



# Vitamin D levels and fracture risk among Hispanic children

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## Abstract

**Purpose** There is a lack of knowledge about whether low vitamin D levels increase the risk of pediatric low-energy fractures among Hispanic population. The objective of this study is to determine whether there is a direct relationship between low vitamin D levels and the incidence of low-energy fractures in Hispanic children.

**Method** Cases included all consecutive patients evaluated with low-energy fractures in the pediatric orthopedic clinic. The control group consisted of all pediatric patients evaluated, without fractures, who had bone and joint pain complaints in the general pediatric clinic. The main focus was to compare cases and controls in relation to their vitamin D levels. Cases and controls were compared using *t* tests for means of quantitative variables and Chi-square tests.

**Results** A total of 201 subjects, distributed as cases ( $n = 107$ ) and controls ( $n = 94$ ), were included in this study. One hundred twelve (55.7%) of the total study population were males. The mean age for the study population was 8.6 years old ranging from 1 year to 18 years, and standard deviation = 4.0 years. The median age for the study population was 9 years. The mean vitamin D level for the cases was 32.6 ng/dl (SD = 10.9); the mean vitamin D level for controls was 32.3 ng/dl (SD = 13.4). This difference was not statistically significant ( $t = 0.18$ , 95% CI – 3.2 to 3.9;  $p = 0.854$ ).

**Conclusion** A direct relationship between low vitamin D levels and fracture risk in a Hispanic pediatric population was not established.

**Levels of Evidence** III.

**Keywords** Vitamin D · Hispanic population · Fracture risks

## Introduction

Vitamin D plays an essential role in the homeostasis of several metabolic processes such as the absorption and maintenance of calcium levels, which is fundamental for the functioning of the nervous system, teeth and bone structure [1, 2]. The main

component of vitamin D is cholesterol, which through various metabolic processes is transformed into 25-hydroxycholecalciferol by a catalytic hydroxylation reaction that occurs when ultraviolet light contacts the skin. Then, it travels to the kidney to be hydroxylated into 1, 25-hydroxycholecalciferol, which is the active form. The latter is necessary for the absorption

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of calcium in the kidneys [3]. Deficiency of vitamin D has been associated with diabetes, cardiovascular illness, immune regulation diseases and bone mineralization defects [4–6]. In the pediatric population, hypovitaminosis D is also associated with the development of rickets, obesity, sickle cell, childhood cancers, chronic inflammatory diseases and deficient bone growth [1, 7–10]. Increased melanin, impaired renal function, limited sunlight exposure, season, age, obesity and decreased intake of vitamin D have been presented as risk factors of vitamin D deficiency [1, 11–13]. In fact, there has been an increasing amount of evidence highlighting the general population trend toward low vitamin D levels [1, 14–20].

It has been established that to maintain normal calcium levels during a low vitamin D state in adults it is necessary to increase bone turnover rate, which predisposes them to a fracture [5, 14–20]. Some suggest that this finding could be extrapolated to pediatric populations [14–20]. However, evidence about the true relationship between low vitamin D and the risk of suffering a fracture in the general pediatric population is not well established [1, 14–26]. The vast majority of research has focused on the Caucasian population, which has shown inconsistent data among fractured pediatric patients versus chronically ill patients or normal “healthy” children [1, 14, 16, 17, 19–21]. Other ethnicities have received less attention in the current publications; for example, only one study has addressed the vitamin levels and the fracture risk relation among the African-Americans pediatric population living in the USA mainland [15]. Nothing has been published about the relation between vitamin D levels and fracture propensity in a pediatric Hispanic population. The current evidence indicates that Hispanics have a higher vitamin D level than African-Americans, but lower than Caucasians [1]. There has not been any case–control study published focused on Hispanic children’s risk of sustaining a low-energy fracture due to vitamin D deficiency.

