

Original Research

Effectiveness of Vitamin D Supplementation in Children with Attention Deficit Hyperactivity Disorder: A Systematic Review of Randomized Controlled Trials

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Abstrak

Attention-deficit/hyperactivity disorder (ADHD) merupakan gangguan neurodevelopmental yang umum dan berdampak signifikan terhadap fungsi serta kualitas hidup. Bukti menunjukkan bahwa vitamin D berperan dalam perkembangan saraf dan regulasi perilaku, dan anak dengan ADHD dilaporkan memiliki kadar serum 25-hidroksivitamin D [25(OH)D] yang lebih rendah. Namun, temuan terkait efektivitas klinis suplementasi vitamin D masih menunjukkan hasil yang tidak konsisten. Penelitian ini bertujuan untuk meninjau secara sistematis efektivitas suplementasi vitamin D pada anak dengan ADHD. Tinjauan sistematis dilakukan sesuai pedoman PRISMA dengan menelusuri PubMed, ScienceDirect, dan Scopus untuk uji klinis acak terkontrol (RCT) yang dipublikasikan antara Januari 2016 hingga Februari 2026. Studi yang memenuhi kriteria melibatkan anak usia ≤ 18 tahun dengan diagnosis ADHD yang menerima suplementasi vitamin D oral. Kualitas studi dinilai menggunakan Joanna Briggs Institute Critical Appraisal Checklist, dan dilakukan sintesis kualitatif. Enam RCT memenuhi kriteria inklusi. Suplementasi vitamin D secara konsisten meningkatkan kadar serum 25(OH)D pada seluruh studi. Namun, efek klinis menunjukkan heterogenitas. Beberapa studi melaporkan perbaikan terbatas pada domain gejala tertentu, terutama inatensi, sementara penurunan yang konsisten pada keparahan ADHD secara keseluruhan tidak ditemukan. Sebagai kesimpulan, suplementasi vitamin D meningkatkan kadar 25(OH)D, tetapi menunjukkan manfaat klinis yang bervariasi pada anak dengan ADHD. Bukti saat ini belum mendukung penggunaannya sebagai terapi tunggal yang definitif, meskipun potensi manfaat sebagai terapi tambahan tidak dapat dikesampingkan. Diperlukan uji klinis acak terkontrol berskala besar dengan kualitas tinggi untuk memperjelas peran klinisnya.

Kata kunci: *Attention deficit hyperactivity disorder; ADHD; Vitamin D; Serum 25(OH)D; Efektivitas.*

Abstract

Attention-deficit/hyperactivity disorder (ADHD) is a common neurodevelopmental disorder that significantly affects functioning and quality of life. Evidence suggests that vitamin D may play a role in neurodevelopment and behavioral regulation, and children with ADHD have been reported to exhibit lower serum 25-hydroxyvitamin D [25(OH)D] concentrations. However, findings regarding the clinical effectiveness of vitamin D supplementation remain inconsistent. This study aimed to systematically review the effectiveness of vitamin D supplementation in children with ADHD. A systematic review was conducted in accordance with PRISMA guidelines by searching PubMed, ScienceDirect, and Scopus for randomized controlled trials (RCTs) published between January 2016 and February

2026. Eligible studies included children aged ≤ 18 years diagnosed with ADHD who received oral vitamin D supplementation. Study quality was assessed using the Joanna Briggs Institute Critical Appraisal Checklist, and a qualitative synthesis was performed. Six RCTs met the inclusion criteria. Vitamin D supplementation consistently increased serum 25(OH)D concentrations across studies. However, clinical effects were heterogeneous. Some studies reported modest improvements in specific symptom domains, particularly inattention, whereas consistent reductions in overall ADHD severity were not observed. In conclusion, vitamin D supplementation improves serum 25(OH)D levels but demonstrates variable clinical benefits in children with ADHD. Current evidence does not support its use as a definitive standalone treatment, although potential benefits as an adjunctive therapy cannot be excluded. Further high-quality, large-scale RCTs are needed to clarify its clinical role.

