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Effectiveness and Safety of Vitamin D3 Supplementation in Children Across India: A Retrospective Real-World Evidence Study

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Abstract

Objective: To assess the real-world effectiveness and safety of vitamin D3 supplementation in children. ***Design:*** A retrospective, multicentre, observational real-world evidence study. ***Subjects/Patients:*** Children aged 0–12 years with documented vitamin D deficiency who received vitamin D3 supplementation for at least two months were included. ***Methods:*** Data from electronic health records (2014–2024) were analyzed. Outcomes assessed included changes in serum vitamin D levels, clinical improvements, and adverse effects. ***Results:*** A total of 1,942 children were evaluated. Mean serum vitamin D levels significantly increased from 18.01 ng/mL (±8.73) to 35.29 ng/mL (±13.53) following supplementation ($p < 0.001$). Greater improvement was observed in children with poorer baseline health. Adverse events were reported in only 0.21% of participants, and were mild, primarily involving transient gastrointestinal symptoms. ***Conclusion:*** Vitamin D3 supplementation is effective in correcting vitamin D deficiency and improving health outcomes in children, with minimal side effects. These findings offer valuable real-world evidence supporting its clinical use in Indian pediatric populations. Further randomized controlled trials are recommended to confirm these results and guide optimal dosing strategies.

Keywords: ***Cholecalciferol, Pediatric health, Serum vitamin D level, Vitamin D deficiency.***

Introduction

Vitamin D is an essential nutrient required by children to regulate calcium metabolism and bone health. Vitamin D deficiency poses a significant burden on healthcare systems globally, particularly in the pediatric population [1]. A recent epidemiological analysis estimated the global vitamin D deficiency, defined by serum 25-hydroxyvitamin D (25(OH)D) concentrations less than 30 nmol/L, to be prevalent in 15.7% of the general population between 2000-2022 [2]. Approximately 490 million individuals in India are affected by vitamin D deficiency, with children and adolescents comprising around 31% of this population [3]. Numerous studies conducted across diverse regions of India consistently report significantly higher prevalence of vitamin D deficiency across all pediatric ages. This condition affects 62% to 95.7% of neonates and breastfed infants aged 0-6 months, 46% to 80% aged 0.5-5 years, and 37.8% to 97.5% aged 5-20 years [4]. The aforementioned data highlights the substantial burden of vitamin D deficiency among children in India.

According to Indian and international guidelines concerning vitamin D, concentrations of serum 25(OH)D are classified as sufficient when exceeding 50 nmol/L as sufficient, insufficient when between 30 and 50 nmol/L, and concentrations below 30 nmol/L are deficient within the pediatric and adolescent populations [5]. Prolonged or severe vitamin D deficiencies impair intestinal absorption of crucial minerals such as calcium and phosphorus [6]. An extended period of malabsorption causes hypocalcemia, triggering secondary hyperparathyroidism, thereby increasing urinary phosphate excretion and accelerating skeletal demineralization. The interplay of these underlying mechanisms can contribute to the development of osteomalacia and osteoporosis in adults, whereas in children, it presents as rickets and osteomalacia[6].

The primary source of vitamin D is sunlight exposure to skin, and the consumption of vitamin D precursors as a part of the diet. However, vitamin D deficiency remains prevalent even in regions with adequate ultraviolet (UV) radiation and in developed countries with established vitamin D fortification programs aimed at mitigating this deficiency [7]. Notably, despite receiving significant sun exposure and UV radiation throughout the year, a subcontinent like India reports alarmingly high number of cases with vitamin D deficiency. This scenario is believed to occur due to a combination of factors, including limited direct exposure to sunlight, deficient diet, increased skin pigmentation, air pollution reducing UV penetration, genetic predisposition, and a higher body fat distribution [8,9]. Dietary factors that may contribute to an elevated risk of vitamin D deficiency include inadequate intake of vitamin D and calcium, excessive consumption of phytates and phosphates,

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caffeine intake, and lactose intolerance [10]. These factors collectively predispose children in India to vitamin D deficiency, underscoring the need for proactive management strategies.

