Journal of Carcinogenesis
Covering Genesis to Therapeutics

Journal of Carcinogenesis, ISSN: 1477-3163
2025; Vol 24: Issue 6s, https://carcinogenesis.com/

# Comparison of Different Vitamin D Supplementation Regimens in the Management of Hypovitaminosis D among Children Aged 1 to 5 Years: An Observational Study

**Shrikant M Mane[1], Anuja U Paul[2]**

[1]Consultant Paediatric Cardiologist, Paediatric Cardiology, KIMS- UAIMS Hospital, Sangli

[2]Assistant Professor, Department of Pathology, Bharati Vidyapeeth [Deemed to be University] Medical College & Hospital, Sangli

Corresponding Author:

Name: Dr Anuja U Paul

Designation: Assistant Professor

Department: Department of Pathology

Institute: Bharati Vidyapeeth [Deemed to be University] Medical College & Hospital, Sangli

Mail ID: paul.uddhav@gmail.com

## ABSTRACT

**Background:** The management of hypovitaminosis D requires therapeutic supplementation of vitamin D along with calcium. In India, a single oral dose of 600,000 IU vitamin D is commonly prescribed for hypovitaminosis D and rickets, as no standardized national guideline exists. This study aimed to compare the efficacy and safety of three different vitamin D regimens—300,000 IU single dose, 600,000 IU single dose, and 60,000 IU weekly for 10 weeks—in children aged 1 to 5 years with documented hypovitaminosis D.

**Methods:** This observational study included children between 1–5 years diagnosed with hypovitaminosis D. Participants were grouped based on supplementation regimen: (i) 60,000 IU sachet weekly for 10 weeks, (ii) 300,000 IU stat orally, and (iii) 600,000 IU stat orally. Serum vitamin D levels were assessed before and after therapy.

**Results:** All three regimens resulted in significant improvement in serum vitamin D levels. The highest proportion of children achieving sufficiency was observed in the 600,000 IU stat group. However, two cases of hypervitaminosis D occurred in this group. Comparatively, both the 60,000 IU weekly and 300,000 IU stat regimens showed effective correction of deficiency with a safer profile.

**Conclusion:** While all three vitamin D regimens are effective in treating hypovitaminosis D in young children, the 600,000 IU stat regimen is associated with a risk of hypervitaminosis. Therefore, 60,000 IU weekly or 300,000 IU stat dosing may be safer alternatives.

***Keywords:*** *Vitamin D Deficiency, Cholecalciferol, Preschool, Dose-Response Relationship, Hypervitaminosis D.*

**How to Cite:** Shrikant M Mane, Anuja U Paul., (2025) Comparison of Different Vitamin D Supplementation Regimens in the Management of Hypovitaminosis D among Children Aged 1 to 5 Years: An Observational Study, *Journal of Carcinogenesis*, *Vol.24, No.6s*, 341-345.

## 1. INTRODUCTION

Vitamin D, often termed the “sunshine hormone,” is synthesized in human skin following exposure to ultraviolet-B (UVB) radiation and subsequently activated to exert its biological functions. Historically described as the anti-rachitic factor or sunlight vitamin, it is now recognized as a steroid hormone regulating a wide spectrum of genetic and cellular processes.[1,2] These include inhibition of excessive cell proliferation, promotion of cell differentiation, modulation of immune responses, and protection of normal cells against malignant transformation.

Vitamin D is unique among vitamins because it can be synthesized endogenously and also functions as a hormone. It regulates the production of proteins that control the cell cycle, thereby slowing uncontrolled growth and facilitating the maturation of specialized cells, including osteoblasts, enterocytes, and keratinocytes. This regulatory role explains its involvement in bone resorption and intestinal calcium absorption. In addition, its immunomodulatory effects may influence host responses to infections, providing a potential explanation for the association between hypovitaminosis D and conditions such as type 2 diabetes, autoimmune diseases, tuberculosis, and certain malignancies [3]

Dietary sources of vitamin D are limited, with fish liver oils, egg yolks, shiitake mushrooms, liver, and organ meats serving as the most relevant contributors. Nonetheless, cutaneous synthesis remains the predominant source, accounting for nearly 90% of total vitamin D acquisition.[4]

Despite abundant sunlight, vitamin D deficiency is highly prevalent in India and represents the most common nutritional deficiency worldwide. Several factors contribute to this paradox, including traditional clothing practices, darker skin pigmentation, urbanization, indoor lifestyles, air pollution, vegetarian dietary habits, limited food fortification, and socioeconomic barriers. The management of hypovitaminosis D typically requires supplementation with therapeutic doses of vitamin D, often combined with calcium. In India, single-dose regimens of 600,000 IU are frequently used in the treatment of hypovitaminosis D and rickets, although no formal national guidelines currently exist. The recommended dosing and duration of vitamin D supplementation vary globally, largely based on expert consensus rather than robust clinical evidence.[5]

The present study aimed to evaluate the efficacy of different supplementation regimens—300,000 IU single dose, 600,000 IU single dose, and 60,000 IU weekly for 10 weeks—in children aged 1 to 5 years with confirmed hypovitaminosis D.