Keywords: *Attention-deficit/hyperactivity disorder; ADHD; Vitamin D; Serum 25(OH)D; Efficacy*

BACKGROUND

According to the DSM-5-TR, attention-deficit/hyperactivity disorder (ADHD) is a neurodevelopmental disorder characterized by persistent patterns of inattention, hyperactivity, and impulsivity that interfere with functioning and development. ADHD substantially impacts daily functioning and quality of life, resulting in impairments across academic, social, and occupational functioning (1–3).

The prevalence of ADHD varies across age groups, with estimates of 7.6% in children aged 3–11 years and 5.6% in adolescents aged 12–18 years, while the global prevalence in adults is approximately 3.1% (4,5).

Although the exact etiology of ADHD remains unclear, it is widely recognized as a multifactorial disorder involving genetic and environmental factors. These include prenatal complications, traumatic brain injury, and nutritional deficiencies, which may disrupt dopaminergic and noradrenergic neurotransmission and contribute to dysfunction in frontostriatal circuits involved in attention and behavioral regulation (6,7).

Current management strategies for ADHD include pharmacological and non-pharmacological approaches. Stimulant medications, such as methylphenidate and amphetamine derivatives, are considered first-line therapy, while non-stimulant agents serve as alternative options and behavioral interventions are commonly used as adjunctive treatments (8,9). However, treatment response remains suboptimal in a subset of patients, and long-term use of stimulant medications may be associated with adverse effects that can limit adherence, highlighting the need for safer and more targeted adjunctive therapies (10).

Emerging evidence suggests that vitamin D plays a role in neurodevelopment and brain function. It acts as a neurosteroid and influences brain regions such as the cerebellum, striatum, and hippocampus. Vitamin D is also involved in the regulation of neurotrophic factors, synaptic plasticity, and signaling pathways, including mTOR and the oxytocin system, which are implicated in attention and behavioral control. Several studies have reported lower serum 25-hydroxyvitamin D [25(OH)D] levels in children with ADHD compared to healthy controls (11,12). In addition, some interventional studies suggest that vitamin D supplementation may improve certain

behavioral symptoms, particularly when combined with standard pharmacotherapy (13). Furthermore, reductions in inflammatory markers following supplementation have been reported, suggesting potential biological mechanisms underlying these effects (14). However, other studies have demonstrated no significant clinical improvement despite increased serum vitamin D levels (15).

Importantly, the existing evidence remains inconsistent and is limited by heterogeneity in study design, population characteristics, dosing regimens, and outcome measures. Furthermore, much of the available evidence is derived from studies with varying methodological quality, making it difficult to draw definitive conclusions regarding the clinical effectiveness of vitamin D supplementation in children with ADHD.

Therefore, this study aims to systematically review the effectiveness of vitamin D supplementation in children with ADHD, with a focus on evidence derived from randomized controlled trials.

METODE

Search Strategy and Selection Criteria

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were used to conduct this systematic review (16). A comprehensive literature search was performed in PubMed, ScienceDirect, and Scopus to identify relevant studies published between January 2016 and February 2026. The search strategy was developed using a combination of free-text terms and relevant synonyms related to the intervention and condition. The main search terms included: ("Vitamin D" OR cholecalciferol OR ergocalciferol) AND ("Attention Deficit Hyperactivity Disorder" OR ADHD). The search strategy was adapted for each database. Only articles published in English were included, and duplicate records were removed prior to screening.

Study Selection Process

The study selection process was conducted in a stepwise manner, including title screening, abstract screening, and full-text assessment for eligibility. Eligibility criteria were defined based on the PICOS framework: (1) Population: Children (aged ≤ 18 years) diagnosed with ADHD; (2) Intervention: oral vitamin D supplementation (at any dose and duration), administered as monotherapy or as an adjunct to standard ADHD treatment; (3) Comparison: placebo, control group, standard ADHD therapy, without vitamin D supplementation, or other therapeutic interventions; (4) Outcomes: any outcome measures related to ADHD treatment; and (5) Study design: randomized controlled trials (RCTs). Three reviewers (OP, DA, and ML) independently screened all identified studies. Discrepancies during the selection process were resolved through discussion, and when necessary, consultation with a fourth reviewer (SU) was performed to achieve consensus. The selection process was documented using a PRISMA flow diagram to ensure transparency and reproducibility.

