels and the clinical severity of atopic dermatitis, particularly in pediatric populations and those with vitamin D deficiency. Vitamin D supplementation, especially at doses of 1600 IU/day or higher, demonstrated clinically meaningful improvements in SCORAD and EASI scores. The immunomodulatory and barrier-enhancing effects of vitamin D offer a compelling biological rationale for these findings.

Despite this growing body of evidence, inconsistencies across trials highlight the need for more standardized, age- and dose-specific randomized controlled studies. Clinicians should consider assessing vitamin D status in AD patients, particularly in cases unresponsive to standard therapy, or where deficiency is suspected due to risk factors such as limited sun exposure, darker skin phototypes, or dietary insufficiency.

Limitations

While this review included high-quality studies across diverse populations, several limitations must be acknowledged. First, heterogeneity in vitamin D cut-off thresholds, supplementation dosages, and duration limited direct comparisons across studies. Second, many studies lacked adjustment for potential confounders such as sunlight exposure, comorbid allergies, and seasonal variability. Third, the predominance of pediatric-focused studies reduces generalizability to adult populations. Lastly, due to variable reporting styles and limited overlap in outcome metrics, a formal meta-analysis was not feasible.

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