

Bone Health in Pediatric Fracture Patients: A DEXA Study

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Abstract

Vitamin D deficiency is widespread in children and is associated with increased fracture severity. Previous studies have shown mixed results on the impact of vitamin D supplementation on bone health parameters measured on dual-energy x-ray absorptiometry (DEXA) scan. This is the first longitudinal DEXA study in a pediatric fracture population. Pediatric fracture patients with vitamin D levels below 20 ng/mL were counseled to take vitamin D and calcium per a serum-based protocol. Patients underwent baseline DEXA within the initial 12 weeks post fracture and had follow-up scans at 6 and 12 months. 48 patients were enrolled, 32 patients completed two DEXA scans, and 19 completed three DEXA scans. There was a significant increase in lumbar spine BMC, TBLH BMD, and TBLH BMC between DEXA 1 and 2 ($p < 0.001$). A positive trend in DEXA parameters is suggested between DEXA 1 and DEXA 3. Height adjusted z-scores (HAZ) were calculated which showed no statistical significance, p -values > 0.05 . In this group, there are no significant changes in TBLH, BMC or BMD z-scores one year after fracturing despite vitamin D and calcium supplementation. This suggests that children returning to collision sports may be at continued risk for refracture and future studies are needed.

Keywords

Bone Health, Pediatric, Fracture, Vitamin D, DEXA, Osteoporosis, Osteopenia, Vitamin D Deficiency

1. Introduction

Vitamin D is an important nutrient that impacts skeletal development by controlling levels of parathyroid hormone (PTH) and increasing calcium absorption

[1] [2]. Vitamin D is primarily obtained from the sun, but 5% is from dietary intake [3]. Vitamin D deficiency is especially widespread in the winter. Even in areas with year-round sun, most children are found to have low vitamin D levels [4] [5]. In a survey of vitamin D levels in children in the US, 70% of the population was found to be either deficient or insufficient regardless of season (Vitamin D level less than 30 ng/mL serum 25(OH)D) [6].

Recent research has correlated low vitamin D levels with fracture severity and need for surgical treatment of fractures [7]. A study of Australian children showed 52% of pediatric patients with fractures were vitamin D deficient (<11.6 ng/mL serum 25(OH)D) and low Vitamin D levels have been positively correlated with forearm fracture risk in African American children [8] [9]. The large number of fracture patients with vitamin D deficiency lends evidence to the fact that vitamin D is a necessary component for bone health.

Randomized controlled studies have shown mixed results, with some studies finding little to no impact of vitamin D on bone health parameters including bone mineral content (BMC) or bone mineral density (BMD) measured on dual-energy x-ray absorptiometry (DEXA) scan [10] [11]. A study conducted in Lebanese adolescents given either a placebo, 200 IU/day vitamin D, or 2000 IU/day, did not find significant changes in overall BMC or BMD [11].

Other studies have found a positive impact of vitamin D on bone health and BMD [12] [13] [14] [15]. One randomized control trial found higher BMD in those taking vitamin D supplementation of 35 ug/week (1400 international units (IU)) or 350 ug/week, (14,000 IU) versus the control group [15]. Lehtonen *et al.* found 27% higher lumbar spine BMD in Tanner stage III or IV females with “higher” serum level of 25(OH)D (mean = 18.1 ng/mL) compared to “low” serum 25(OH)D levels (mean = 7.7 ng/mL) suggesting that the last premenarchal years are the most important for vitamin D to have an impact on overall BMD [14].

A study examining adolescent Finnish girls found a 14.3% increase in femur BMC in those taking 5 ug (200 IU) Vitamin D3 daily, versus 17.2% increase in femur BMC in the group receiving 10 ug (400 IU) compared to placebo after 1 year of intervention ($p = 0.024$) [13].

Research suggests that providing calcium and vitamin D together is more successful than either alone [1] [16] [17]. With 80% or better compliance with vitamin D and calcium supplementation, there was a 25% reduction in hip fractures in adults compared to control [17].

