Vitamin D Status in Full-term Exclusively Breastfed Infants versus Full-term Breastfed Infants Receiving Vitamin D Supplementation in Thailand: A Randomized Controlled Trial

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Abstract

**Background:** Many international medical organizations recommend vitamin D supplementation for infants, especially exclusively breastfed infants. In Thailand, however, data regarding the vitamin D status in Thai infants are lacking. Such data would help to support physician decisions and guide medical practice.

**Methods:** Full-term, exclusively breastfed infants were randomized into two groups at 2 months of age to continue exclusive breastfeeding either without vitamin D supplementation (control group, \( n = 44 \)) or with vitamin D\(_3\) supplementation at 400 IU/day (intervention group, \( n = 43 \)) until 6 months of age. At 6 months, the serum vitamin D (25OHD) of the infants and their mothers, serum bone marker, and infants' growth parameters were compared between the two groups.

**Results:** The infants' serum 25OHD concentration was lower in the control group than intervention group (20.57 ± 12.66 vs. 46.01 ± 16.42 ng/mL, \( p < 0.01 \)). More infants had vitamin D sufficiency (25OHD of >20 ng/mL) in the intervention group than control group (93.0% vs. 43.2%, \( p < 0.01 \)). Vitamin D supplementation in breastfed infants increased the mean serum 25OHD concentration by 25.66 ng/mL (95% confidence interval, 19.07–32.25; \( p < 0.001 \)) and contributed to an 88.7% decrease in the prevalence of vitamin D insufficiency/deficiency (relative risk, 0.11; 95% confidence interval, 0.04–0.35; \( p < 0.01 \)).

**Conclusions:** Most full-term, exclusively breastfed Thai infants have serum vitamin D concentration below sufficiency level at 6 months of age. However, vitamin D supplementation (400 IU/day) improves their vitamin D status and prevents vitamin D deficiency.

**Trial registration:** The study was pre-registered in the Thai Clinical Trials Registry (TCTR20190622001) on 22/06/2019.

**Background**

Vitamin D plays an important role in bone metabolism and affects many extraskeletal organ systems (1). Severe vitamin D deficiency may cause rickets in infants or children and osteomalacia in adults. The natural production of vitamin D in the skin through sunlight exposure is the primary source of vitamin D in humans. Direct dietary vitamin D intake from natural foods, fortified foods, and supplements is another source of vitamin D for the body. Despite improved nutritional knowledge and medical care, vitamin D deficiency and infantile rickets remain significant global public health challenges in developed and developing countries (2, 3).

During the first year of life, breastfeeding is one of the most critical factors to child survival, nutrition, development, and maternal health. The World Health Organization and the United Nations Children's Fund recommend that infants should be exclusively breastfed for the first 6 months of life (4). However, breastfed infants are known to be at risk of vitamin D deficiency, especially in areas of high latitude, because the vitamin D content in breast milk can vary depending on the maternal vitamin D status and is
often low (5, 6). Moreover, infants' exposure to sunlight may be limited because of their geographical location; their parents' culture, beliefs, or practices; or other reasons. As a result, many international medical organizations, including the American Academy of Pediatrics, recommend vitamin D supplementation for infants, especially those who are exclusively breastfed (7, 8). Despite these international recommendations, adherence to the guidelines is still problematic in many countries (9, 10). Previous studies have revealed barriers to vitamin D supplementation in infants, including physicians' beliefs that infants in their geographic area are exposed to adequate sunlight or that breast milk provides sufficient vitamin D, making supplementation unnecessary (11).

In Thailand, routine vitamin D supplementation for exclusively breastfed infants has not been widely practiced. Reasons for this include physicians' belief that infants' vitamin D status is adequate without supplementation, the lack of obvious clinical signs of vitamin D deficiency during the exclusive breastfeeding period, and the difficulty finding suitable vitamin D preparations in Thailand. Most importantly, the local healthcare authorities have not established a national consensus to guide pediatricians on vitamin D supplementation in infants. Currently, data on the vitamin D status among breastfed infants in Thailand are very scarce. There is not enough evidence to establish a guideline to support physician decisions or guide medical practice; therefore, research in this field is urgently needed.

This study was performed to evaluate the effect of vitamin D supplementation on the vitamin D status of exclusively breastfed infants during the first 6 months of life. In addition, the associations among the vitamin D status, serum bone markers, and growth parameters of infants were evaluated.

