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ORIGINAL ARTICLE

Serum 25-hydroxyvitamin D status among Saudi children with and without a history of fracture

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Abstract
Background The significance of vitamin D deficiency in the incidence of bone fractures in children has been under investigated. Here, we aimed to associate serum 25-hydroxyvitamin D levels and fractures in Saudi children.
Materials and methods This cross-sectional study was conducted in 1022 Saudi children without fracture history [476 boys (age 14.56 ± 1.81, BMI 22.38 ± 5.81) and 546 girls (age 13.57 ± 1.67, BMI 22.24 ± 4.94)] and 234 Saudi children with a history of fracture [148 boys (age 14.25 ± 1.39, BMI 22.66 ± 6.08) and 86 girls (age 13.76 ± 1.35, BMI 21.33 ± 1.35)]. Anthropometric and fasting serum biochemical data were collected. Serum 25-hydroxyvitamin D level was assessed using electrochemiluminescence.
Results Mean circulating 25-hydroxyvitamin (25OH) D level in subjects with a history of fracture was significantly lower in both boys ($p < 0.01$) and girls ($p < 0.01$) than those without, however both groups had low mean 25(OH) D levels. Furthermore, age was positively associated with 25-hydroxyvitamin D in boys ($p < 0.05$) and negatively in girls ($p < 0.05$) with a history of fracture.
Conclusion In conclusion, vitamin D levels were significantly lower in children with a history of bone fractures in both boys and girls than those without such a history; even in the absence of fracture history, vitamin D status correction is warranted in the general Saudi pediatric population.

Keywords Vitamin D · History of fracture · Children · Arab

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Introduction

Vitamin D is an essential nutrient, known for its role in regulating calcium absorption and bone mineralization [1, 2]. Vitamin D deficiency and insufficiency (hypovitaminosis D) have been associated with rickets, metabolic bone disease, and rarely hypocalcaemia during infancy and childhood [3, 4]. Serum 25-hydroxyvitamin D [25(OH)D] is considered the best marker of vitamin D repletion status, and there is increasing evidence that low serum 25(OH)D is common in both children and adults [5]. Serum 25(OH) D levels persistently below 50/nmol may lead to hypocalcemia, secondary hyperparathyroidism, osteoporosis, and osteomalacia, respectively, in adults or rickets, including growth hormone deficiency in children [6, 7].

Osteoporotic fractures, which are increasingly common worldwide, are associated with considerable morbidity, mortality, and cost to the health care system [8]. Fractures are one of the most severe consequences of weak bone, and deficiency of vitamin D has been identified as one of the most common risk factor [9]. Vitamin D deficiency was identified as a risk factor for fragility hip fracture in the

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elderly population [10]. However, fractures in children are largely ignored, in spite of being quite common, having a significant impact on daily activities, and might be indicative of increased fracture risk in adulthood [11]. Recent evidence suggests that pediatric fractures are increasing in incidence and result in substantial health care costs [8, 12].

Several studies revealed the high prevalence of vitamin D deficiency in adult women with hip fractures [13–15]. However, limited data are available regarding vitamin D deficiency as a risk factor for fractures in children. Recent studies in the Middle East have shown an increased incidence of vitamin D deficiency across this region of year-round sunlight in all age groups, including children [16], probably because of cultural full-body coverings (especially girls) restricts children from sun exposure during daytime [17]. In spite of the well-known relation between vitamin D and bone health, the significance of vitamin D deficiency in the pathogenesis of fractures in Saudi children remains unclear. The purpose of this study was to determine the relation between vitamin D deficiency and fracture history among Saudi boys and girls.