## 2. MATERIALS AND METHODS

This observational study encompassed 124 children aged 1 to 5 years, diagnosed with vitamin D deficiency at the pediatric outpatient department of Lilavati Hospital, Mumbai, from November 2013 to November 2014. The study was approved by Institutional Ethics Committee - Lilavati Hospital and Research Centre. We included children with suspected and confirmed hypovitaminosis D (less than 30 ng/dl) in the study. The study excluded individuals with renal disease, hepatic disorders, lipid malabsorption, parathyroid diseases, and those undergoing calcium and vitamin D supplements. Upon obtaining parental consent, we collected comprehensive data regarding indicators of vitamin D deficiency, including irritability, weakness, leg cramps, frontal sweating, recurrent colds, a pronounced forehead, and broader wrists, in addition to measuring their weight and height/length. Thorough general and systemic assessments were performed. The children involved in the study were categorized into three groups. Group A consists of 44 children administered 60,000 IU of vitamin D, Group B includes 41 children administered 300,000 IU of vitamin D, and Group C comprises 39 children administered 600,000 IU of vitamin D. Blood samples were taken at the start of the study to check the vitamin D levels in children who might have low vitamin D. Children with low vitamin D levels were randomly given vitamin D supplements, which included 60,000 IU sachets for 10 weeks, a one-time dose of 300,000 IU of arachitol, and a one-time dose of 600,000 IU of arachitol, along with calcium supplements like Syp. Calcimax for 3 months. After three months, blood concentrations of vitamin 25(OH)D were re-evaluated for all participating children.

Venous blood samples were collected from participants to assess serum 25(OH)D concentrations. The Elecsys and Cobas e (Roche/Hitachi) apparatus employed a specialized testing technique known as electrochemiluminescence immunoassay (ECLIA) to quantify the concentration of 25(OH)D in the bloodstream. The minimal detection threshold of this method was 3 ng/ml.

The reference range for serum vitamin D levels is as follows: deficiency is defined as below 20 ng/ml, insufficiency ranges from 20 to 30 ng/ml, and sufficiency is classified as 30 to 100 ng/ml. Qualitative data were expressed as frequency and percentage. The relationship between different categories was examined using the chi-square test with a correction for all $2 \times 2$ tables, and Fisher's exact test was employed for $2 \times 2$ tables when the chi-square test results were unreliable due to small sample sizes. Data from adjacent rows of tables exceeding 2x2 were combined, and the chi-square test was repeated if more than 20.0% of the cells had an expected count of fewer than 5. Quantitative data were presented as mean ± standard deviation and median with interquartile range (IQR). The comparison of quantitative data across the three treatment groups was conducted using one-way ANOVA, provided the data met the normality criterion. If the data didn't meet the normality requirement, the Kruskal-Wallis test was used, along with a suitable follow-up test if the RM ANOVA p-value showed significant results. Pre- and post-treatment vitamin D levels (ng/ml) in each treatment group were examined using a paired t-test if the data was normally distributed, and the Wilcoxon signed-rank test if it was not. Results were visually shown where applicable. The majority of analyses were performed utilizing SPSS Version 17. Our study determined an efficient vitamin D dosage that elevates blood levels to between 30-100 ng/ml after three months of supplementation, with safety criteria demonstrating that this dosage does not increase vitamin D levels beyond 100 ng/ml.

## 3. RESULTS:

This observational study included 124 children aged 1–5 years with hypovitaminosis D. The mean age was 2.9 years; 62 (50.0%) were between 1–3 years and 62 (50.0%) between 3–5 years. Males comprised 51.6% of the cohort. Of the total, 84 children (67.7%) were classified as vitamin D deficient (<20 ng/ml), while 40 (32.3%) were insufficient (20–30 ng/ml). The mean height and weight were 93.19 cm and 13.86 kg, respectively, with a mean pre-treatment vitamin D level of 16.21 ng/ml. The most common clinical manifestations were frontal bossing (92.7%) and recurrent respiratory infections (87.9%), followed by wrist widening (72.6%), leg cramps (65.3%), weakness (62.9%), forehead sweating (26.6%), irritability (22.6%), and bow legs (17.7%) (Table 1).