The Indian Academy of Pediatrics (IAP) provides age-specific guidelines for vitamin D supplementation. Recommended daily dosages include 2,000 international units (IU) for neonates and children aged between 1 month and 1 year, and 3,000-6,000 IU for children and adolescents aged 1-18 years [11]. However, excessive supplementation may result in hypercalcemia and hypercalciuria, which leads to gastrointestinal symptoms, fatigue, neuropsychiatric disturbances, and in severe cases, renal failure [12].

Therefore, controlled supplementation is recommended to improve vitamin D levels while minimizing any chances of developing adverse effects. Vitamin D deficiency is highly prevalent in India but often goes undiagnosed and untreated. Furthermore, there is a lack of clinical studies addressing the safety and effectiveness of vitamin D3 supplementation as a therapy for vitamin D-deficient children. To bridge the gap, the present retrospective study focuses on the evaluation of the real-world impact of vitamin D3 supplementation in children, by investigating the changes in serum blood vitamin D levels, symptom resolution, and the incidence of any adverse events.

Methods

Study design

The present study is a retrospective multi-center study evaluating the effectiveness of vitamin D3 supplementation in the Indian pediatric population with documented deficiency or associated symptoms. Data was collected from electronic health records across multiple centers (167) in India, spanning a period of 10 years from March 2014 to March 2024.

Study population

The study population includes: 1) Children aged 0 to 12 years, 2) A confirmed clinical diagnosis of vitamin D deficiency or exhibited symptoms suggestive of deficiency, and 3) Those who have received vitamin D3 supplementation for at least two months during the study period. Patients with medical conditions affecting vitamin D metabolism or incomplete medical records were excluded.

Data collection

Data was collected from electronic health records, including demographic information, clinical data, co-morbidities, and adverse events. Patient demographics included age, height, weight, and gender. The overall health was assessed using a self-rated health (SRH) scale for child ageing ≥8 years and the parent proxy scale for those children ageing less than 8 years [13,14] at baseline and post vitamin D3 supplementation. It was categorized as excellent, very good, good, fair, poor and very poor. The serum 25(OH) vitamin D levels were measured at baseline and post vitamin D3 supplementation. Any adverse events that occurred during the supplementation period were also documented.

Data analysis

Both descriptive and inferential statistics were applied. Descriptive statistics were applied to assess self-reported overall health and calculated as percentage changes with mean and SD. Continuous variables such as age, height, weight, and serum 25(OH) vitamin D levels were reported as means and standard deviations (SD). The categorical variables were represented as frequencies and percentages. Paired t-tests were performed to compare baseline and endpoint levels. Statistical Package for the Social Sciences [SPSS], Version 26 was used for carrying out the statistical analyses, with a significance threshold set at 5%.

Ethical Considerations

The study ensured ethical conduct by complying with the ethical principles outlined in the Declaration of Helsinki, prioritizing the rights, well-being, and confidentiality of participants. Approval from the local institutional ethics committee was taken before initiating the study for all sites. All collected data was anonymized to protect patient confidentiality. Strict measures were undertaken to secure and maintain data integrity. Informed consent was waived due to the retrospective nature of the study.

Results

Demographic data

The study population consisted of 1,942 participants, with a mean age of 6.03 years (± 4.28). Among the participants, males represented 65.40% (n = 1,272), while females accounted for 34.45% (n = 670). The average height and weight were 102.13 (± 29.98) cm and 22.70 (± 15.87) kg, respectively.

Efficacy of Vitamin D3 Supplementation

The primary efficacy outcome showed a marked improvement in serum Vitamin D levels following supplementation. The mean Vitamin D levels at baseline were 18.01 ng/mL (± 8.73), significantly increasing to 35.29 ng/mL (± 13.53) at the endpoint ($p = 0.001$) as shown in Table 1.