Data Extraction and Quality Assessment

The data were extracted and systematically organized using a standardized data collection form. The aforementioned form encompassed the following elements: the primary author, the year of publication, the study design, the participant characteristics (i.e., age and body mass index [BMI]), the sample size, the details of the intervention and comparator, the outcomes and measurement instruments, and the main findings.

The methodological quality and risk of bias of the included studies were assessed using the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for randomized controlled trials (17). The assessment instrument was chosen based on the study's design, particularly the Revised JBI Critical Appraisal Checklist for Randomized Controlled Trials (RCTs). Each study was evaluated across 13 items, with responses categorized as “yes,” “no,” “unclear,” or “not applicable.” To enhance transparency, the overall methodological quality of each study was determined based on the number of “yes” responses, with studies categorized as high quality (≥ 10 “yes”), moderate quality (7–9 “yes”), and low quality (≤ 6 “yes”). The assessment was conducted independently by two reviewers (OP and DA) and subsequently verified by additional reviewers (ML and SU) to ensure consistency.

Data Analysis

The characteristics of the included studies were summarized in tables and described in narrative form. Due to heterogeneity in study design, patient characteristics, interventions, comparators, and outcomes, a qualitative synthesis was undertaken. The findings were analyzed across studies and presented with an emphasis on the primary outcomes.

RESULT AND DISCUSSION

Literature Search

The initial database search identified 170 records (PubMed: 32, ScienceDirect: 103, Scopus: 35). After removing duplicates, 167 records remained for title and abstract screening. A total of 30 full-text articles were assessed for eligibility, of which 24 were excluded for not meeting the inclusion criteria. Finally, six studies met all eligibility criteria and were included in this systematic review (Figure 1).