The main purpose of this study is to determine whether there is a correlation between vitamin D levels and the risk of a low-energy pediatric fracture in a Hispanic population. We compared levels of vitamin D, calcium, phosphorus, blood urea nitrogen (BUN), creatinine, parathyroid hormone (PTH) and alkaline phosphatase (ALP) of children who sustained a low-energy fracture to those of children without a fracture. We hypothesized that Hispanic children with fractures would have significantly higher prevalence of vitamin D deficiency and insufficiency than children without fractures.

## Method

This was a case–control study approved by the Institutional Review Board at Ponce Health Sciences University, Ponce, Puerto Rico. Data were collected through a medical record

review of all consecutive pediatric patients evaluated due to a low-energy fracture at the Mayaguez Medical Center Pediatric Orthopedic Clinic—Puerto Rico during a 6-month period, from January to July 2017 (107 pts.). We defined low-energy fracture as the one sustained during what is considered normal daily activity or from a standing position, in contrast to those fractures secondary to vehicle accident or secondary to a fall from over 10 feet which are considered as high-energy fracture [14, 17, 18]. The control group consisted of 94 pediatric patients evaluated during the same time period, without fractures, who had bone and joint pain complaints at Mayaguez Medical Center Pediatric Clinics. Case inclusion criteria were pediatric patients (< 18 years) who suffered a low-energy fracture confirmed by a plain radiograph and required evaluation at the orthopedic pediatric clinic. Following current and ongoing clinical evidence [14, 17, 21], a comprehensive metabolic panel, phosphorus, parathyroid hormone (PTH) and 25-hydroxyvitamin D levels are routinely required to all patients evaluated who have suffered a fracture and bone/joint pain. Metabolic panel includes levels of calcium, blood urea nitrogen (BUN), creatinine and alkaline phosphatase. Vitamin D deficiency was defined as a 25-hydroxyvitamin D level  $\leq 20$  ng/mL, insufficiency as within the 20–30 ng/mL range and normal above 30 ng/mL [3, 14, 20]. The serum samples were ordered at the initial evaluation, and results were brought back by the legal guardian of the patient in the follow-up medical visit.

Exclusion criteria of cases and controls are as follows: an underlying bone mineralization disorder (e.g., osteomalacia or osteogenesis imperfecta), chronic diseases that directly affect bone density (e.g., chronic kidney disease, cancer or sickle-cell disease), wheelchair bound (e.g., cerebral palsy, spina bifida, spinal atrophy or syndromic), use of antiepileptic medication and chronic use of oral steroids. Also, high-energy fractures were excluded from the case sample.

Demographic variables, such as age, sex, location and mechanism of fracture, and season were collected through the revision of medical records. Additionally, weight and height were used in order to calculate body mass index (BMI). BMI percentiles were determined by using the Centers for Disease Control Charts (2000). Subjects were classified as underweight, normal, overweight or obese according to accepted criteria based on BMI percentiles. All the above-mentioned information was recorded following standard clinical protocol.

## Statistical analysis

Statistical analysis was done using SPSS®. Descriptive statistics included frequency distributions and percentages for categorical variables while means and standard deviations for quantitative variables. Cases and controls were compared using *t* tests for means of quantitative variables and

Chi-square tests for categorical variables. A logistic regression analysis was done to estimate adjusted associations between fractures and relevant variables, eliminating any possible confounding effects.

## Results

A total of 201 subjects, distributed as cases ( $n = 107$ ) and controls ( $n = 94$ ), were included in this study. One hundred twelve (55.7%) of the total study population were males. The mean age for the study population was 8.6 years old, ranging from 1 year to 18 years of age and standard deviation = 4.0 years. The median age for the study population was 9 years. The age group distribution was 63 (31.3%) from 0 to 6 years old, 100 (49.8%) from 7 to 12 years old and 38 (18.9%) 13 years and older. Mean BMI for the study sample was 19.6 kg/m<sup>2</sup>, ranging from 8.9 to 48.9 kg/m<sup>2</sup> and standard deviation = 6.0 kg/m<sup>2</sup>. The median BMI for the study group was 18.1 kg/m<sup>2</sup>.