Materials and methods

Subjects and experimental design

In this cross-sectional study, a total of 1256 Saudi children aged 12–17 years; 1022 without a history of fracture (476 boys and 546 girls) and 234 (148 boys and 86 girls) with a history of fracture were recruited from four Primary Health Care Centers (PHCCs) within Riyadh, Saudi Arabia from mid-2013 to early 2015. Written informed consent was obtained from parents, as well as a verbal assent for children, prior to inclusion in the study. Approval was obtained from the Ethics Committee of the College of Science Research Center, King Saud University, Riyadh, Saudi Arabia. All participants completed a questionnaire on demographic information, general health status, and past medical history, including the history of confirmed fracture type [e.g. major (high-energy impact trauma requiring orthopedic surgery treatment) and minor (low-to-moderate-energy impact trauma that does not require such treatment] and location (e.g., lower and upper extremities and other skeletal parts).

Physical examination was carried out by the attending physician who ensured the exclusion of subjects with conditions that require immediate medical attention like cardiac, kidney or liver disease, psychiatric conditions, and/or use of medications known to affect body weight and bone health (such as steroids). Likewise, subjects, whose past or present medical history, include that the diagnosis of rickets either clinically through X-ray and/or with metabolic signs (elevated ALP or PTH, or low phosphate or calcium) was excluded.

Weight and height were recorded to the nearest 0.2 kg and 0.5 cm, respectively, using an appropriate international standard scale (Digital Pearson Scale, ADAM Equipment Inc., USA). Blood pressure was measured using an appropriate mercury sphygmomanometer. Blood pressure was measured twice with a 5-min interval and the mean of the two readings was recorded.

Fasting blood samples (>8 h) were withdrawn by a staff nurse and centrifuged for serum isolation. The collected sera were then transferred to a pre-labeled tube, stored in ice, and delivered to the Biomarkers Research Program (BRP) at King Saud University, Riyadh, KSA for immediate storage at −20 °C until analysis. Fasting blood glucose (FBG) level and lipid profile were measured using a chemical analyzer (Konelab20XTi, Thermo Electron Corporation, Vantaa, Finland). Serum 25(OH) D was measured using COBAS e-411 automated analyzer (Roche Diagnostics, Indianapolis, IN, USA) in a DEQAS-certified laboratory (BRP). For serum 25(OH)D assay, the inter- and intra-assay coefficients of variation (CV) were 8.0 and 5.6 %, respectively, with a lower detection limit (LOD) of <10 nmol/l). Vitamin D deficiency was defined based on the recommendations of Misra and colleagues [deficiency (<37.5 nmol/l); insufficiency (37.5–50 nmol/l) and sufficiency (>50 nmol/l)] [18].

Statistical analyses

Data analyses were carried out using the Statistical Package for the Social Sciences software (SPSS 16.0; SPSS Inc, Chicago, IL, USA). Data were expressed as mean ± standard deviation (SD). A Kolmogorov–Smirnov test was performed to assess continuous variables for normality. All non-Gaussian parameters were logarithmically or square root transformed to normalize prior to correlations and parametric analyses. Independent Student *t* test was employed to compare means between groups of normally distributed data. Mann–Whitney *U* test was performed for non-Gaussian variables. p values <0.05 were considered statistically significant.

Results

A total of 234 (18.6 %) subjects reported to have had a history of fracture. All were considered minor fractures (low-to-moderate-energy trauma not requiring surgical treatment). A majority of these fractures were located in the arms, hands, and fingers [$n = 123$ (52.6 %)] followed by ankle, foot, and toes [$N = 78$ (33.3 %)] (not included in the table).

All the anthropometric and laboratory characteristics of the study participants are presented in Table 1. Vitamin D deficiency prevalence was significantly higher in the fracture than the non-fracture group (76.1 vs. 58.2; $p < 0.001$).

Mean serum 25(OH)D level and HDL cholesterol were also significantly lower ($p < 0.001$) in the history of fracture group than the non-fracture group.

Table 2 presents clinical characteristics of the participants with subjects that were divided into males and females. Serum 25(OH)D level was significantly lower ($p < 0.001$) in both boys and girls with fracture than in the non-fracture group (Fig. 1). Furthermore, in boys, total cholesterol, HDL cholesterol, and triglycerides were significantly lower ($p < 0.01$) in the fracture group than the non-fracture group, while only total cholesterol levels were significantly higher ($p < 0.01$) in girls with a history of fracture than in non-fracture group.