**Methods**

This open-label randomized controlled trial was conducted at Chakri Naruebodindra Medical Institute, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Samut Prakan, Thailand from July 2019 to October 2020. The study protocol was approved by the Ramathibodi Hospital Institutional Review Board (ID 10-61-58). The study was pre-registered in the Thai Clinical Trials Registry (TCTR20190622001) on 22/06/2019.

**Study population and randomization**

The study participants were recruited from healthy full-term infants and their mothers who attended the well-baby clinic at Chakri Naruebodindra Medical Institute for a routine 2-month infant checkup and immunization. To be eligible, the infants were required to be 6 to 12 weeks old when they entered the study. Only mothers who performed exclusive breastfeeding and had an intention to continue exclusive breastfeeding until the infants were 6 months old were approached for their consent to participate in the trial. The exclusion criteria were premature infants with a gestational age of <37 weeks at birth, infants with a congenital anomaly, introduction of formula milk and/or complementary foods before 6 months of age, and participant withdrawal. After the mothers had provided informed consent, the infants were randomized into two groups: the control group and the intervention group. Randomization was performed using opaque, sealed, sequentially numbered envelopes opened after informed consent. Each envelope
contained a computer-generated block of four intervention order randomization assignments. An enrollment log was kept to ensure all envelopes were accounted for and used in the correct order.

**Intervention**

Routine health supervision and immunization were provided to both groups of participants under individualized physician discretion. Infants in the intervention group were given 400 mg/day of vitamin D supplementation (400 mg/day) in the form of a daily 1-mL multivitamin drop (composition per mL: vitamin A, 2000 IU; vitamin B₃, 2 mg; vitamin B₆, 2 mg; vitamin B₉, 1.8 mg; vitamin B₁₂, 5 mcg; vitamin C, 40 mg; vitamin D₃, 400 IU; nicotinamide, 15 mg; dexamethasone) (Munti-Vim drops; B.L. Hua & Co., Ltd., Bangkok, Thailand). The multivitamin drop was used in the study because there was no commercially available infant vitamin D-only preparation in Thailand at the time of the study. No placebo was given to the infants in the control group.

At 4 months of age, follow-up appointments were made for all infants to ensure compliance with the study protocol and to refill the vitamin D supplementation in the intervention group. At 6 months of age, follow-up appointments were made for all infants and their mothers to conclude the study and collect blood samples. Both appointments at 4 and 6 months of age were performed in accordance with the infants' routine checkup and immunization schedule visits.

**Data collection**

The infants' demographic data (place of birth, season at birth, gestational age, and sex) and anthropometric data (weight, length, and head circumference) at birth and at the 2-month visit were collected at the time of study enrollment. At the 4- and 6-month visits, the infants' anthropometric measurements were repeated. At the 6-month visit, the following laboratory data were obtained for each infant: serum concentrations of vitamin D [25-hydroxyvitamin D₂ (25OHD₂), 25-hydroxyvitamin D₃ (25OHD₃), and total 25-hydroxyvitamin D₃ (25OHD)]), intact parathyroid hormone (iPTH), calcium, phosphorous, and alkaline phosphatase (ALP). Maternal age and serum vitamin D concentrations were also collected at the 6-month visit.

**Biochemical analyses**

Serum vitamin D (25OHD₂, 25OHD₃, and 25OHD) was analyzed using liquid chromatography-tandem mass spectrometry assays (6490 Triple Quad LC/MS; Agilent Technologies, Santa Clara, CA, USA). The iPTH concentration was measured using an electrochemiluminescence immunoassay (cobas e601; Roche Diagnostics, Basel, Switzerland). The plasma concentrations of calcium, phosphorous, and ALP were measured using an automated analyzer (cobas c501; Roche Diagnostics). Vitamin D deficiency was defined as a 25OHD concentration of <12 ng/mL, insufficiency as 25OHD of 12 to 20 ng/mL, and sufficiency as 25OHD of >20 ng/mL (8).

**Sample size estimation**
A power calculation was used to calculate the sample size needed to evaluate the primary outcome (infants' 25OHD concentrations). A pilot study of 34 full-term, exclusively breastfed infants aged 1 to 6 months in our institution (Ramathibodi Hospital, Bangkok) showed that the infants' mean 25OHD concentration was 13.6 ± 7.7 ng/mL (unpublished data). We hypothesized that vitamin D supplementation would increase the 25OHD level by at least 50% in the intervention group or to a mean 25OHD concentration of up to 20.4 ng/mL (sufficiency level) with a standard deviation similar to that in the control group. According to this assumption, 40 infants in each group were required to detect a post-intervention difference in the 25OHD concentration with an alpha of 0.01, 90% power, two-sided. To allow for attrition, an additional 20% or 10 subjects were added to each group. Therefore, 50 was selected as the total number of infants in each group.

