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Association of Vitamin D Levels and Pediatric Long Bone Fractures in Vajira Hospital: A Case-Control Study

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Purpose: Vitamin D is essential for bone metabolism. The incidence of pediatric fractures in Thailand is increasing. Although vitamin D deficiency is associated with fracture risk in adults, its association with fracture risk in children remains unclear. This study aimed to compare the mean 25-hydroxyvitamin D [25(OH)D] levels in pediatric patients with and without fractures and to evaluate calcium, phosphate, and parathyroid hormone levels.

Methods: This case-control study included 60 pediatric patients with long bone fractures and 60 patients without fractures in the control group, matched for age, sex, underlying disease, sun exposure, and milk consumption. Patients with fractures were recruited from Vajira Hospital, whereas controls were obtained from a prior database. Patients with high-energy trauma or chronic conditions affecting 25(OH)D levels were excluded. Blood levels of 25(OH)D, calcium, phosphate, and parathyroid hormone were compared between the groups.

Results: Mean 25(OH)D levels were not significantly different between the fracture (23.3 ± 7.0 ng/mL) and nonfracture groups (21.2 ± 6.1 ng/mL) (p = 0.08). Calcium levels were slightly higher in the fracture group (9.6 ± 0.5 mg/dL) than in the nonfracture group (9.4 ± 0.4 mg/dL) (p = 0.04). Phosphate and parathyroid hormone levels were not significantly different between groups.

Conclusions: No significant differences in 25(OH)D levels were observed between children with and without fractures, suggesting that other factors may contribute to fracture risk. Although calcium levels were slightly higher in the fracture group than in the nonfracture group, the difference was not clinically significant.

Keywords: fracture, pediatrics, vitamin D deficiency, vitamin D insufficiency

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The incidence of pediatric fractures ranges from 12 to 36 fractures per 1,000 children per year and varies by geographic region, age, and sex[1]. The incidence of pediatric fractures in Thailand has been increasing annually[2]. Fractures can limit patients' activity, are time-consuming to treat, and often lead to financial burdens. They may also result in long-term complications, such as malunion or chronic pain[3].

Aside from trauma, modifiable causes of fractures may include obesity, milk consumption, limited physical activity, and vitamin D deficiency[4-11]. Although vitamin D deficiency is associated with fractures in adults[12], its impact on children remains unclear[13]. Some studies have reported a significant correlation between vitamin D and fractures[7,11,14], whereas others have found no association[4,6,15].

This discrepancy may be attributed to differences in geography, sun exposure, diet, lifestyle, and individual behaviors influencing vitamin D metabolism[16]. Most studies have been conducted in Western or temperate-climate countries with limited UV exposure and marked seasonal variation. By contrast, Thailand, a tropical country located near the equator, receives abundant year-round UV radiation, which theoretically favors sufficient vitamin D synthesis. However, a recent study showed that Thai children and adults remain at risk of vitamin D insufficiency[17].

In this study, we aimed to determine the 25(OH)D levels in Thai pediatric patients with long bone fractures and compare them with those in patients without fractures from the pediatric outpatient department. We hypothesized that pediatric patients with long bone fractures would have lower 25(OH)D levels than those without fractures.

METHODS

This study was approved by the Institutional Ethics Committee of the Faculty of Medicine, Vajira Hospital at Navamindradhiraj University (COA 029/2562). The study design was a case-control analysis of two groups.

The inclusion criteria for the case group were pediatric patients aged 2–12 years who were admitted to Vajira Hospital between 2019 and 2021 for the treatment of long bone fractures, including fractures of the humerus, radius, ulna, femur, tibia, and fibula. The exclusion criteria were high-energy trauma, evaluated using the Landin classification[18], which included falls from heights greater than 3 m, motor vehicle injuries, and injuries from heavy objects. We also excluded patients with significant chronic diseases (including liver disease, kidney disease, malabsorption, or colostomy) and those taking medications that affect vitamin D metabolism, such as anticonvulsants (including phenytoin and phenobarbital), glucocorticoids, and rifampicin.

The control group was derived from a prior study titled "Vitamin D Deficiency among Children at Vajira Hospital; Prevalence and Risk Factors," conducted in 2017 by Punyashthira and Sinsophonphap, both of whom are co-authors of the present manuscript. The original study was approved by the Institutional Ethics Committee of the Faculty of Medicine, Vajira Hospital at Navamindradhiraj University (COA 77/2560). Although the study has not been formally published, the data were ethically collected and used after obtaining the authors' consent. The study included children aged 7–15 years attending outpatient services. The exclusion criteria for the control group included patients who covered all body parts outdoors, were strictly vegetarian, had a significant chronic disease, or were taking medications that affected 25(OH)D levels.