Among cases, 84 (78.5%) had fractures of the upper extremity and 23 (21.5%) had fractures of the lower extremity. A total of 48 subjects (44.9%) had forearm fractures; most of them occurred during a fall at school.

Cases and controls were compared using independent samples *t* test for the means of quantitative variables. These results are shown in Table 1. The two groups were not different except for the mean values of parathyroid hormone (PTH) and alkaline phosphatase (ALP), which showed statistically significant differences between the two groups. Cases had significantly lower mean values of PTH than controls and had significantly higher levels of alkaline phosphatase than controls.

Cases and controls were compared by their sex distribution. A total of 64 (59.8%) of cases and 48 (51.1%) controls were male. The difference in sex distribution between the two groups was not statistically significant ( $X^2 = 1.55$ ;  $p = 0.213$ ). The Odds Ratio for being male (cases vs control) was 1.4 (95% CI 0.82–2.5). Cases and controls were also compared according to BMI categories. These results are shown in Table 2. The differences between the two groups were not statistically significant.

The main focus of the results was to compare cases and controls in relation to their vitamin D levels. This was done in two different manners. Mean levels of vitamin D were calculated for each group and compared with independent samples *t* test. The mean vitamin D level for the cases was 32.6 ng/dl (SD = 10.9); the mean vitamin D level for controls was 32.3 ng/dl (SD = 13.4). This difference was not statistically significant ( $t = 0.18$ ;  $p = 0.854$ ). The mean vitamin D difference between the groups was 0.3 ng/dl (95% CI – 3.2, 3.9). Cases and controls were also compared dividing the subjects into three groups, according to whether they had normal, insufficient or deficient levels of Vitamin D. The results of this comparison are shown in Table 3. These results were also not statistically significant.

Two variables (PTH and alkaline phosphatase) were associated with fracture risks in our population, conversely, sex, age and vitamin D levels have been found relevant by previous studies [14–18]. For this reason, a multivariate analysis was done to look for adjusted measures of association of all independent variables of interest and fractures (cases) erasing any possible confounding effects between these variables. A logistic regression analysis was done using age, male sex, PTH, ALP levels and vitamin D levels as independent variables, and fracture (case) as the dependent variable. The results of this analysis are shown in Table 4. The multivariate model was consistent with the previous crude analysis, showing a statistical association of PTH levels and alkaline phosphatase levels with fractures. Age, male sex and vitamin D levels were not associated with the presence of fracture.

**Table 2** Comparison of cases and controls by BMI categories

BMI Category	Control (%)	Cases (%)
Underweight	29 (31.2)	33 (31.3)
Normal	48 (50.5)	53 (49.5)
Overweight	14 (15.1)	13 (12.1)
Obese	3 (3.2)	8 (7.1)
Total	94 (100.0)	107 (100.0)

$X^2$  for linear trend = 0.21;  $p = 0.649$

**Table 1** Comparison of cases and controls by quantitative variables

Variable	Mean cases	Mean control	<i>T</i> (p)	Mean difference (95% CI)
BMI (kg/m <sup>2</sup> )	20.2	19.0	1.39 (0.167)	1.2 (– 0.5, 2.9)
Calcium (mg/dL)	9.8	9.7	1.03 (0.306)	0.1 (– 0.1, 0.2)
Phosphorus (mg/dL)	5.0	5.4	– 0.32 (0.747)	– 0.4 (– 2.4, 1.7)
BUN (mg/dL)	11.8	11.9	– 0.23 (0.822)	– 0.1 (1.3, 1.0)
Creatinine mg/dL	0.5	0.5	0.21 (0.832)	0.0 (0.0, 0.1)
PTH (pg/ml)	27.0	33.7	– 3.39 (0.001)	– 6.7 (– 10.6, – 2.8)
Alk Phosph (U/L)	268.0	213.3	2.64 (0.009)	54.7 (13.7, 95.6)

**Table 3** Comparison of cases and controls by vitamin D level categories

Vitamin D level category	Control (%)	Cases (%)
Deficient	5 (5.6)	11(10.6)
Insufficient	45 (47.8)	38 (35.1)
Normal	44 (46.7)	58 (54.3)
Total	94 (100.0)	107 (100.0)