Employing Pearson correlation analysis (Table 3), 25(OH)D was positively associated with age, total cholesterol, HDL cholesterol, triglycerides, and FBG in the overall population ($p < 0.01$). In boys from the non-fracture group, 25(OH)D level was positively associated with age, serum total cholesterol, HDL cholesterol, and triglycerides ($p < 0.01$), while 25(OH)D levels were positively associated with age ($p < 0.05$), total cholesterol ($p < 0.01$), and triglycerides ($p < 0.01$) in the bone fracture group. In girls from the non-fracture group, HDL cholesterol was positively associated ($p < 0.05$) with 25(OH)D level. In girls from the fracture group, age was negatively associated with serum 25(OH)D level ($p < 0.05$).

Table 1 Clinical characteristics of subjects

	Without fracture	With fracture	*p* value
N	1022	234	
Vitamin D status (%)			0.000
Deficiency	595 (58.2)	178 (76.1)	
Insufficiency	365 (35.7)	46 (19.6)	
Sufficiency	62 (6.1)	10 (4.3)	
Age (years)	14.03 ± 1.81	14.07 ± 1.39	0.744
Body mass index (kg/m^2)	22.30 ± 5.35	22.15 ± 5.57	0.703
Systolic blood pressure (mmHg)	116.96 ± 16.05	118.06 ± 16.80	0.356
Diastolic blood pressure (mmHg)	71.94 ± 15.59	71.04 ± 13.71	0.333
Total cholesterol (mmol/l)	4.83 ± 0.99	4.80 ± 1.01	0.646
HDL-cholesterol (mmol/l)	1.27 ± 0.37	1.19 ± 0.29	0.003
Glucose (mmol/l)	5.44 ± 1.95	5.27 ± 0.95	0.218
Triglycerides (mmol/l)[#]	1.28 ± 0.85	1.17 ± 0.63	0.069
25(OH)D (nmol/l)[#]	38.74 ± 22.25	30.71 ± 18.48	0.000

Data presented as mean ± SD

[#] Non-Gaussian; *p* value significant at <0.05

Discussion

The main findings of this study were a significantly lower level of 25(OH)D in both boys and girls having a history of fracture, and furthermore, age was positively associated with 25(OH)D in boys, while it was negatively associated in girls with a history of fracture.

Bone fractures are a common childhood problem and in an estimate in the Caucasian population, up to 50 % of boys and 40 % of girls were shown to sustain at least one fracture before the age of 18 years [3, 19, 20]. However, the data on fractures are limited in Saudi children and adolescents and, to the best of our knowledge, there are no data available regarding the relation between serum 25(OH)D concentrations and incidence of fracture in children. Despite the high prevalence of vitamin D deficiency among the Saudi population of all ages, including children [16,

Table 2 Clinical characteristics of the male and female subjects

	Males		Females	
	Without fracture	With fracture	Without fracture	With fracture
N	476	148	546	86
Age (years)	14.56 ± 1.81	14.25 ± 1.39	13.57 ± 1.67	13.76 ± 1.35
Body mass index (kg/m^2)	22.38 ± 5.81	22.66 ± 6.08	22.24 ± 4.94	21.33 ± 1.35
Systolic blood pressure (mmHg)	119.02 ± 15.97	118.14 ± 17.34	115.19 ± 15.93	117.90 ± 15.92
Diastolic blood pressure (mmHg)	71.14 ± 13.64	71.89 ± 14.01	72.64 ± 11.57*	69.59 ± 1.11
Total cholesterol (mmol/l)	5.33 ± 1.31**	4.63 ± 0.91	4.52 ± 0.52**	5.08 ± 1.11
HDL-cholesterol (mmol/l)	1.32 ± 0.36**	1.19 ± 0.31	1.25 ± 0.37	1.19 ± 0.27
Glucose (mmol/l)	5.72 ± 2.74*	5.23 ± 0.68	5.27 ± 1.19	5.35 ± 1.29
Triglycerides (mmol/l)[#]	1.48 ± 1.13**	1.10 ± 0.56	1.16 ± 0.56	1.29 ± 0.73
25(OH)D (nmol/l)[#]	37.52 ± 22.53**	30.10 ± 20.66	39.81 ± 21.98**	32.21 ± 11.58