Children were distributed evenly across treatment groups according to age and baseline vitamin D status (Table 2). In the 60,000 IU weekly group, 33 (75.0%) achieved sufficiency, 5 (11.4%) remained insufficient, and 6 (13.6%) remained deficient; no cases of hypervitaminosis D were observed. In the 300,000 IU single-dose group, 35 (85.4%) attained sufficiency and 6 (14.6%) remained insufficient, with no cases of deficiency or hypervitaminosis D. In the 600,000 IU single-dose group, 35 (89.7%) reached sufficiency, 1 (2.6%) remained insufficient, 1 (2.6%) remained deficient, and 2 (5.1%) developed hypervitaminosis D (levels >100 ng/ml). Overall, 103 (83.1%) of all treated children attained sufficiency, 12 (9.7%) were insufficient, 7 (5.6%) remained deficient, and 2 (1.6%) developed hypervitaminosis D (Table 3).

Statistical analysis revealed no significant difference in outcomes between the 60,000 IU and 300,000 IU groups, nor between the 300,000 IU and 600,000 IU groups. A significant difference was observed, however, between the 600,000 IU and 60,000 IU groups with respect to post-treatment vitamin D levels and change from baseline (Table 4).

**Table 1: Baseline characteristics of study participants**

| Characteristics | Number | Percentages (%) |
|---|---|---|
| **Age** | | |
| 1-3 years | 62 | 50% |
| 3-5 years | 62 | 50% |
| **Gender** | | |
| Male | 64 | 51.6 |
| Female | 60 | 48.4 |
| **Pre-treatment levels of Vitamin D** | | |
| Deficiency (less than 20ng/ml) | 84 | 67.7 |
| Insufficiency (20-30ng/ml) | 40 | 32.3 |
| **Presenting complaints** | | |
| Frontal bossing | 115 | 92.7% |
| Repeated respiratory infections | 109 | 87.9% |
| Wrist widening | 90 | 72.6% |
| Leg cramps | 81 | 65.3% |
| Weakness | 78 | 62.9% |
| Forehead sweating | 33 | 26.6% |
| Irritability | 28 | 22.6% |
| Bow leg | 22 | 17.7% |
| Chest deformity | 0 | 0.0% |
| Spine deformity | 0 | 0.0% |
| **Anthropometric measurements** | **Mean** | **SD** |
| Height | 93.19 cm | 9.15 |
| Weight | 13.86 Kg | 2.65 |

**Table 2: Distribution of study participants in groups who received different doses of vitamin D**

| Characteristics | Treatment groups according to different doses of vitamin D | | | Total Number (%) | P value |
|---|---|---|---|---|---|
| | 60,000 IU/week Number (%) | 3 lakh IU stat Number (%) | 6 lakh IU stat Number (%) | | |
| **Age groups** | | | | | |
| 1-3 years | 26 (59.1) | 20 (48.8) | 16 (41.0) | 62 (50) | 0.25 |
| 3-5 years | 18 (40.9) | 21 (51.2) | 23 (59) | 62 (50) | |
| Total | 44 (100) | 41 (100) | 39 (100) | 124 (100) | |
| **Pretreatment levels of vitamin D** | | | | | |
| Deficiency (<20 ng/ml) | 29 (65.9) | 28 (68.3) | 27 (69.2) | 84 (67.7) | 0.94 |
| Insufficiency (20-30 ng/ml) | 15 (34.1) | 13 (31.7) | 12 (30.8) | 40 (32.3) | |
| Total | 44 (100) | 41 (100) | 39 (100) | 124 (100) | |

**Table 3: Distribution of study participants according to post-treatment levels of vitamin D**

| Treatment groups according to various doses of vitamin D | Post-treatment vitamin D levels | | | | Total |
|---|---|---|---|---|---|
| | Sufficiency Number (%) | Insufficiency Number (%) | Deficiency Number (%) | Hypervitaminosis Number (%) | |
| 60,000 IU/week | 33 (75) | 5 (11.4) | 6 (13.6) | 0 (0) | 44(100) |
| 3 lakh IU stat | 35 (85.4) | 6 (14.6) | 0 (0) | 0 (0) | 41 (100) |
| 6 lakh IU stat | 35 (89.7) | 1 (2.6) | 1 (2.6) | 2 (5.1) | 39 (100) |
| Total | 103 (83.1) | 12 (9.7) | 7 (5.6) | 2 (1.6) | 124 (100) |