$\chi^2$  for linear trend=0.07;  $p=0.791$

**Table 4** Logistic regression—association between different variables and event of fracture

Variable	$\chi^2$	$p$	OR (95% confidence interval)
Age	0.35	0.552	0.965 (0.859, 1.085)
Male sex	0.34	0.561	1.293 (0.544, 3.072)
Vitamin D (ng/dl)	1.98	0.159	0.973 (0.936, 1.011)
PTH (pg/dl)	8.31	0.004	0.934 (0.892, 0.978)
Alkaline phosphatase (U/l)	6.37	0.012	1.006 (1.001, 1.010)

## Discussion

Published data gathered in the last decade shows conflicting findings on how hypovitaminosis D increases the fracture possibility in a pediatric population [1, 14–26]. The literature search shows a universal tendency of low vitamin D level values with a direct correlation with several risk factors such as diet, geographical location, sun exposure, skin type, vitamin D supplementation and the presence of obesity [1, 14–26]. There is a relative consensus that vitamin D level less than 20 ng/ml is considered a deficiency, less than 30 ng/ml is insufficient and more than 30 ng/ml is accepted as normal [14, 18, 20]. Kapisnki et al. [25] reported 12 ng/ml as the mean lower vitamin D level in a fractured polish group of patients, and Ceroni et al. [16] presented the mean upper vitamin D level (31 ng/ml) in a Swiss fractured group of patients. Even though not all the published articles had a control group, the vitamin D values reported in the control groups ranged from 16 to 32.7 ng/ml [1, 14–16, 18, 19, 21, 22, 24, 25]. Our data confirms a similar tendency in our Hispanic population, having 32 ng/ml as a mean value in both groups. This finding placed our group of patients in the lower portion of the normal spectrum (30–100 ng/ml), as the rest of the races.

The prevalence of vitamin D deficiency percentage in a pediatric fracture population had been reported to be between 5 and 47% [1, 14–24]. In those publications that use a control group, the deficiency percentage ranged from 4 to 40.8% [1, 14–19, 22, 23]. Regarding vitamin D

insufficiency levels, the same pattern was found among published studies [1, 14–22]. In our Hispanic group, the vitamin D deficiency level ranged from 6% (control group) to 10% (fractured group) and within the insufficiency range from 32% (fractured group) to 43% (control group). As reported in the literature, Afro-American population presented the higher percentage of deficiency and insufficiency of vitamin D levels, and the lower percentage found in the Caucasian patients [15–17, 19, 21, 23]. The disparity in vitamin D mean levels in the literature clearly confirmed the universal tendency of low levels of vitamin D with a strong link to geographical or skin type influences [1, 14–19, 23]. Also, the data analysis validates that the Hispanic population will have a similar vitamin D behavior as the Caucasian group of patients. This research helps to fill the gap between what is known among Caucasians and other ethnic minorities regarding vitamin D status.

The natural pathway of the vitamin D starts with a catalytic hydroxylation reaction that occurs when ultraviolet light contacts the skin to generate 25-hydroxycholecalciferol, which travels to the kidney to be hydroxylated into 1, 25-hydroxycholecalciferol, being the active form. The latter is necessary for the absorption of calcium in the kidneys [3]. Calcium is one of the major mineral component of the bone and responsible of the bone strength [27, 28]. Therefore, theoretically deficient bone strength will be associated with a low calcium level. It is expected that a complete evaluation of the pathway between the vitamin D level and the fracture risk required an assessment of the participation of calcium, phosphorus, BUN, creatinine, ALP and PTH as components of the calcium–bone homeostasis. With different conclusions, few studies in the past had considered this assessment as important in their evaluation of the relation of vitamin D levels and pediatric fracture risk. Schilling et al. [20] found that lower vitamin D levels were associated with higher incidences of hypocalcemia and elevated alkaline phosphatase without hypophosphatemia. El-Sakka et al. [24] found a significant low calcium level and vitamin D level in the fracture group with significant elevated ALP level. Olney et al. [18], James et al. [17] and Saglan et al. [26] did not report any metabolic panel disturbance associated with hypovitaminosis D. In our study, there was no correlation between calcium and vitamin D levels, in agreement with previous reports where the calcium concentration remains normal in patients with low vitamin D levels [17, 18]. Nevertheless, we found higher ALP level in those patients with fracture that correlate with El-Sakkar et al. [24] and Schilling findings [20]. ALP levels usually rise above normal after a fracture due to its biochemical action which is important in bone turnover and healing [28]; parathyroid hormone levels were found considerably higher in the control cohort than in cases, a finding that has not been previously described and not expected at all since vitamin