Data presented as mean ± standard deviation

[#] Non-Gaussian; * significance at the 0.05 level and ** significance at the 0.01 level

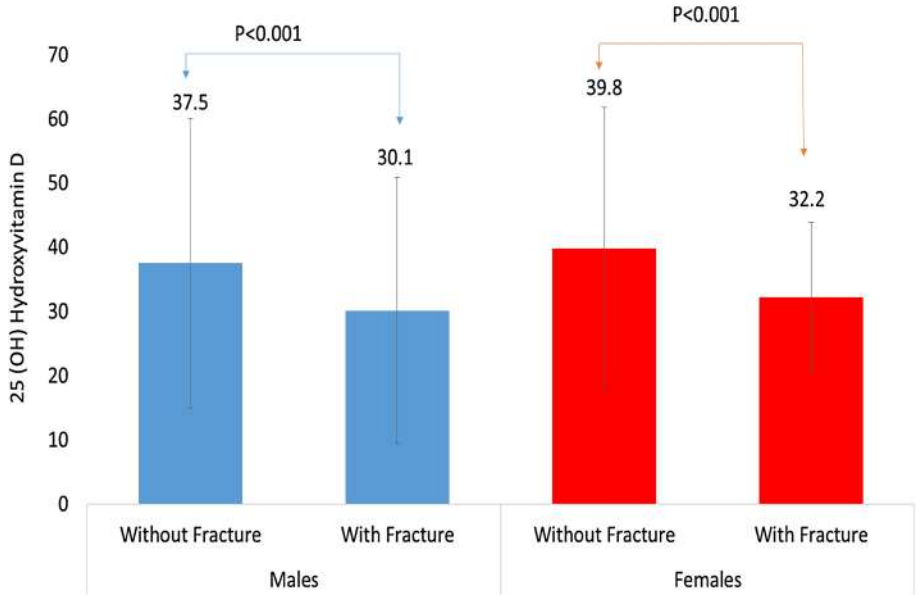

Fig. 1 Mean 25(OH D) (nmol/l) levels (standard deviation) in boys and girls with and without a history of fractures

Table 3 Association between Log 25(OH)D with clinical parameters of all subjects, males, and females

Parameters	All Subjects			Males			Females		
	All	W/O fracture	With fracture	All	W/O fracture	With fracture	All	W/O fracture	With fracture
N	1256	1022	234	624	476	148	632	546	86
Age (years)	0.08**	0.08**	0.08	0.24**	0.25**	0.18*	−0.05	−0.03	−0.26*
Body mass index (kg/m^2)	0.01	0.01	0.05	0.18	0.01	0.06	0.01	0.004	0.11
Systolic blood pressure (mmHg)	−0.02	−0.03	0.04	0.05	0.04	0.04	−0.06	−0.07	0.11
Diastolic blood pressure (mmHg)	0.06*	0.08*	−0.06	0.07	0.12*	−0.04	0.03	0.03	−0.03
Total cholesterol (mmol/l)	0.19**	0.17**	0.27**	0.35**	0.29**	0.37**	−0.01	0.02	−0.04
HDL-cholesterol (mmol/l)	0.15**	0.14**	0.11	0.20**	0.18**	0.15	0.11**	0.11*	0.03
Glucose (mmol/l)	0.08*	0.09**	−0.03	0.11*	0.11	−0.03	0.06	0.08	−0.06
Triglycerides (mmol/l)[#]	0.13**	0.24**	0.09**	0.23**	0.18**	0.28**	0.02	0.02	0.09

Data presented as coefficient (*R*)

[#] Non-Gaussian; * significance at 0.05 level; ** significance at 0.01 level

17], deficiency/insufficiency of vitamin D in children suffering fractures has not been studied until now.