**Statistical analysis**

A univariate analysis was performed to identify significant differences between the groups. Student's t-test was used for continuous variables, and the results are presented as mean ± standard deviation. The Mann–Whitney U test was used if the distribution was not normal, and the results are presented as median (interquartile range). Pearson's chi-square test or Fisher's exact test was used for categorical variables, and the results are presented as total number (%). Multivariate linear regression analysis was used to determine the factors associated with infants' 25OHD concentration. To demonstrate the differences in serum bone markers between infants with and without vitamin D sufficiency, univariate analysis was applied using an infant serum 25OHD concentration of <20 ng/mL as the independent variable. A p-value of <0.05 was considered statistically significant. Stata Statistical Software version 15.1 (StataCorp LLC, College Station, TX, USA) was used for all statistical analyses.

**Results**

One hundred mother–infant pairs were randomized to the control and intervention groups according to the study protocol. At the end of the study, 44 and 43 mother–infant pairs in the control and intervention groups, respectively, had completed the study. Figure 1 shows the number of study participants and the reasons for exclusion. The mean age of the infants at the time of enrollment and the end of the study were comparable between the control and intervention groups (65 ± 4 vs. 67 ± 6 days, p = 0.07 and 184 ± 4 vs. 184 ± 4 days, p = 0.86, respectively).

The infants' weight at birth and enrollment was slightly lower in the intervention group than in the control group. There were no significant differences in the other baseline characteristics of the mothers and infants between the two groups. The demographic data and infants' birthing season are shown in Table 1.

At 6 months, the mean 25OHD concentration was lower in the control group than intervention group (20.57 ± 12.66 vs. 46.01 ± 16.42 ng/mL, p < 0.01), as shown in Table 2. The prevalences of vitamin D insufficiency and deficiency were lower among infants in the intervention group. Serum bone markers, including calcium, phosphorus, ALP, and iPTH, as well as infants' growth parameters, were comparable...
between the two groups. No infants in the study had a clinical manifestation of vitamin D toxicity or clinical rickets.

The mean 25OHD concentration of all lactating women in the study was 24.43 ± 7.64 ng/mL. The maternal 25OHD concentrations were not different between the two groups (25.08 ± 7.75 vs. 23.75 ± 7.64 ng/mL, respectively; p = 0.42). The overall prevalence of vitamin D insufficiency and deficiency among lactating women was 27.6% (24 of 87) and 2.3% (2 of 87), respectively. There was no difference in the prevalence of vitamin D insufficiency and deficiency in lactating women between the two groups (Table 2).

Multivariate linear regression analysis, which included the study group (control or intervention), maternal 25OHD concentration, infants' age, weight at enrollment, sex, and birth season, showed that vitamin D supplementation increased the infants' mean 25OHD concentration by 25.66 ng/mL [95% confidence interval (CI), 19.07–32.25]; p < 0.001. The model also showed the association of the maternal and infants' 25OHD concentrations (β = 0.52; 95% CI, 0.11–0.94; p = 0.013) independent of whether the infants were receiving vitamin D supplementation. Other factors were not significant predictors of the infants' 25OHD concentration. In addition, the binary regression model showed that vitamin D supplementation reduced vitamin D insufficiency and deficiency by 88.7% (relative risk, 0.11; 95% CI, 0.04–0.35; p < 0.01).

The associations between serum bone markers and infants' vitamin D status were analyzed, as shown in Table 3. The iPTH concentration was 13.72 pg/mL higher in infants with a 25OHD concentration of <20 ng/mL than in those with a normal 25OHD concentration. No associations were found between other serum bone markers and infants' vitamin D status.

Discussion

This is the first study in Thailand to compare the vitamin D status of breastfed infants with and without vitamin D supplementation during the exclusive breastfeeding period. Vitamin D supplementation increased the 25OHD concentration and decreased the prevalence of vitamin D insufficiency and deficiency in breastfed infants. We found that the 25OHD concentration among unsupplemented breastfed infants was low and that fewer than half had vitamin D sufficiency. In addition, we found that approximately 30% of lactating women had serum vitamin D concentration below sufficiency level.