This study aims to study the effects of providing supplemental vitamin D and calcium on total BMC and BMD at 6 months and 12 months in pediatric fracture patients. A fracture population in children has not been studied. This is a special situation since having a fracture causes systemic release of a cascade of growth factors in the body to allow for fracture healing. The hypothesis is that this population will react differently to supplementation than those without fractures. Parathyroid hormone (PTH) and osteocalcin have been shown to increase after a fracture [18] [19]. Levels of insulin-like growth hormone 1 (IGF-1)

were lower and remained lower in fracture patients one-year post-fracture compared to non-fracture patients [18]. There is also increased secretion of tumor necrosis factor- α and interleukins during fracture healing that work to recruit necessary cells to heal the bone [20]. Mesenchymal stem cells are particularly important in fracture healing and are recruited in part by BMPs, SDF-1, and CXCR-4 [20]. Overgrowth has been reported as a common occurrence in fracture patients. Bones on the same limb of the body as the fracture may grow longer than the contralateral side, due to the increased blood flow, and factors needed for bone formation [21]. Overgrowth is largely completed by 18 months post-fracture [21].

This is the first study to examine changes in DEXA parameters over time in a pediatric fracture population taking supplemental vitamin D and calcium. This study seeks to contribute to a body of knowledge on pediatric bone health, which is currently lacking as most studies focus on bone health in older populations. Information from this study can help with counseling children on safe return to sports based on DEXA results.

2. Methods

Institutional Review Board approval was obtained, and all patients gave informed consent before participating in the study. This study was conducted by using a sample of pediatric patients with a recent fracture and serum vitamin D level below 20 ng/mL. Patients were counseled by the orthopedic surgeon to take vitamin D and calcium as per a serum-based supplementation protocol. Patients with levels between 12 and 20 ng/ml were recommended 4000 IU daily, and patients below 12 ng/mL were recommended 7000 IU daily, both with follow-up levels to determine if the dose of vitamin D was enough to raise their levels.

Patients underwent a baseline DEXA scan within the initial 12 weeks post fracture and had follow-up DEXA scans at 6 months and 12 months. Patients presenting with a fracture and a vitamin D level less than or equal to 20 ng/mL were offered enrollment in this study if they were able to get a DEXA scan in the first 12 weeks after the fracture occurred.

Patients exclusion criteria included: endocrinopathies, malabsorption syndromes, hematologic disorders, cancer, bone disorders, spine disorders/scoliosis, collagen vascular diseases, nutritional/eating disorders, organ failure/transplantation, kidney/liver disease among others. All fractures are eligible other than spine or pelvis because spine DEXA is being used. Fractures causing the patients to be non-ambulatory for at least four weeks due to expected loss of bone from non-ambulation were excluded. DEXAs cannot be performed if the patient is wearing a cast; thus those wearing a cast beyond 12 weeks from the date of injury were excluded.

When patients agreed to participate in the study, they were given an initial survey to complete which documented patient demographics, previous fractures, sports and exercise activities, family history of bone disease, diet, and current supplementation. Patients received a stipend totaling \$125 for participating in

the study, with \$25 given as a gift card after the first DEXA, and \$50 gift cards given at the second and third DEXA scans to increase patient compliance.

At the time of the DEXA scan, a short survey was completed asking self-reported vitamin D, calcium, and multivitamin compliance and to self-identify their Tanner stage of development.

Patients were contacted via phone reminders about scheduling DEXA scans and continuing to take vitamins. Patients were considered compliant if at their follow-up scans, they reported taking vitamin D for at least four days per week.

3. Results

48 patients were enrolled, 32 patients completed the first two DEXA scans, and 19 completed the study with three DEXA scans. Demographics including Tanner stage at time of initial DEXA are presented in **Table 1**.

Table 1. Demographics.

	n = 48
Age, mean (SD)	12.375 (0.397)
Ethnicity, n (%)	
Hispanic or Latino	17 (35.42%)
NOT Hispanic or Latino	30 (62.5%)
Unknown/Not Reported	1 (2.08%)
Race, n (%)	
Asian	5 (10.42%)
Black or African American	8 (16.67%)
More Than One Race	1 (2.08%)
Native Hawaiian or Other Pacific Islander	1 (2.08%)
Unknown/Not Reported	3 (6.25%)
White	30 (62.5%)
Skin Tone, n (%)	
Dark	16 (34.04%)
Light	31 (65.96%)
Gender, n (%)	
Female	20 (41.67%)
Male	28 (58.33%)
Age menarche or puberty, n, mean (SD)	16, 12.063 (2.016)
Height (inches), mean (SD)	60.834 (6.158)
Weight (pounds), mean (SD)	111.38 (37.38)
BMI, mean (SD)	20.654 (4.731)
Tanner Stage Girl, n (%)	
I	2/14, (14.29%)
II	4/14, (28.57%)
III	1/14, (7.14%)
IV	7/14, (50%)
Tanner Stage Boy, n (%)	
I	5/23, (21.74%)
II	4/23, (17.39%)
III	5/23, (21.74%)
IV	6/23, (26.09%)
V	3/23, (13.04%)