In this study, we observed lower vitamin D levels among boys and girls having a history of fractures than those without. This is the first study from the Arabian region that confirms an association between low serum 25(OH)D concentrations and higher incidence of bone fractures, with incidence defined as the number of new cases in a defined population in a given time period, equal for both groups for comparison. Recently, in a preliminary study published in 2010 by Ryan et al. [21], a significant proportion (59 %) of African American children with fractures was vitamin D-insufficient, and furthermore, the authors noted that this prevalence was higher than the baseline levels reported in similar populations. Another study, Ryan et al. [12] supported an association between vitamin D deficiency and lower bone mineral density, with increased odds of forearm fracture among African American children. On the other hand, some studies failed to observe any association between vitamin D deficiency and increased the incidence of fractures. In a study by Chan et al. [22], children under 12 years who had sustained a fracture were not different from those without fractures with respect to vitamin D level. Similarly, Farr et al. [23] assessed 25(OH)D status in children aged 8–15 years who had sustained a mild or moderate impact distal radial fractures but did not find any difference in 25(OH)D status between children with and without a history of fractures.

Despite the above inconsistencies, other studies have shown a decrease in fracture incidence following vitamin D supplementation, which indirectly confirm the association between vitamin D and fractures [24]. A randomized double-blind controlled trial of 100,000 IU oral vitamin D3 (cholecalciferol) supplementation versus placebo given every 4 months for 5 years found a 22 % reduction for any first fracture and a 33 % reduction for a first fracture in the common osteoporotic sites [25]. In another study, Parchi et al. [26] in a case report also confirmed the effect of vitamin D on fracture healing in a young boy with a hypovitaminosis D.

In this study, we observed that fractures in boys were more prevalent than in girls ($n = 148$ vs. 86). This might relate to higher outdoor activities, such as sports in boys compared to girls and also physiological difference in this age group due to timing of pubertal growth—the bones of the girls are maturing and the boys still have relatively weaker bones due to rapid bone growth at age 13–14 years. This hypothesis is consistent with higher incidence of fractures in Caucasian children, in which up to 50 % of boys and 40 % of girls sustain at least one fracture in their childhood [3].

Another highlight in the present study was the positive association of age and 25-hydroxyvitamin D in boys, while it was negatively associated in girls having a history of fracture. One explanation for this observation may be conservative social and religious practices imposed on girls and the fact that advancing age in girls is more often covered compared to boys of similar age. However, the peak age of incidence of childhood fractures is fairly constant in the literature with around age 14 for boys and age 11 for girls, with a sharp decline in the rate afterwards [11].

It is important to mention none of the subjects had rickets even among those whose 25(OH) vitamin D was <34 nmol/l as previously observed by Atapattu et al. [27]. In the presence of normal calcium intake, simple vitamin D deficiency has not been associated with rickets or fractures. Rickets, however, is associated with fractures [28–30]. The question of whether a state of pre-rickets (with histological osteomalacia but no radiological signs of rickets) exists, where fracture risk is already increased cannot be answered in the present study. Nevertheless it is clear that serum 25(OH)D is lower among those with a fracture history than those without. This has clinical implications, since it has been observed that circulating 25(OH)D affects mineralization process [31] and even seasonal variations affect growth in pre-pubertal children [32].

There were certain limitations of this study. The measurement of cause and effect relation was not possible because of the cross-sectional design of the study. Information on time since fracture is also not available and could have greatly added value to the study. Another limitation was that 25(OH)D measurements were performed after the fracture and may not accurately reflect pre-fracture exposure.

In conclusion, our data indicate an association between vitamin D status and bone fractures in Saudi children. Because fracture rates in children are increasing and bone health status in childhood may directly impact adult bone health, opportunities to intervene during childhood should be pursued. Given the high prevalence of vitamin D deficiency in Saudi children with and without fracture, a strong consideration should be given for routine vitamin D testing and correction in the Saudi pediatric population.