Limited data are available on the vitamin D status in breastfed infants in Thailand. The mean 25OHD concentration in unsupplemented breastfed infants in our study was comparable with that in breastfed infants born in summer in Greece (19.4 ± 2.8 ng/ml) (12). The Greece study also showed a significantly higher 25OHD concentration in infants born in summer than in winter. In contrast to countries located in the northern and southern hemispheres with marked seasonal variations in weather, especially in summer and winter, Thailand has only three seasons with relatively abundant sunlight all year round. This may explain the lack of a significant association of infants' birth season with the serum vitamin D concentration. Our study showed that unless they were receiving vitamin D supplementation, 56.8% of
breastfed infants at 6 months of age had serum vitamin D concentration below sufficiency level. The prevalence of vitamin D insufficiency or deficiency among infants in tropical countries was previously expected to be low because of the large amount of sunlight in these areas. The prevalences of vitamin D insufficiency and deficiency (≤ 20 ng/mL) among unsupplemented breastfed infants in the present study are comparable with those reported in Hong Kong (60%) (13). The prevalences were lower than those reported in India (90%) (14), Taiwan (86.1%) (15), Qatar (83%) (16), and Japan (76.9%) (17) but higher than those in Boston, MA, USA (40%) (18), Kenya (23.4%) (19), and Indonesia (16.7%) (20). The variation in these reported prevalences was likely caused by multiple factors, such as the infants' age, ethnicity, geographical location, and study methodology. Interestingly, an Indonesian study revealed much lower prevalences of vitamin D insufficiency and deficiency than in the present study despite the fact that Indonesia and Thailand are located at similar latitudes in the Southeast Asia region. The authors described the traditional morning sunbathing practice in the study area, which might be one of the factors that contributed to the relatively high serum vitamin D concentration among the infants in this area (20).

Our results showed that 400 IU of vitamin D supplementation daily increased the serum 25OHD concentration and contributed to an 88% reduction in the prevalences of vitamin D insufficiency and deficiency among breastfed infants. Our findings are consistent with previous studies that showed low prevalences of vitamin D deficiency and insufficiency (≤ 20 ng/mL) when exclusively breastfed infants were supplemented with 400 IU of vitamin D daily (21, 22, 23). A recent systematic review determined the effect of vitamin D supplementation in breastfed infants compared with placebo (24). The authors found six and four randomized controlled trials that determined the primary outcome of infants' vitamin D concentration and vitamin D status, respectively. This systematic review indicated that vitamin D supplementation at 400 IU/day for breastfed infants may increase the serum 25OHD concentration and reduce the incidence of vitamin D insufficiency. However, the study was unable to confirm the benefits of vitamin D supplementation on vitamin D deficiency, the bone mineral content, the incidence of biochemical or radiological rickets, and the risk of detrimental effects in infants.

Serum bone markers, including iPTH and ALP, were not different between the control and intervention groups in our study. However, we found that the serum iPTH concentration was 13.7 pg/mL higher in infants with vitamin D deficiency and insufficiency (≤ 20 ng/mL) than in those with vitamin D sufficiency. This finding indicates the effect of vitamin D deficiency on infants' bone health.

There is a concern regarding vitamin D toxicity while giving vitamin D supplements to infants. No infants in our study had a serum 25OHD concentration of > 100 ng/mL, the level regarded as toxicity (8). Our study also showed that serum calcium and phosphorus were not higher in the intervention group than in the control group. This finding is consistent with a recent systematic review regarding vitamin D supplementation in breastfed infants (25).

The vitamin D concentration and prevalences of vitamin D insufficiency and deficiency among the lactating women in our study were comparable with the results of a previous study from Thailand, which reported a mean vitamin D concentration of 24.64 ± 7.72 ng/mL at delivery; concentrations of < 20 ng/mL
were found in 34.0% of women (26). Vitamin D insufficiency and deficiency in lactating women have been reported in many parts of the world. A global study showed that the mean vitamin D concentration was 28.08 ng/mL in Cincinnati, 19.44 ng/mL in Shanghai, and 19.28 ng/mL in Mexico City. Vitamin D concentrations of < 20 ng/mL were found at 4 weeks postpartum in 17%, 52%, and 62% of mothers in Cincinnati, Shanghai, and Mexico City, respectively (27). The vitamin D status of lactating women should be a topic of concern because it affects the vitamin D status in breastfed infants, as shown in our study. The maternal vitamin D status during pregnancy is directly correlated with the fetal and neonatal vitamin D status, and this relationship continues during lactation (28).