General Health Outcomes

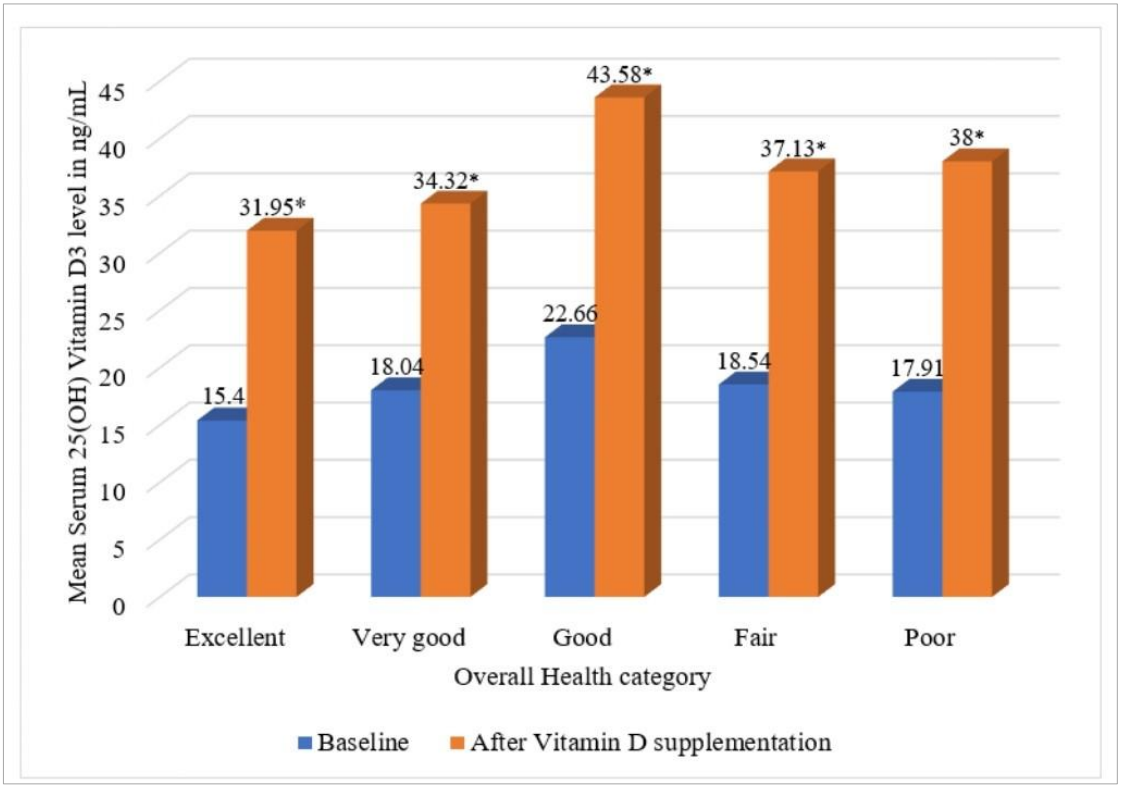
Post-supplementation assessments revealed significant improvements in self-reported general health. A substantial proportion of participants rated their health as "Excellent" (36.40%) or "Very Good" (34.24%), while only a small fraction reported "Fair" (9.05%) or "Poor" (4.11%). Further analysis of health outcomes based on Vitamin D levels demonstrated a consistent pattern of improvement across all health categories. Participants in the "Excellent" health category experienced a mean increase of 16.55 ng/mL in Vitamin D levels ($p = 0.001$), while those in the "Poor" category exhibited an even larger mean increase of 20.09 ng/mL ($p = 0.001$). Notably, this trend underscores the responsiveness of individuals with poorer health to supplementation, indicating a potentially greater benefit for those starting with lower baseline health scores. Across all categories, the increases in Vitamin D levels were statistically significant (**Figure 1**).

Safety Profile

The safety assessment indicated that the supplementation regimen was highly tolerable. An overwhelming majority of participants (99.79%) reported no adverse events. Only a minimal proportion (0.21%, n = 4) experienced mild gastrointestinal symptoms, which were transient and self-limiting.

Table 1: Change in the Serum Vitamin D levels after Vitamin D3 supplementation

Vitamin D	Number (N)	Mean	Standard deviation (SD)	p value
Baseline	1718	18.01	8.73	0.001*
Endpoint	1406	35.29	13.53	
* p value significant at 95% CI calculated through paired t test				



*Paired T test applied, *p value =<0.001*

Fig. 1: Improvement in Mean Serum 25(OH) Vitamin D levels after vitamin D3 supplementation in overall health categories

Discussion

This real-world, retrospective study highlights the effectiveness and safety of vitamin D3 supplementation in addressing vitamin D deficiency among Indian children. The observed significant increase in mean serum 25(OH)D levels-from a baseline of 18.01 ng/mL to 35.29 ng/mL-confirms the therapeutic benefit of supplementation. Notably, children with poorer initial health experienced greater increases in serum levels, suggesting that the degree of baseline deficiency may predict a more pronounced response. Beyond biochemical improvement, a majority of participants reported enhancements in general well-being, bone development, and immune function. The relationship between improved serum levels and clinical outcomes aligns with current understanding of the multifaceted role of vitamin D in pediatric physiology, particularly in supporting musculoskeletal and immune health.