There was a significant increase seen in lumbar spine BMC, TBLH BMD, and TBLH BMC between DEXA 1 and 2 ($p < 0.001$, **Table 2**). A positive trend in DEXA parameters is suggested between DEXA 1 and DEXA 3, although not statistically significant. There was not a significant change in lumbar spine Z-score, TBLH Z-score, right or left femoral neck z-scores between DEXA 1 and 2 or DEXA 2 and 3 (**Table 2**).

Height adjusted z-scores (HAZ) were calculated using the Children's Hospital of Philadelphia's Pediatric Z-Score Calculator by Zemel [22]. Paired t-tests comparing changes from HAZ 1 to HAZ 3 for all measurements showed no statistical significance, p-values > 0.05 ($p = 0.178$; 0.066 ; 0.087 ; 0.313 ; **Figure 1**).

Table 2. DEXA data.

	DEXA 1	DEXA 2	DEXA 3	p-value TP1 and TP2	p-value TP2 and TP3
	n = 32	n = 32	n = 19		
Height in inches at time of 1st DEXA, n, mean (SD)	32, 60.89 (6.36)	32, 62.24 (5.79)	1, 57 (*)	<0.001	unable to calc
Weight in pounds at time of 1st DEXA, n, mean (SD)	32, 116.36 (41.26)	32, 123.23 (43.49)	1, 94.8 (*)	<0.001	unable to calc
BMI at time of 1st DEXA, n, mean (SD)	32, 21.494 (5.282)	32, 21.828 (5.527)	-	0.179	unable to calc
L/S BMD, n, mean (SD)	32, 0.9564 (0.1972)	32, 0.9538 (0.2528)	19, 1.0189 (0.2195)	0.908	0.013
L/S Z Score, n, mean (SD)	32, 0.116 (1.267)	32, 0.016 (1.298)	19, 0.347 (1.111)	0.034	0.917
L/S BMC, n, mean (SD)	32, 40.77 (14.54)	32, 43.04 (15.17)	19, 43.92 (16.23)	<0.001	0.005
TBLH BMD, n, mean (SD)	32, 0.9189 (0.1461)	32, 0.9445 (0.1558)	19, 0.9696 (0.1613)	<0.001	0.008
TBLH Z Score, n, mean (SD)	25, 0.304 (1.368)	25, 0.316 (1.422)	14, 0.516 (1.347)	0.851	0.06
TBLH BMC, n, mean (SD)	32, 1536 (576)	31, 1614 (602)	19, 1719 (665)	<0.001	0.005
Right Femoral Neck BMD, n, mean (SD)	19, 0.9961 (0.1629)	21, 1.0045 (0.1679)	14, 1.0486 (0.1868)	0.251	0.161
Right Femoral Neck Z score, n, mean (SD)	19, -0.016 (1.326)	21, 0.081 (1.443)	14, 0.5 (1.468)	0.636	0.591
Right Femoral Neck Z BMC, n, mean (SD)	19, 4.517 (1.028)	21, 4.55 (1.083)	14, 4.708 (1.143)	0.21	0.535
Left Femoral Neck BMD, n, mean (SD)	20, 1.0243 (0.1635)	21, 1.0149 (0.1577)	14, 1.0723 (0.1862)	0.897	0.069
Left Femoral Neck Z score, n, mean (SD)	20, 0.27 (1.449)	21, 0.167 (1.412)	14, 0.679 (1.396)	0.285	0.38
Left Femoral Neck Z BMC, n, mean (SD)	20, 4.521 (0.914)	21, 4.479 (1.013)	14, 4.761 (1.09)	0.425	0.036
Grip strength #1 (average of test trials), n, mean (SD)	32, 42.66 (17.13)	32, 48.47 (18.59)	18, 49.83 (15.35)	0.001	0.226