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Compliance with ethical standards

Author contributions Nasser M. Al-Daghri conceptualized and designed the study, and approved the final manuscript as submitted. Shakilur Rahman and Shaun Sabico contributed in the preparation and revision of the manuscript, carried out the initial analyses, reviewed and revised the manuscript, and approved the final manuscript as submitted. Naji Aljohani, Abdulrahman Al-Ajlan, Omar Al-Attas, and Majed Alokail and George Chrousos edited, critically reviewed, and approved the final version of the manuscript as submitted.

Conflict of interest None.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Written informed consent was obtained from parents, as well as a verbal assent for children, prior to inclusion in the study.

References

1. Lieben L, Carmeliet G, Masuyama R (2011) Calcemic actions of vitamin D: effects on the intestine, kidney and bone. Best Pract Res Clin Endocrinol Metab 25:561–572
2. Marcelli C, Chavoix C, Dargent-Molina P (2015) Beneficial effects of vitamin D on falls and fractures: Is cognition rather than bone or muscle behind these benefits? Osteoporos Int 26:1–10
3. Moon RJ, Harvey NC, Davies JH, Cooper C (2014) Vitamin D and skeletal health in infancy and childhood. Osteoporos Int 25:2673–2684
4. Wagner CL, Greer FR (2008) Prevention of rickets and vitamin D deficiency in infants, children, and adolescents. Pediatrics 122:1142–1152
5. Alemzadeh R, Kichler J, Babar G, Calhoun M (2008) Hypovitaminosis D in obese children and adolescents: relationship with adiposity, insulin sensitivity, ethnicity, and season. Metabolism 57:183–191