As per the recent guidelines of the Indian Academy of Pediatrics released in 2022, patients are classified as deficient, insufficient, or sufficient when the serum 25(OH) Vitamin D levels are <12, <20, and >20 ng/ml respectively [5]. In our cohort, mean post-supplementation levels surpassed this threshold, indicating successful correction of deficiency. Prior studies corroborate these outcomes. For example, Forno et al. (2020) observed a significant rise in serum 25(OH)D in asthmatic children after supplementation, with 94.4% of treated patients achieving sufficiency versus only 40.7% in the placebo group [15]. Similarly, Javadfar et al. (2020) demonstrated a mean increase of over 30 ng/mL in children with autism following vitamin D3 therapy [16].

Pediatric patients also reported significant improvements in immunity after vitamin D3 supplementation. Previous research has elucidated the role of vitamin D supplementation in enhancing immune function across various conditions. In patients with chronic renal failure and vitamin D-resistant rickets, impaired natural killer (NK) cell activity has been observed. Supplementation with the active form of vitamin D, 1,25-dihydroxyvitamin D (1,25D), has been shown to restore and normalize NK cell functionality in these individuals, highlighting its immunomodulatory potential [17,18]. A meta-analysis demonstrated that daily or weekly supplementation significantly reduces the number of episodes of acute respiratory tract infections [18].

Additionally, Castillo et al. (2020) reported a marked reduction in the need for intensive care unit admission among patients receiving oral vitamin D supplementation. Only 1 out of 50 supplemented patients required ICU care, compared to 13 out of 26 in the control group [19]. A growing body of evidence supports the role of vitamin D supplementation in alleviating infection rates in pediatric populations. Emerging research also points to its protective effects against autoimmune disorders, asthma, and other allergic conditions [20]. Based on present findings along with existing research, vitamin D supplementation represents a vital intervention for improving immune function, preventing infections, and mitigating the risk of immune-related disorders in children.

The majority of the participants reported an improvement in their bone health. Contrary to the present study, Ganmaa et al. (2017) reported the results from two randomized trials enrolling 113 children, 12 to 15 years of age with severe vitamin D deficiency [21]. The study aimed to assess the impact of supplementation on the overall growth of the children. However, changes in various growth parameters like the body mass index (BMI), height, and weight were statistically insignificant, when compared between the supplementation and placebo groups. There was a lack of growth despite the increase in serum vitamin D levels in the supplementation group [22]. Nonetheless, this difference can be attributed to the discrepancy within the dosing regimen, where they administered a low dose of 800 IU per day, while the present study administered 4000 IU per day. Therefore, high doses of vitamin D potentially improve bone health and function.

Vitamin D deficiency plays a critical role in the pathogenesis of osteoporosis through its active metabolite, 1,25 dihydroxy Vitamin D [Calcitriol]. This biologically active form is crucial for

regulating mineral metabolism and bone remodeling, exerting its effects by modulating the structure and function of osteoblasts and osteoclasts [22]. These two cells are the predominant structures, present in the bones. Additionally, vitamin D deficiency is a primary determinant of developing rickets, a clinical condition in children characterized by delayed or failed mineralization of growth plates in developing bones. This condition is frequently reported in children under the age of two, with the highest incidence occurring between 3 and 18 months of age [23]. Based on the clinical relevance of vitamin D deficiency in causing severe bone defects, vitamin D supplementation is an important approach to maintaining bone health and preventing severe skeletal disorders. This therapy is particularly crucial in children, whose growing bones are highly susceptible to the adverse effects of vitamin D deficiency. Skeletal disorders at such a young age can lead to permanent impairments, significantly affecting quality of life. Therefore, proactive management of vitamin D deficiency, including vitamin D3 supplements, is essential to safeguard healthy bone development and long-term well-being.