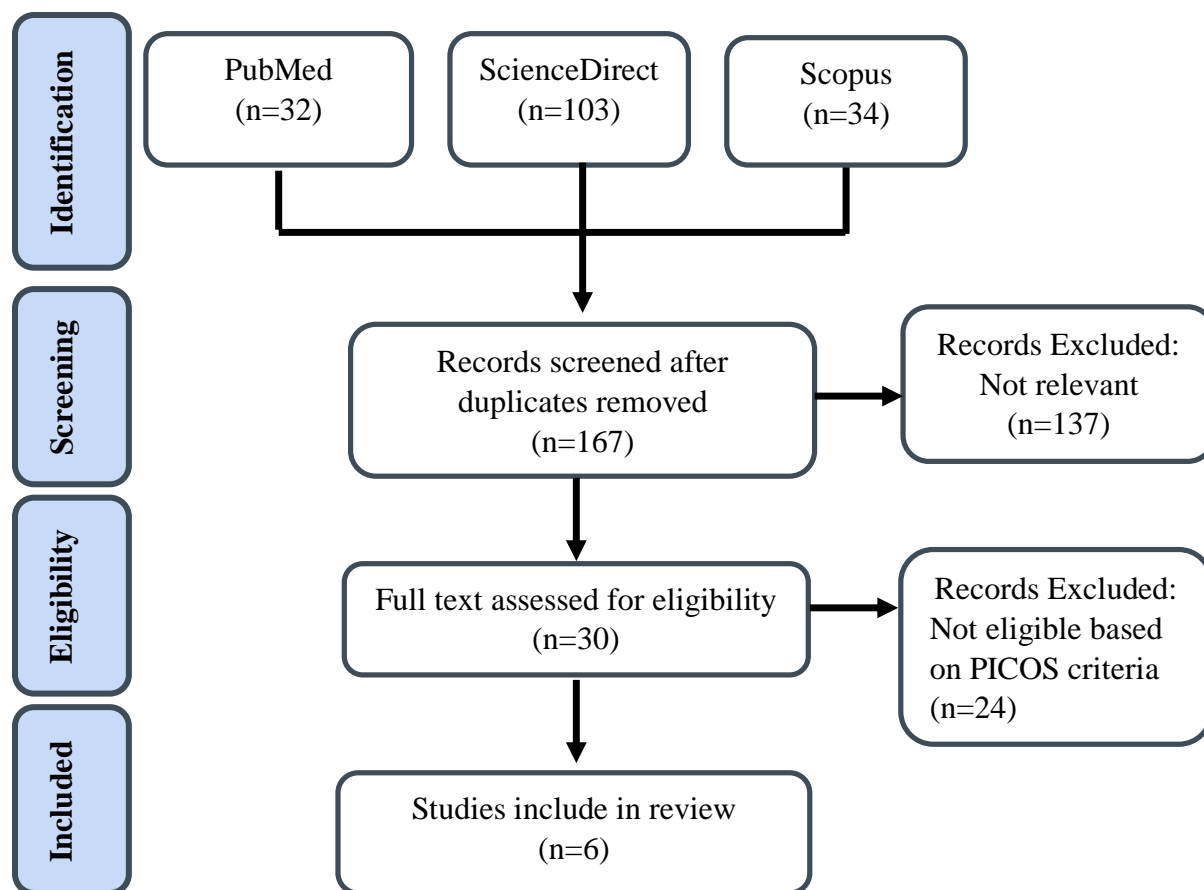


Figure 1. PRISMA flowchart of study selection process

Risk of Bias Assessment

The results of the critical appraisal of methodological quality and risk of bias are presented in Table 1. All six studies were evaluated across Domains I–V using 13 assessment items (Q1–Q13). Based on predefined criteria, all studies were classified as high quality, with at least ten “yes” responses across the checklist items.

However, several studies did not fully meet specific criteria, particularly within Domain II (allocation concealment and blinding of participants and personnel) and Domain V (statistical analysis and completeness of reporting). Minor concerns were also noted in Domain III (outcome measurement and assessor blinding), particularly for items such as Q7 and Q11. Although these limitations were not sufficient to downgrade the overall quality classification, they may introduce potential bias in specific domains. Therefore, the overall risk of bias across the included studies was considered low risk.

Table 1. Results of the JBI critical appraisal tool for risk of bias assessment in RCTs

Study	D-I			D-II			D-III			D-IV	D-V			Quality
	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13	
Samadi et al. 2022	√	√	√	√	√	√	√	√	√	√	X	√	√	High
Honarvar et al. 2022	√	√	√	√	√	√	√	√	√	√	X	√	√	High
Hemamyet al. 2021	√	X	√	√	√	√	√	√	√	√	X	√	√	High
Dehbokri et al. 2019	√	X	√	√	√	√	√	√	√	√	X	√	√	High
Elshorbagy, et al. 2018	√	X	√	√	√	√	X	√	√	√	X	√	√	High
Mohammadpour et al., 2016	√	X	√	√	√	√	X	√	√	√	X	√	√	High

Effectiveness of Vitamin D Supplementation in Children with ADHD

The present review included six randomized controlled trials evaluating the effect of vitamin D supplementation in children with ADHD. Across all included studies, vitamin D supplementation consistently increased serum 25(OH)D concentrations, whether administered as daily dosing (2000 IU/day) or weekly high-dose regimens (50,000 IU/week). However, improvements in clinical and biological outcomes were not consistent across studies and appeared to depend on the endpoints assessed and specific study characteristics. The characteristics and main findings of the included studies are presented in Table 2 and provide the basis for the following analysis.