The primary outcome was the difference in blood 25(OH)D levels between the fracture and non-fracture groups. Secondary outcomes included additional blood tests relevant to bone metabolism and fracture risk in children, including parathyroid hormone, serum calcium, and serum phosphate levels. These biomarkers play crucial roles in bone metabolism; calcium and phosphate are essential for bone mineralization, whereas parathyroid hormone regulates calcium and phosphate homeostasis and influences bone remodeling. We also evaluated average sun exposure time and milk consumption as additional lifestyle-related variables associated with vitamin D status.

All patients underwent blood testing in a non-fasting state, either at the time of admission (fracture group) or during outpatient visits (control group), without standardization of the time of day. Samples were processed within 2 h of collection. All biochemical tests were performed at the Central Laboratory of Vajira Hospital. Serum 25(OH)D levels were measured using the 25(OH)hydroxyvitamin D assay on the Roche Cobas e801 analyzer module, which demonstrated no significant diffe-

rences compared with the gold-standard isotope-dilution liquid chromatography–tandem mass spectrometry method[19].

Statistical Analysis

A sample size of 61 patients per group was required, based on a case-control study by Thompson,[11] with an alpha of 0.05 and a beta of 0.2. Statistical analyses were conducted using STATA software (version 14.0; StataCorp LP, College Station, TX, USA). Because of the large amount of data in the non-fracture group, we employed 1:1 propensity-score matching to minimize confounding factors. Propensity scores were calculated using baseline covariates, including age (continuous), sex, underlying disease, sun exposure time, and average milk consumption. The nearest-neighbor method without replacement was used to pair each fracture case with the most similar control. Because the control dataset comprised children aged 7–15 years, exact age matches for children aged 2–6 years were unavailable; therefore, younger patients were matched with the closest available controls based on their propensity scores. Interval data between the two groups were compared using the Student t test, whereas categorical data were analyzed using the chi-square test. A p-value < 0.05 was considered statistically significant.

RESULTS

Between February 2019 and January 2022, 60 fracture cases and 60 controls were compared. Table 1 presents the patients' demographic data. The mean age of the non-fracture group was significantly higher (8.3 ± 1.6 years) than that of the fracture group (7.3 ± 2.9 years; p = 0.021). Sex distribution and body mass index did not differ significantly between the groups (p = 0.45 and p = 0.30, respectively). The fracture group reported high daily milk consumption (2.8 ± 1.1 vs. 2.3 ± 0.6 glasses/day; p = 0.003), while sun exposure time was similar (p = 0.15).

The supracondylar humerus (43.3%) was the most common fracture site, followed by the distal radius (25%) and forearm (10%). Less frequent sites included the clavicle, radial neck, lateral condyle of the humerus, medial epicondyle of the humerus, transphyseal humeral separation,

Table 1 Demographic characteristics and laboratory results of the fracture and nonfracture groups.

	Fracture Group (n = 60)	**Nonfracture Group (n = 60)**	***p* value**	**95% CI**
Age (years)	7.3 ± 2.9	8.3 ± 1.6	0.021	–1.84 to –0.16
Gender (%)			0.45	
Male	40 (67)	34 (57)		
Female	20 (33)	26 (43)		
BMI (kg/m²)	17.3 ± 3.7	18.1 ± 5.0	0.3	–2.37 to 0.77
Milk consumption (glasses/day)	2.8 ± 1.1	2.3 ± 0.6	0.003	0.18 to 0.82
Sun exposure (hours/day)	3.0 ± 1.2	2.7 ± 1.2	0.15	–0.13 to 0.73
25(OH)D levels (ng/mL)	23.3 ± 7.0	21.2 ± 6.1	0.08	–0.25 to 4.45
Vitamin D insufficiency (12-20 ng/mL)	19 (31.7)	30 (50)	0.063	
Vitamin D deficiency (<12 ng/mL)	1 (1.7)	1 (1.7)	1	
Calcium level (mg/dL)	9.6 ± 0.5	9.4 ± 0.4	0.04	0.04 to 0.36
Phosphate level (mg/dL)	4.9 ± 0.6	4.7 ± 0.8	0.18	-0.05 to 0.45
Parathyroid hormone level (pg/mL)	38.8 ± 17.7	34.9 ± 14.5	0.18	-1.89 to 9.69