**Table 5** Vitamin D and pediatric fracture risk relation

References	Study sample	Association vitamin D and fracture risks	Ethnicity
Olney et al. [18]	68 fractured 57 non-fractured	No	Multiethnic
Schilling et al. [20]	118 fractured	No	Multiethnic
Ceroni et al. [16]	100 fractured	No	Swiss
Ryan et al. [15]	100 fractured 100 non-fractured	Yes	Afro-Americans
James et al. [17]	181 fractured	Yes	Multiethnic
Contreras et al. [1]	100 fractured 100 non-fractured	No	Multiethnic
Fabricant et al. [21]	58 fractured 103 CKD patients	Yes	Multiethnic
Gorter et al. [23]	189 fractured	Yes	Dutchs
El-Sakka et al. [24]	23 fractured 23 non-fractured	Yes	Egyptians
Minkowitz et al. [22]	369 fractured 662 non-fractured	No	Multiethnic
Thompson et al. [14]	60 fractured 60 no fractured	Yes	Multiethnic
Karpinski et al. [25]	100 fractured 127 non-fractured	Yes	Polish
Saglam et al. [26]	30 fractured 30 non-fractured	Yes	Turkish
Anderson et al. [19]	206 fractured 343 non-fractured	No	Canadian

D, phosphorus and calcium levels were relatively similar in both groups. Although the difference is statistically significant, it is not clinically relevant.

From 2007 to 2017, the relation between vitamin D levels and pediatric fracture risk had been evaluated in 14 studies with a great inconsistency of conclusions [1–26] (See Table 5). This inconsistency had been based on the methodological differences in the analysis, such as different vitamin D values, cohorts with dissimilar group of age, different type of fracture energy, different ethnicities. Other dissimilarities were patient selection, the use of a control group or not, different selection of patients in the control group and statistical analysis or outcomes. In summary, our study method consisted in all consecutive Hispanic patients with low-energy fracture less than 18 years of age during a 6-month period who were evaluated with a similar group of healthy patient as control cohort. This study took place in a Caribbean island without seasonal variance with a relatively high sun exposure. The conclusions were based on the comparison among fracture and control groups' vis-à-vis vitamin D values and categories. There was a minimal difference between mean vitamin D levels among cases and controls. Surprisingly, there were a higher percentage of controls with deficient or insufficient vitamin D levels than cases. Our findings suggest that in a Hispanic pediatric population vitamin D status does not impact fracture risk. The study

weakness resides in that we did not gather information about mean weekly milk intake and vitamins supplementation.

## Conclusion

Data show no association between vitamin D status and fracture risk in Hispanics. Our study starts to fill the evidence gap of what is known about the vitamin D status and fracture risk association in Hispanics. On the other hand, we found that nearly 50% of the study sample had vitamin insufficiency. It is a startling finding since Puerto Rico is near the equatorial line where there are minimal seasonal changes and there are no extended periods without sunlight. Our results add to the emerging body of evidence that there is a trend toward vitamin D deficiency in the world and suggest that it is secondary to a genetic predisposition or other social–demographic and environmental factors. Further studies are needed to evaluate the reasons for low vitamin D levels in the Hispanic population that live close to the equatorial line.

## Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflict of interest.

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