To the best of our knowledge, this is the first study in Thailand to investigate the vitamin D status in exclusively breastfed infants and lactating women and to evaluate the effect of breastfed infants’ vitamin D supplementation on the vitamin D status in these infants. At the time of our study, there was no official national guideline regarding vitamin D supplementation in healthy infants. Routine vitamin D supplementation for exclusively breastfed infants has not been widely practiced by the pediatricians and general physicians who provide care for the children in the community, possibly because of lack of guidance and supporting evidence specific to the Thai population. This facilitated performance of the present randomized controlled trial, in which infants in the control group were not given vitamin D supplementation. As increasing evidence worldwide indicates the universal presence of vitamin D deficiency in exclusively breastfed infants, and once the international medical community's authorities acknowledge the global recommendation, future studies performed in a similar fashion would likely be considered unethical.

This study has some limitations. This was an open-label study without a placebo in the control group, which could have led to bias. However, several measures were used to reduce bias, including blinding the infants’ growth assessment personals from the group allocation and targeting the objective outcome measurements. Compliance with the protocol was based solely on the parents' interview, which could have been inaccurate. Some parents might have provided infant formula or complementary food to the infants without disclosure to the study team. The infants’ baseline vitamin D concentrations were not assessed in our trial; however, the infants’ baseline characteristics in both groups were comparable. Most participants in this study lived in Samut Prakan province, a city located on the outskirts of Bangkok. Therefore, the data may not represent populations in other areas of Thailand.

**Conclusions**

Although Thailand is located in the tropical climate zone and has relatively abundant sunlight all year round, vitamin D insufficiency is not uncommon in nursing mothers and infants in Thailand. Almost one-third of lactating mothers and more than half of full-term, exclusively breastfed infants at 6 months of age have serum vitamin D concentrations below sufficiency level. However, vitamin D supplementation (400 IU/day) for these infants improves their vitamin D status and prevents vitamin D deficiency.

**Abbreviations**
Declarations

Ethics approval and consent to participate

The study protocol was approved by the Ramathibodi Hospital Institutional Review Board (ID 10-61-58). Individual informed consent of the mother and their infant in the study was obtained from the mother prior to participating in a trial. All the experiment protocol involving humans subjects was in accordance with the institutional ethical standards and the Helsinki Declaration.

Consent for publication

Not applicable

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare no conflict of interest.

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Authors' contributions

CR and OD designed the study. OD prepared the randomization sequence. CR, SS, PW, NS, and SA performed the subject recruitment, intervention group assignment, follow-up, and data collection. OD analyzed the data. CR drafted the original manuscript. OD revised the final manuscript and supervised the overall project. All authors read and approved the final manuscript.

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Tables

Table 1. Baseline characteristics of study population
| Characteristics                          | Exclusively breastfed without vitamin D supplementation (control group) | Exclusively breastfed with vitamin D supplementation (intervention group) | p-value |
|-----------------------------------------|------------------------------------------------------------------------|--------------------------------------------------------------------------|---------|
|                                         | n = 44                                                                  | n = 43                                                                   |         |
| **Mother**                              |                                                                        |                                                                          |         |
| Age, years                              | 31.1 ± 4.2                                                              | 31.3 ± 5.4                                                               | 0.84    |
| **Infant**                              |                                                                        |                                                                          |         |
| Sex, male                               | 21 (47.7)                                                               | 16 (37.2)                                                                | 0.32    |
| Inborn                                  | 26 (59.1)                                                               | 22 (51.2)                                                                | 0.46    |
| Gestational age, weeks                  | 38 ± 1                                                                  | 38 ± 1                                                                   | 0.79    |
| Small for gestational age               | 7 (15.9)                                                                | 6 (14.0)                                                                 | 0.80    |
| Large for gestational age               | 1 (2.3)                                                                 | 1 (2.3)                                                                  | 1.00    |
| **Seasons at birth**                    |                                                                        |                                                                          | 0.75    |
| Cool season, Nov-Feb                    | 20 (45.5)                                                               | 23 (53.5)                                                                |         |
| Hot season, Mar-Jun                     | 11 (25.0)                                                               | 9 (20.9)                                                                  |         |
| Rainy season, Jul-Oct                   | 13 (29.5)                                                               | 11 (25.6)                                                                |         |
| **At birth**                            |                                                                        |                                                                          |         |
| Weight, g                               | 3012 ± 373                                                              | 3176 ± 375                                                               | 0.05    |
| Length, cm                              | 49.1 ± 1.9                                                              | 49.4 ± 2.3                                                               | 0.51    |
| Head circumference, cm                  | 33.5 ± 1.5                                                              | 33.9 ± 1.3                                                               | 0.16    |
| **At enrollment**                       |                                                                        |                                                                          |         |
| Weight, g                               | 4997 ± 423                                                              | 5302 ± 560                                                               | <0.01   |
| Length, cm                              | 56.6 ± 2.0                                                              | 57.5 ± 1.9                                                               | 0.93    |
| Head                                    | 38.4 ± 1.2                                                              | 38.6 ± 1.3                                                               | 0.38    |
Data are presented as mean ± standard deviation or n (%).