**Table 4: Comparison of outcomes among different treatment groups**

| Vitamin D levels | Treatment groups compared | Mean difference | Standard error | p value |
|---|---|---|---|---|
| Post-treatment Vitamin D levels | 60000 IU vs. 3 lakh IU | 11.30 | 1.44 | >0.05 |
| | 60000 IU vs. 6 lakh IU | 28.43 | 3.5 | **<0.05*** |
| | 3 lakh IU vs. 6 lakh IU | 17.13 | 2.13 | >0.05 |
| Pre to post treatment Vit. D levels change (ng/ml) | 60000 IU vs. 3 lakh IU | 9.24 | 1.18 | >0.05 |
| | 60000 IU vs. 6 lakh IU | 28.43 | 3.5 | **<0.05*** |
| | 3 lakh IU vs. 6 lakh IU | 19.19 | 2.3 | >0.05 |

## 4. DISCUSSION

Vitamin D, despite being labeled a vitamin, functions more as a hormone and is mainly synthesized endogenously through cutaneous photosynthesis rather than obtained from the diet. It was previously considered uncommon in India until a landmark study from Delhi in 2000 revealed hypovitaminosis D in nearly 90% of participants. Scientific evidence regarding optimal therapeutic regimens that are effective, affordable, and safe remains limited.[6]

The present study included 124 children with clinically suspected and biochemically confirmed hypovitaminosis D, evaluated between November 2013 and November 2014.

The mean age was 2.99 ± 1.18 years (median 2.95 years), with equal distribution between the 1–3 years and 3–5 years groups. Males accounted for 51.6% and females 48.4%. Rabea et al. (2012) studied children aged 6 months–2 years and reported 40% males and 60% females, with a mean age of 14.9±5.7 months.[7] Billoo et al. (2009) evaluated children aged 6 months–3 years, comprising 63% boys and 37% girls, with a mean age of 12.8 ± 6.6 months.[8]

In our study, the mean weight was 13.86±2.65 kg and mean height 93.19±9.15 cm. The most frequent features were frontal bossing (92.7%) and recurrent respiratory infections (87.9%), followed by wrist widening (72.6%), leg cramps (65.3%), weakness (62.9%), sweating (26.6%), irritability (22.6%), and bowlegs (17.7%). Rabea et al.[7] found frontal bossing and recurrent infections in 46.7%, while Soliman et al.[9] reported wrist widening (90%), bowed legs (70%), and frontal bossing (57.5%) as common signs.Of the 124 children, 67.7% had deficiency (<20 ng/ml) and 32.3% had insufficiency (20–30 ng/ml). Jain et al. (2011) reported deficiency in 66.7%, insufficiency in 19.8%, and severe deficiency in 27.1%.[10] Agarwal et al. (2013) also found high prevalence, with 83.7% deficient and 8.7% insufficient.[11]

After treatment, 83.1% achieved sufficiency (30–100 ng/ml), 9.7% remained insufficient, 5.6% remained deficient, and 1.6% developed hypervitaminosis D (>100 ng/ml). Tellioglu et al. (2012) reported 83.3% sufficiency after oral therapy.[12] Mondal et al. (2014) observed persistent deficiency in 30% of cases despite supplementation, with 4.2% developing hypervitaminosis D.[13]

In our cohort, the mean pre-treatment vitamin D level was 16.21±6.7 ng/ml, increasing to 44.06±18.02 ng/ml post-treatment, with a mean rise of 27.83±17.92. All three regimens were effective: 60,000 IU weekly (pre 16.05±7.39, post 38.14±13.19), 300,000 IU single dose (pre 16.88±6.44, post 41.99±9.21), and 600,000 IU single dose (pre 15.68±6.23, post 52.86±25.31). Similar efficacy has been reported by Tellioglu et al.[12] and Mittal et al.[13] Logan et al. demonstrated that vitamin $D_3$ is superior to vitamin $D_2$,[14] while Aggarwal et al. highlighted improved outcomes when vitamin D was combined with calcium.[15]

In conclusion,in all three treatment groups (60,000 IU weekly for 10 weeks, 300,000 IU single dose, and 600,000 IU single dose), most patients achieved vitamin D sufficiency (30–100 ng/ml). The 600,000 IU single-dose group demonstrated a significantly greater rise in vitamin D levels compared to the other two regimens. While all regimens were effective, two cases of hypervitaminosis D occurred in the 600,000 IU group, suggesting that 60,000 IU weekly and 300,000 IU single-dose therapies may represent safer options. The study could be further strengthened by including additional biochemical markers, such as serum calcium and alkaline phosphatase to better assess both the efficacy and safety of supplementation. Notably, to our knowledge, no previous research has directly compared all three regimens, making this study an important contribution to optimizing treatment strategies for hypovitaminosis D.

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