Abbreviations: n, number; CI, confidence interval; BMI, body mass index; kg/m², kilogram per square meter; ng, nanogram; mL, milliliter; mg, milligram; dL, deciliter; pg, picogram.
The data are presented as mean ± standard deviation or number (%).

femoral shaft, ankle, and femoral neck. Most patients underwent closed reduction with Kirschner wire fixation (53.3%) or casting (33.3%), while only a few required multiple screws or external fixation. Open reduction was performed in six cases, using Kirschner wire, plate fixation, or cast immobilization. One patient was managed conservatively with an arm sling.

Mean 25(OH)D levels did not differ significantly between groups, with an average of 23.3 ± 7.0 ng/mL in the fracture group and 21.2 ± 6.1 ng/mL in the non-fracture group ($p = 0.08$). Vitamin D insufficiency (12–20 ng/mL) was observed in 31.7% and 50% of patients in the fracture and non-fracture groups, respectively, with no significant difference ($p = 0.063$). Only one patient in each group had vitamin D deficiency (< 12 ng/mL). Calcium levels were slightly high in the fracture group (9.6 ± 0.5 vs. 9.4 ± 0.4 mg/dL; $p = 0.04$). No significant differences were found in phosphate levels ($p = 0.18$) or parathyroid hormone levels ($p = 0.18$).

When fracture patients were stratified by vitamin D status (normal vs. insufficiency/deficiency), those with normal vitamin D levels were significantly younger (6.6 ± 2.6 vs. 8.7 ± 3.0 years; $p = 0.007$) and had higher calcium levels (9.7 ± 0.5 vs. 9.3 ± 0.6 mg/dL; $p = 0.005$), greater daily milk consumption (3.0 ± 1.1 vs. 2.4 ± 1.2 glasses/day; $p = 0.03$), and longer sun exposure (3.3 ± 1.1 vs. 2.7 ± 1.0 h/day; $p = 0.022$). There were no significant differences in sex distribution ($p = 0.84$), phosphate levels ($p = 0.52$), or parathyroid hormone levels ($p = 0.19$). These findings are summarized in Table 2.

Table 2 Demographic characteristics and laboratory results of fracture patients according to vitamin D status.

	Normal vitamin D (n = 40)	**Vitamin D insufficiency and deficiency (n = 20)**	***p* value**	**95% CI**
Age (years)	6.6 ± 2.6	8.7 ± 3.0	0.007	–3.59 to –0.60
Gender (%)			0.84	
Male	27 (67.5)	13 (65)		
Female	13 (32.5)	7 (35)		
Milk consumption (glasses/day)	3.0 ± 1.1	2.4 ± 1.2	0.03	0.07 to 1.28
Sun exposure (hours/day)	3.3 ± 1.1	2.7 ± 1.0	0.022	0.10 to 1.25
Calcium level (mg/dL)	9.7 ± 0.5	9.3 ± 0.6	0.005	0.13 to 0.70
Phosphate level (mg/dL)	4.9 ± 0.6	5.0 ± 0.6	0.515	-0.43 to 0.22
Parathyroid hormone level (pg/mL)	36.4± 15.3	43.6 ± 21.3	0.186	-18.19 to 3.69

Abbreviations: n, number; CI, confidence interval; mg, milligram; dL, deciliter; pg, picogram; mL, milliliter.
The data are presented as mean ± standard deviation or number (%).

DISCUSSION

The incidence of pediatric fractures in Thailand has increased over the years, leading to significant financial and time-related burdens[2]. While studies in adults have established a relation between vitamin D and fractures[12], the literature presents mixed findings in pediatric patients. In our study, we found that the mean 25(OH)D levels did not differ significantly between the fractured and non-fractured groups. This finding is consistent with those of Anderson et al.[15] and Contreras et al.[6], who also found no association between serum 25(OH)D levels and fracture risk in pediatric populations.