**Table 2. Study results**
| Characteristics | Exclusively breastfed without vitamin D supplementation (control group) n = 44 | Exclusively breastfed with vitamin D supplementation (intervention group) n = 43 | p-value |
|-----------------|----------------------------------------------------------------------------------|----------------------------------------------------------------------------------|---------|
| **Mother**      |                                                                                   |                                                                                   |         |
| **Vitamin D levels** |                                                                                   |                                                                                   |         |
| 25OHD<sub>2</sub>, ng/mL | 0.10 ± 0.38                                                                         | 0.08 ± 0.37                                                                         | 0.83    |
| 25OHD<sub>3</sub>, ng/mL | 24.97 ± 7.77                                                                         | 23.67 ± 7.70                                                                         | 0.44    |
| 25OHD (total), ng/mL | 25.08 ± 7.75                                                                         | 23.75 ± 7.64                                                                         | 0.42    |
| **Vitamin D (25OHD) status** |                                                                                   |                                                                                   | 0.25    |
| Deficiency, <12 ng/mL | 1 (2.3)                                                                             | 1 (2.3)                                                                             |         |
| Insufficiency, 12–20 ng/mL | 9 (20.5)                                                                            | 15 (34.9)                                                                           |         |
| Sufficiency, >20 ng/mL | 34 (77.3)                                                                            | 27 (62.8)                                                                           |         |
| **Infant**      |                                                                                   |                                                                                   |         |
| **Vitamin D levels** |                                                                                   |                                                                                   |         |
| 25OHD<sub>2</sub>, ng/mL | 0.00 ± 0.00                                                                         | 0.00 ± 0.00                                                                         | -       |
| 25OHD<sub>3</sub>, ng/mL | 20.57 ± 12.66                                                                         | 46.01 ± 16.42                                                                         | <0.01   |
| 25OHD (total), ng/mL | 20.57 ± 12.66                                                                         | 46.01 ± 16.42                                                                         | <0.01   |
| **Vitamin D (25OHD) status** |                                                                                   |                                                                                   | <0.01   |
| Deficiency, <12 ng/mL | 11 (25.0)                                                                            | 0 (0.0)                                                                             |         |
| Insufficiency, 12–20 ng/mL | 14 (31.8)                                                                            | 3 (7.0)                                                                             |         |
### Table 3. Prediction of serum bone markers at serum 25OHD concentration of ≤20 ng/mL

| Serum bone markers | Beta (95% confidence interval) | p-value |
|--------------------|--------------------------------|---------|
| Calcium            | $-0.099 (-0.255$-$0.056$)      | 0.208   |
| Phosphorous        | $-0.149 (-0.343$-$0.045$)      | 0.129   |
| ALP                | $13.899 (-13.026$-$40.724$)    | 0.308   |
| iPTH               | $13.724 (4.160$-$23.288$)      | 0.005   |

ALP, alkaline phosphatase; iPTH, intact parathyroid hormone

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Data are presented as mean ± standard deviation, n (%), or median (interquartile range).

Δ represents the increment in each parameter from 2 to 6 months.

25OHD$_2$, 25-hydroxyvitamin D$_2$; 25OHD$_3$, 25-hydroxyvitamin D$_3$; 25OHD, total 25-hydroxyvitamin D; ALP, alkaline phosphatase; iPTH, intact parathyroid hormone
Figure 1
Flow chart of study participants