Table 2. Summary of Studies Evaluating the Effectiveness of Vitamin D Supplementation in Children with ADHD

No	Source/Study Design	Population	Intervention	Comparison	Outcome	Main Finding
1	Samadi et al., 2022 (19) RCT	Children 6–12 years with ADHD, on methylphenidate <1 year N = 75	Vitamin D3 2000 IU/day 3 months	Placebo 3 months	IL-6, TNF- α , 25(OH)D	Significant reduction in IL-6 and/or TNF- α levels in intervention group compared to placebo ($p < 0.05$). Serum 25(OH)D significantly increased.
2	Honarvar et al., 2022 (20) RCT	Children 6–12 years with ADHD on methylphenidate <1 year N = 75	Vitamin D3 2000 IU/day 3 months	Placebo 3 months	PON-1, TAC, 8-Isoprostane, 25(OH)D	Serum 25(OH)D significantly increased ($p < 0.001$). No statistically significant differences in oxidative stress markers between groups ($p > 0.05$).
3	Hemamy et al., 2021(14) RCT	Children with ADHD on methylphenidate N = 66	Vitamin D 50,000 IU/week Magnesium 6 mg/kg/day 8 weeks	Placebo 8 weeks	25(OH)D	Serum levels of 25-hydroxyvitamin D3 and magnesium increased significantly in the intervention group compared to the control group. Also, a significant improvement in the behavioral function and mental health of children with ADHD was shown by children who received vitamin D plus magnesium.
4	Dehbokri et al., 2019 (18) RCT	Children with ADHD	Vitamin D (50,000 IU/week) 6 weeks	Placebo 6 weeks	ADHD scores, 25(OH)D	There was a significant increase in serum 25(OH)D levels ($p < 0.05$) and a significant improvement in ADHD symptoms, especially inattention, compared to the placebo group.

5	Elshorbagy et al., 2018 (12) RCT	Children with ADHD N= 50	Vitamin D	Without Vitamin D	ADHD severity, 25(OH)D	There was a significant lower serum vitamin D levels than controls (p = 0.0009). Vitamin D supplementation in deficient children was associated with improvement in cognitive function and behavioral domains (inattention, hyperactivity, impulsivity).
6	Mohammadpour et al., 2018 (15)	Children (5–12 years) with ADHD, all receiving methylphenidate N= 62	Vitamin D3 2000 IU/day + methylphenidate 8 weeks	Placebo + methylphenidate 8 weeks		There was a significant increase in serum 25(OH)D levels. The evening ADHD symptoms improved (as measured by the WPREMB), but there was no significant effect on the CPRS or ADHD-RS scores compared with the placebo.

Four trials evaluated ADHD symptom severity or behavioral outcomes as primary clinical endpoints. Significant improvements in ADHD symptoms, particularly inattention, were reported following weekly vitamin D supplementation (18). Similarly, children with ADHD were found to have significantly lower baseline vitamin D levels compared with controls, and supplementation in deficient children was associated with improvements in cognitive and behavioral domains, including inattention, hyperactivity, and impulsivity (12). Improved behavioral function and mental health outcomes were also observed when vitamin D was administered in combination with magnesium (14). However, because vitamin D was provided alongside magnesium, the independent effect of vitamin D alone cannot be clearly determined. In contrast, no significant reduction in total ADHD rating scale scores was found despite marked increases in serum 25(OH)D concentrations, although improvements were noted in evening behavioral symptoms (15). These findings suggest that vitamin D supplementation may influence specific symptom domains rather than producing a generalized reduction in overall ADHD severity.

These differences in clinical outcomes may reflect variations in study design and intervention characteristics, including differences in vitamin D dosage, duration of supplementation (ranging from 6 weeks to 3 months), and the outcome measures used to assess ADHD symptoms. Such variability highlights the diversity of approaches used in the included trials and provides important context when interpreting the overall findings.

Importantly, four of the six trials involved children who were already receiving methylphenidate, meaning that vitamin D was primarily evaluated as an adjunctive therapy rather than as a standalone treatment. Therefore, the observed improvements may reflect an additive or supportive effect alongside stimulant medication rather than an independent therapeutic action. This also suggests a potential complementary role of vitamin D in enhancing treatment outcomes when used in combination with standard therapy.