The present study population did not observe any severe adverse events, while only 0.2% reported mild gastrointestinal disorders. These symptoms were transient and not significantly associated with vitamin D supplementation. These findings are in alignment with a previous meta-analysis that studied vitamin D supplementation safety profile. The study revealed no significant correlation between high doses of vitamin D supplementation and the incidence of severe adverse events or death.22 While few events were seen, the rate of incidence was similar between the supplementation and control groups. Furthermore, hypercalcemia, which is a known risk of vitamin D supplementation was higher in those receiving a bolus dose compared to daily low doses [24]. Therefore, the absence of adverse events can be due to daily dosing and avoiding vitamin D levels exceeding 50 ng/ml. Overall, supplementation demonstrated a good safety profile, with no serious episodes of adverse events.

The present study is a valuable addition to the literature, as the data on vitamin D supplementation as a therapy for deficiency in children is limited, and even scarce in Indian patients. The study gathered first-hand information about the patients, providing results based on real-world supplementation. A large sample population was enrolled which strengthens the reliability of the findings. Furthermore, a multi-center approach generalizes the result to the broad patient population of India. The efficacy and safety data of vitamin D supplementation provided by the present investigation are valuable for pediatric physicians in managing vitamin D deficiency.

Certain limitations of the study must be considered. First, the observational study design limits the quality of evidence, requiring randomized clinical trials to definitively establish the effectiveness and safety of vitamin D3 supplementation. Second, there may exist potential confounding factors such as BMI, comorbidities, and other health-related variables, which were not accounted for in the study, potentially influencing the outcomes. Third, the study did not collect data on drug compliance, leaving uncertainties about adherence to the supplementation regimen among participants. Fourth, a comparator group or control group is absent, which restricts the ability to evaluate the intervention against standard practices or alternative approaches. These limitations highlight the need for future controlled studies to validate the findings and address these gaps.

In conclusion

The present study findings provide evidence supporting the effectiveness and safety of vitamin D3 supplementation in addressing pediatric vitamin D deficiency in India. An increase in serum vitamin D levels improves bone development, immunity, and general health outcomes, which were statistically significant. The supplementation regimen demonstrated an excellent safety profile, with only mild and transient gastrointestinal adverse events reported in a small percentage of participants. This study contributes valuable real-world data, addressing a significant gap in the literature concerning pediatric vitamin D3 supplementation in India. However, future randomized controlled trials should be conducted to explore optimal dosing strategies and improve therapeutic approaches for vitamin D deficiency in children.

Declarations

Conflict of interest declaration

None

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Nil

Contributors

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Ethical Clearance

Approved

Trial details

A retrospective, multicentre, observational real-world evidence study

Supplementary Material

None

References

[1] Antonucci R, Locci C, Clemente MG, Chicconi E, Antonucci L. Vitamin D deficiency in childhood: old lessons and current challenges. J Pediatr Endocrinol Metab. 2018;31:247-260. doi:10.1515/jpem-2017-0391

[2] Cui A, Zhang T, Xiao P, Fan Z, Wang H, Zhuang Y. Global and regional prevalence of vitamin D deficiency in population-based studies from 2000 to 2022: A pooled analysis of 7.9 million participants. Front Nutr. 2023;10:1070808. doi:10.3389/fnut.2023.1070808

[3] Cashman KD, Sheehy T, O'Neill CM. Is vitamin D deficiency a public health concern for low middle income countries? A systematic literature review. Eur J Nutr. 2019;58(1):433-453. doi:10.1007/s00394-018-1607-3

[4] Surve S, Chauhan S, Amdekar Y, Joshi B. Vitamin D deficiency in Children: An update on its Prevalence, Therapeutics and Knowledge gaps. Indian J Nutr. 2017;4:167

[5] Gupta P, Dabas A, Seth A, et al. Indian Academy of Pediatrics Revised (2021) Guidelines on Prevention and

Treatment of Vitamin D Deficiency and Rickets. Indian Pediatr. 2022;59:142-158.

[6] Sizar O, Khare S, Goyal A, Givler A. Vitamin D Deficiency - StatPearls - NCBI Bookshelf. StatPearls Publ. Published online 2024.