Vitamin D deficiency and insufficiency remain major global public health problems across all age groups, even in countries with adequate ultraviolet light exposure. Factors that affect

25(OH)D levels beyond geographical location[16] include avoidance of strong sunlight, use of sun protection products, malnutrition, liver and kidney disease, hyperparathyroidism[5], and use of certain drugs such as steroids or antiepileptic medications. A 2014 meta-analysis by Palacios demonstrated that vitamin D deficiency is a major public health problem worldwide among all age groups[20]. In our study, the mean 25(OH)D levels in both groups were below 30 ng/mL, which is considered optimal for bone health, particularly in high-risk children, such as those with fractures. Using the definition of vitamin D insufficiency (12–20 ng/mL) [21], approximately one-third (31.7%) of the patients in the fracture group and half (50%) of those in the non-fracture group were classified as vitamin D-insufficient; however, this difference was not statistically significant. Vitamin D deficiency (<12 ng/mL) was rare in both groups (1.7%)[21].

Vitamin D is essential for bone mineralization and the maintenance of bone quality by regulating calcium metabolism and skeletal homeostasis[8]. Vitamin D deficiency can impair bone strength and reduce bone mineral density, thereby increasing the risk of fractures in adults[22]. Despite the known role of vitamin D in bone metabolism, we did not observe a significant difference in serum 25(OH)D levels between groups. This suggests that vitamin D insufficiency may be common among Thai children, regardless of fracture status. Other factors not evaluated in our study—including the summer season[23], younger maternal age, birth order, and maternal alcohol misuse—have also been reported to influence pediatric fracture risk[24].

Several additional differences were observed between the groups. Patients in the non-fracture group were significantly older than those in the fracture group. This may reflect the high incidence of fractures in younger children, who typically have less mature motor coordination and are more prone to falls. Despite being younger, the fracture group had high daily milk consumption, which may reflect age-specific dietary habits, as younger children generally consume more milk than older ones. Hohoff et al. reported that dietary intake decreased with age and continued to decline into adulthood in both boys and girls[25]. The calcium level was slightly high in the fracture group, although both groups remained within the normal physiological range. This difference may also be attributable to the younger age of the fracture group, as younger children tend to have slightly high serum calcium levels[26]. Although this difference reached statistical significance, it is unlikely to be clinically meaningful. No significant differences in phosphate or parathyroid hormone levels were observed between the groups.

Interestingly, the fracture group had a slightly higher mean 25(OH)D level and lower prevalence of vitamin D insufficiency than those of the non-fracture group, although the difference was not statistically significant. This finding may be attributed to lifestyle factors. As shown in Table 2, children with normal vitamin D levels reported higher milk consumption and longer sun exposure than those with low vitamin D levels. Considering that the fracture group reported higher milk intake and comparable or greater sun exposure than those of the control group, these factors may partly explain their relatively high vitamin D levels. Similar observations have been reported in previous pediatric studies, indicating that milk consumption and environmental factors can influence serum vitamin D levels[27].

Based on our findings, routine vitamin D screening for pediatric fractures or supplementation for fracture prevention in healthy children may not be justified. However, the high rate of insufficiency in both groups supports the importance of nutritional counseling, safe sun exposure, and public awareness campaigns as part of general pediatric care. These findings highlight the need for public health efforts focused on improving vitamin D status in the Thai pediatric population.

This study had several limitations owing to heterogeneity between the case and control groups. The fracture group included children aged 2–12 years, whereas the control group included children aged 7–15 years. Although propensity-score matching was performed using key covariates,

including age, exact age matches for children younger than 7 years were not available because of the age range of the control dataset. Consequently, the younger patients were matched with the most similar available controls based on their propensity scores. Future studies with age-matched or age-stratified designs in Thai children are recommended to clarify fracture-related risk factors.

Moreover, because only one patient in each group had vitamin D deficiency, the study may not adequately represent the effects of vitamin D deficiency on fracture risk. Additionally, the control data were collected in 2017, whereas the case data were obtained between 2019 and 2022, which may introduce temporal bias. Differences in nutritional practices and public health awareness during this period may have influenced vitamin D levels. Information on sunscreen use, which may affect cutaneous vitamin D synthesis, was not collected in this study and should be assessed in future investigations. Finally, although our target sample size was 61 patients with a power of 80%, we were able to recruit only 60 patients because of the COVID-19 pandemic, which may have minimally reduced the study's statistical power.

CONCLUSION

There were no significant differences in 25(OH)D, phosphate, or parathyroid hormone levels between children with and without fractures. This finding suggests that vitamin D alone may not be a key determinant of fracture risk. Although serum calcium levels were slightly higher in the fracture group, the difference was minimal and not clinically significant.

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