Two trials evaluated biological markers as primary outcomes. Reductions in pro-inflammatory cytokines following vitamin D supplementation have been reported, suggesting a potential role of vitamin D in modulating inflammatory processes in children with ADHD (19). In contrast, no significant changes were observed in oxidative stress markers including paraoxonase-1, total antioxidant capacity, and 8-isoprostane despite improved vitamin D status (20). These findings indicate that the biological effects of vitamin D may be pathway specific and warrant further investigation.

Despite the heterogeneity of supplementation protocols across studies, the correction of vitamin D deficiency was consistently achieved. However, clinical responses varied. Intervention durations ranged from six weeks to three months, which may not have been sufficient to produce sustained neurobehavioral changes. In addition, most studies included relatively small sample sizes, potentially limiting statistical power and contributing to variability in findings. Evidence from observational and meta-analytic studies further supports an association between vitamin D status and ADHD. Significantly lower serum 25(OH)D levels have been reported in children with ADHD compared with healthy controls, and vitamin D concentrations have been found to be negatively correlated with SNAP-IV scores. Children presenting with concurrent vitamin A and

vitamin D deficiencies demonstrated greater inattention and overall symptom severity, suggesting that combined micronutrient deficiencies may influence symptom expression (21).

Small but statistically significant reductions in total ADHD scores, including inattention and hyperactivity, have been observed following vitamin D supplementation (22). A meta-analysis of 13 observational studies found that children with ADHD had significantly lower serum vitamin D concentrations, and low vitamin D status was associated with an increased risk of ADHD. Suboptimal perinatal vitamin D levels were also linked to a higher likelihood of ADHD later in life (13). Consistently lower serum 25(OH)D concentrations have also been reported across multiple clinical studies involving children with ADHD (22).

More recently, a comprehensive meta-analysis of 37 studies reported a pooled mean difference of -6.55 ng/mL in serum vitamin D concentrations between ADHD and control groups. Vitamin D deficiency was associated with nearly a twofold increased risk of ADHD, and maternal deficiency during pregnancy was significantly linked to ADHD risk in offspring. Importantly, pooled analyses of randomized trials demonstrated modest but statistically significant improvements in total ADHD scores and inattention symptoms following supplementation, whereas findings for hyperactivity remained inconsistent (23).

Additional clinical evidence indicated that approximately half of supplemented participants experienced improvement in symptom scores, and greater increases in serum 25(OH)D levels were associated with greater symptom reduction. However, not all children responded to supplementation, suggesting heterogeneity in treatment effects and indicating that vitamin D deficiency may act as a modifying factor influencing symptom severity rather than serving as a primary etiological cause of ADHD (21).

Although several studies assessed comparable clinical outcomes, a quantitative meta-analysis was not performed in this review due to differences in intervention protocols, duration, and the use of combination therapies, which may affect the comparability of pooled results. Therefore, a qualitative synthesis was considered appropriate to provide a balanced interpretation of the available evidence.

Overall, current evidence indicates that vitamin D supplementation reliably improves serum 25(OH)D concentrations and may provide modest benefits in certain ADHD symptom domains, particularly inattention and when used as an adjunct to stimulant therapy. While clinical effects are not uniform, these findings highlight the potential role of vitamin D as a supportive therapeutic option. Future well-designed randomized controlled trials with standardized protocols and longer durations are needed to further clarify the clinical effectiveness and independent role of vitamin D supplementation.

CONCLUSION

The findings of this systematic review indicate that vitamin D supplementation in children with ADHD consistently improves serum 25(OH)D levels but demonstrates inconsistent effects on clinical symptom improvement. Although some evidence suggests modest benefits in specific symptom domains, particularly inattention, overall reductions in total ADHD severity were not consistently observed.

Therefore, based on currently available randomized controlled trials, vitamin D supplementation cannot be definitively considered an effective standalone treatment for ADHD. However, it may offer potential benefits when used alongside other treatments, especially for children with vitamin D deficiency. Researchers need to conduct further high quality, large scale randomized controlled trials to strengthen the evidence and clarify its clinical role.

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