[7] Palacios C, Gonzalez L. Is vitamin D deficiency a major global public health problem? J Steroid Biochem Mol Biol. 2014;144 Pt A:138-145. doi:10.1016/j.jsbmb.2013.11.003

[8] Aparna P, Muthathal S, Nongkynrih B, Gupta S. Vitamin D deficiency in India. J Fam Med Prim Care. 2018;7:324. doi:10.4103/jfmpc.jfmpc_78_18

[9] Mandlik R, Kajale N, Ekbote V, et al. Determinants of Vitamin D status in Indian school-children. Indian J Endocrinol Metab. 2018;22:244. doi:10.4103/ijem.IJEM_622_17

[10] Khadilkar A, Kajale N, Oza C, et al. Vitamin D status and determinants in Indian children and adolescents: a multicentre study. Sci Rep. 2022;12:16790. doi:10.1038/s41598-022-21279-0

[11] Khadilkar A, Khadilkar V, Chinnappa J, et al. Prevention and treatment of vitamin D and calcium deficiency in children and adolescents: Indian Academy of Pediatrics (IAP) guidelines. Indian Pediatr. 2017;54:567-573. doi:10.1007/s13312-017-1070-x

[12] Galior K, Grebe S, Singh R. Development of Vitamin D Toxicity from Overcorrection of Vitamin D Deficiency: A Review of Case Reports. Nutrients. 2018;10:953. doi:10.3390/nu10080953

[13] Idler EL, Benyamini Y. Self-rated health and mortality: a review of twenty-seven community studies. J Health Soc Behav. 1997;38:21–37. doi: 10.2307/2955359.

[14] Zhang, T., Lu, G. & Wu, X.Y. Associations between physical activity, sedentary behaviour and self-rated health among the general population of children and adolescents: a systematic review and meta-analysis. BMC Public Health 20, 1343 (2020). https://doi.org/10.1186/s12889-020-09447-1

[15] Forno E, Bacharier LB, Phipatanakul W, et al. Effect of Vitamin D3 Supplementation on Severe Asthma Exacerbations in Children With Asthma and Low Vitamin D Levels: The VDKA Randomized Clinical Trial. JAMA. 2020;324:752. doi:10.1001/jama.2020.12384

[16] Javadfar Z, Abdollahzad H, Moludi J, et al. Effects of vitamin D supplementation on core symptoms, serum serotonin, and interleukin-6 in children with autism spectrum disorders: A randomized clinical trial. Nutrition. 2020;79-80:110986. doi:10.1016/j.nut.2020.110986

[17] Kamboj P, Dwivedi S, Toteja GS. Prevalence of hypovitaminosis D in India & way forward. Indian J Med Res. 2018;148:548-556. doi:10.4103/ijmr.IJMR_1807_18

[18] Martineau AR, Jolliffe DA, Greenberg L, et al. Vitamin D supplementation to prevent acute respiratory infections: individual participant data meta-analysis. Health Technol Assess Winch Engl. 2019;23:1-44. doi:10.3310/hta23020

[19] Entrenas Castillo M, Entrenas Costa LM, Vaquero Barrios JM, et al. "Effect of calcifediol treatment and best available therapy versus best available therapy on intensive care unit admission and mortality among patients hospitalized for COVID-19: A pilot randomized clinical study." J Steroid Biochem Mol Biol. 2020;203:105751. doi:10.1016/j.jsbmb.2020.105751

[20] Mailhot G, White JH. Vitamin D and Immunity in Infants and Children. Nutrients. 2020;12:1233. doi:10.3390/nu12051233

[21] Ganmaa D, Stuart JJ, Sumberzul N, et al. Vitamin D supplementation and growth in urban Mongol school children: Results from two randomized clinical trials. Van Wouwe JP, ed. PLOS ONE. 2017;12:e0175237. doi:10.1371/journal.pone.0175237

[22] Goltzman D. Functions of vitamin D in bone. Histochem Cell Biol. 2018;149:305-312. doi:10.1007/s00418-018-1648-y

[23] Pettifor JM, Thandrayen K, Thacher TD. Vitamin D Deficiency and Nutritional Rickets in Children. In: Vitamin D. Elsevier; 2018:179-201. doi:10.1016/B978-0-12-809963-6.00067-5

[24] Brustad N, Yousef S, Stokholm J, Bønnelykke K, Bisgaard H, Chawes BL. Safety of High-Dose Vitamin D Supplementation Among Children Aged 0 to 6 Years: A Systematic Review and Meta-analysis. JAMA Netw Open. 2022;5:e227410. doi:10.1001/jamanetworkopen.2022.7410