6. Ciresi A, Ciccio F, Giordano C (2014) High prevalence of hypovitaminosis D in Sicilian children affected by growth hormone deficiency and its improvement after 12 months of replacement therapy. J Endocrinol Invest 37:631–638
7. Holick MF (2007) Vitamin D deficiency. N Engl J Med 357:266–281
8. Harvey N, Dennison E, Cooper C (2008) Epidemiology of osteoporotic fractures. In: Rosen CJ (ed) Primer on the metabolic bone diseases and disorders of mineral metabolism (7th edn). ASBMR, pp 198–202
9. Smith JT, Halim K, Palms DA, Okike K, Bluman EM, Chiodo CP (2014) Prevalence of vitamin D deficiency in patients with foot and ankle injuries. Foot Ankle Int 35:8–13
10. Dhanwal DK, Sahoo S, Gautam VK, Saha R (2013) Hip fracture patients in India have vitamin D deficiency and secondary hyperparathyroidism. Osteoporos Int 24:553–557
11. Clark EM (2014) The epidemiology of fractures in otherwise healthy children. Curr Osteoporos Rep 12:272–278
12. Ryan LM, Teach SJ, Singer SA, Wood R, Freishtat R, Wright JL, McCarter R, Tosi L, Chamberlain JM (2012) Bone mineral density and vitamin D status among African American children with forearm fractures. Pediatrics 130:e553–e560
13. Larrosa M, Gomez A, Casado E, Moreno M, Vazquez I, Orellana C, Berlanga E, Ramon J, Gratacos J (2012) Hypovitaminosis D as a risk factor of hip fracture severity. Osteoporos Int 23:607–614
14. Malavolta N, Pratelli L, Frigato M, Mule R, Mascia ML, Gnudi S (2005) The relationship of vitamin D status to bone mineral density in an Italian population of postmenopausal women. Osteoporos Int 16:1691–1697
15. Nurmi I, Kaukonen JP, Luthje P, Naboulsi H, Tanninen S, Kataja M, Kallio ML, Leppilampi M (2005) Half of the patients with an acute hip fracture suffer from hypovitaminosis D: a prospective study in southeastern Finland. Osteoporos Int 16:2018–2024
16. Al-Daghri NM, Al-Attas OS, Alokail MS, Alkharfy KM, El-Kholie E, Yousef M, Al-Othman A, Al-Saleh Y, Sabico S, Kumar S, Chrousos GP (2012) Increased vitamin D supplementation recommended during summer season in the gulf region: a counterintuitive seasonal effect in vitamin D levels in adult, overweight and obese Middle Eastern residents. Clin Endocrinol (Oxf) 76:346–350
17. Al-Othman A, Al-Musharaf S, Al-Daghri NM, Krishnaswamy S, Yusuf DS, Alkharfy KM, Al-Saleh Y, Al-Attas OS, Alokail MS, Moharram O, Sabico S, Chrousos GP (2012) Effect of physical activity and sun exposure on vitamin D status of Saudi children and adolescents. BMC Pediatr 12:92
18. Misra M, Pacaud D, Petryk A, Collett-Solberg PF, Kappy M (2008) Drug and Therapeutics Committee of the Lawson Wilkins Pediatric Endocrine Society. Vitamin D deficiency in children and its management: review of current knowledge and recommendations. Pediatrics 122:398–417
19. Cooper C, Dennison EM, Leufkens HG, Bishop N, van Staa TP (2004) Epidemiology of childhood fractures in Britain: a study using the general practice research database. J Bone Miner Res 19:1976–1981
20. Moustaki M, Lariou M, Petridou E (2001) Cross country variation of fractures in the childhood population. Is the origin biological or "accidental"? Inj Prev 7:77
21. Ryan LM, Brandoli C, Freishtat RJ, Wright JL, Tosi L, Chamberlain JM (2010) Prevalence of vitamin D insufficiency in African American children with forearm fractures: a preliminary study. J Pediatr Orthop 30:106–109
22. Chan GM, Hess M, Hollis J, Book LS (1984) Bone mineral status in childhood accidental fractures. Am J Dis Child 138:569–570
23. Farr JN, Amin S, Melton LJ III, Kirmani S, McCready LK, Atkinson EJ, Muller R, Khosla S (2014) Bone strength and structural deficits in children and adolescents with a distal forearm fracture resulting from mild trauma. J Bone Miner Res 29:590–599
24. Steele B, Serota A, Helfet DL, Peterson M, Lyman S, Lane JM (2008) Vitamin D deficiency: a common occurrence in both high-and low-energy fractures. HSS J 4:143–148
25. Trivedi DP, Doll R, Khaw KT (2003) Effect of four monthly oral vitamin D3 (cholecalciferol) supplementation on fractures and mortality in men and women living in the community: randomised double blind controlled trial. BMJ 326:469
26. Parchi P, Andreani L, Piolanti N, Niccolai F, Cervi V, Lisanti M (2014) Effect of vitamin D in fracture healing in a child: case report. Arch Osteoporos 9:1–3
27. Atapattu N, Shaw N, Hogler W (2013) Relationship between serum 25-hydroxyvitamin D and parathyroid hormone in the search for a biochemical definition of vitamin D deficiency in children. Pediatr Res 74:552–556
28. Chapman T, Sugar N, Done S, Marasigan J, Wambold N, Feldman K (2010) Fractures in infants and toddlers with rickets. Pediatr Radiol 40:1308
29. Ward LM, Gaboury I, Ladhani M, Zlotkin S (2007) Vitamin D-deficiency rickets among children in Canada. CMAJ 177:161–166
30. Hazzazi MA, Alzeer I, Tamimi W, Al Atawi M, Al Alwan I (2013) Clinical presentation and etiology of ostyeomalacia/rickets in adolescents. Saudi J Kidney Dis Transpl 24:938–941
31. Need AG, Horowitz M, Morris HA, Moore R, Nordin C (2007) Seasonal change in osteoid thickness and mineralization lag time in ambulant patients. J Bone Miner Res 22:757–761
32. Andersson B, Swolin-Eide D, Kristrom B, Gelander L, Magnusson P, Albertsson-Wikland K (2015) Seasonal variations in vitamin D in relation to growth in short prepubertal children before and during first year growth hormone treatment. J Endocrinol Invest 38:1309–1317