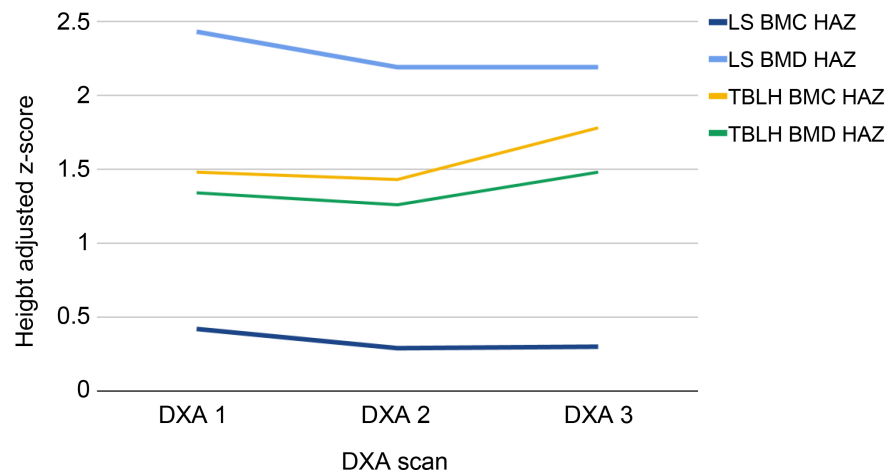


Figure 1. Height adjusted Z-scores over time for all measurements.

ANOVA tests compared the percent change in Tanner stage. While there was no statistical significance, the impact of Tanner stage is very high due to the high R^2 value. The mean percent change by Tanner stage was highest for stage II in each variable except TBLH BMD, where stage III had a higher mean by almost 3%.

Using Wilcoxon Sign Rank and correlation tests, it was determined that there was no significant difference in the time points for the supplementation compliant patients, and there was no significant difference in any of the measurements between compliant and non-compliant patients. A total of 15 patients were compliant, with 4 non-compliant patients.

After BMC and BMD were adjusted for height, there were no statistically significant changes found in any of the measurements.

4. Discussion

This study suggests that vitamin D supplementation in pediatric fracture patients has positive impacts on bone health, measured using DEXA scans obtained over 12-months with a positive trend seen. This is the first longitudinal DEXA study in a pediatric fracture population. In this group, there are no significant changes in TBLH, BMC or BMD z-scores one year after a fracture despite vitamin D and calcium supplementation. This suggests that children returning to collision sports may be at continued risk for injury or refracture and future studies are needed to explore this further.

The hormonal changes that occur after a fracture may be involved in resorbing bone to mobilize calcium for fracture healing and may have lowered the HAZs from DEXA 1 to 2 with no effect on DEXA 3. No one has studied this 6-month time point in this fracture population with or without supplementation and this could be studied further in the future.

Patients grew an average of 1.46 inches (SD = 1.09) during the study, which impacts the size of bones and therefore BMC and BMD. Growth over time was accounted for by calculating the HAZ for each patient, at each measurement, at

each time point. More patients had a negative change after converting to HAZs, so it is likely due primarily to growth in the patients that have caused the increases in the raw data. It is expected that pediatric patients would have increased bone mass and density with the 12-month follow-up period due to normal growth, however, these results suggest a positive trend which may be amplified due to vitamin D and calcium supplementation. Even with the differences in growth, nearly all patients showed some increase in LS and TBLH BMC and BMD, suggesting a role for vitamin D and calcium supplementation.

These study results vary from what is found in the literature. While many studies did not find an impact of vitamin D supplementation on bone mass or density, the doses of vitamin D were lower than the daily recommendations given in this study or much higher and less frequent [10] [11] [23]. Vitamin D supplementation in this study was per vitamin D serum level-based protocol. While other studies only found increases in bone density in the LS, this study showed far fewer positive impacts in that region and instead had increases in the TBLH measurement [12] [13].

Study limitations include a small sample size due to loss to follow-up and adherence to study protocol. Increasing patient compliance to supplementation and to follow-up DEXA scans in the future could improve conclusions that are able to be drawn from the study. Not all participants had follow-up serum 25(OH)D levels drawn as requested. Although repeat vitamin D testing is not advocated by many, this would have been one way to reliably measure whether study participants were compliant with supplementation. Further DEXA studies at 6 months post fracture could help elucidate the hormonal effect of fractures on bone health.

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Contribution Statement

BM: Conceptualization, Methodology, Formal analysis, investigation, Resources, Writing-Review & editing, Supervision, Funding acquisition. JR: Methodology, investigation, writing-original draft & review and editing, project administration. LN: Conceptualization, writing-original draft, project administration. MM: writing-original draft, investigation, data curation. VW: writing-review and editing, data curation, formal analysis. EP: conceptualization, methodology.

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Competing Interests

The authors declare there are no competing interests.

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