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Bone health markers of a representative group of Saudi adolescents in Jeddah

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Summary

Aim: With the high prevalence of postmenopausal osteoporosis in Saudi Women (1), among other factors, failure to achieve peak bone mass (PBM) during puberty was suggested to be the culprit. Bone physiology parameters of a representative sample of adolescents in Jeddah were studied. *Materials and Methods:* Three hundred three adolescents (13-19 years) were selected from seven PHCC by multistage cross-sectional sampling and were studied prospectively. Demographic data, dietary habits, and lifestyle parameters were obtained by direct interview. Serum samples of calcium, phosphate, alkaline phosphatase, parathormone, 25 OH vitamin D, and osteocalcin were collected. Statistical analysis was done using SPSS 16. *Results:* The mean value of 25-hydroxy-vitamin D was 32.55 (50-75) nmol/ml with 89.5 % of the 303 adolescents with insufficient levels (< 50 nmol/L). There was a significant inverse correlation of serum parathormone with 25-hydroxy-vitamin D and calcium ($p = 0.000$ and $p = 0.003$), but no significant correlation of osteocalcin with 25 OH vitamin D. Linear regression of osteocalcin and the independent variables revealed no significant effect. *Conclusion:* Although 25 OH vitamin D levels were less than desirable in almost all adolescents, bone formation marker was normal. Could different genetic factors or microenvironment molecules have effect on bone physiology of Saudi girls? Future longitudinal studies are needed.

Key words: Adolescents; Bone turnover marker (osteocalcin); 25 OH vitamin D; Parathormone.

Introduction

Bone growth accelerates during puberty, in concert with height velocity. Seventeen to eighteen percent of adult height is accrued during puberty [1]. One-half of total body calcium is laid down during puberty. The final peak bone mass occurs around 19 years in adolescents females [2].

Building and maintaining healthy bones helps to reduce the risk of osteoporosis. By 2020, 50% of Americans older than 50 years are estimated to be at risk of osteoporotic fractures [3]. The future risk of osteoporotic fractures among Saudi population is yet to be studied, but there are reports of isolated centers from different parts of the country reporting the prevalence of osteoporosis in the corresponding regions of the Kingdom. *Rouzi et al.* in their study of 707 Saudi postmenopausal women reported 30.01 osteoporosis related fractures (ORF) per 1,000 women [4]. They also reported a prevalence of osteoporosis to be 38.3-47.7% of 1980 Saudi females between ages 50-79 years [5]. Different causes have been proposed including genetic, racial, and ethnic differences, plus vitamin D deficiency.

Severe vitamin D deficiency affecting adolescents causes osteomalacia and can lead to hypocalcemia which may cause tetany or seizures. Chronic vitamin D deficiency could possibly lead to future increased fracture risk in older children, adolescents, and adults [4]. Severe vitamin D deficiency is associated with reduced bone mass in adolescents [6]. Children and adolescents who have higher PBM reduce their risk of osteoporosis later in life [7]. This study was performed to be a baseline of bone health of a representative sample of Saudi adolescents.

Materials and Methods

A cross-sectional sample of adolescents presenting to seven primary healthcare centers (PHCC) were studied from December 15, 2010 to March 22, 2011.Multistage sampling technique was adopted to select the adolescents. One PHCC was selected by simple random sample from each sector PHCCs in Jeddah city. The city includes 40 PHCCs that are divided into six sectors. Then, all patients attending the selected centers were proportionally allocated according to the number of the registered population in each center. Well trained research assistants interviewed the selected adolescents in the selected PHCCs. Each adolescent visited the selected center during the study period and agreed to participate in the study. A consent form was obtained from the adolescent and her parent after explanation of the study. Demographic data of every adolescent was completed in the prepared form by the trained research assistant. It included: weight, height, body mass index (BMI), type and duration of exercise if any, sun exposure, and a detailed dietary history. A sample of blood was collected for estimation of 25 (OH) vitamin D, serum calcium, phosphate, alkaline phosphatase and parathormone (PTH). The study was approved by the ethical committee of King Abdul-Aziz University Hospital. SPSS 16 was used for data entry and analysis.

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Table 1. — *Demographic data of adolescents.*

Characteristic	Mean	SD	SEM
Age	16	1.84	0.106
Weight/kg	55.54	1.79	1.03
Height/m	1.53	7.97	0.46
BMI	23.43	7.02	0.41

BMI: Body mass index, SD: Standard deviation, SEM: Standard error of the mean

Table 2. — *Serum biochemical marker of the study group.*

Biochemical marker	Mean	SD	SEM
Calcium	2.33	0.196	0.013
Phosphate	1.56	0.57	0.038
Alkaline phosphatase	155	15.52	10.3
25-OH vitamin D	32.55	1.65	1.03
Osteocalcin	13.66	6.81	0.43
Parathormone	5.68	2.7	0.17

SD: Standard deviation, SEM: Standard error of the mean

Results

The demographic data of the adolescents are shown in Table 1. Only one adolescent had one child, all others had never been pregnant. The mean BMI of the adolescents was 23.4 kg/m² which is below the normal cutoff set by WHO (25 kg/m²) for this age group, 18.6% of girls were overweight, and 15.8% were obese. The mean serum level of osteocalcin was 13.66 (1-18 ng/ml), and parathormone was 5.68 (n = 5.1 to 8.6 pmol/L) Table 2.

The mean serum level of 25-hydroxy-vitamin D was: 32.55 nmol/L (Table 2). Using IOM criteria, 89.5 % of adolescents had 25 OH vitamin D insufficiency (< 50 nmol/L), while considering the Osteoporosis Canada Guidelines, endocrine Society, National Osteoporosis Foundation (NOF), International Osteoporosis Foundation (IOF) 98% of adolescents were insufficient (< 75 nmol/L) [8]. More than one-third of the adolescents (34.4%) had severe deficiency (< 25 nmol/L).

There was no significant correlation of serum osteocalcin with 25 OH vitamin D ($p = 0.167$) or PTH ($p = 0.856$) although it did positively correlate with serum calcium ($p = 0.002$).

The expected inverse correlation of serum PTH with 25 OH vitamin D and serum calcium is seen in this study ($p = 0.000$ and $p = 0.003$), also alkaline phosphatase correlated negatively with serum 25 OH vitamin D ($p = 0.014$) (Table 3). Linear regression of the bone turnover marker (osteocalcin) and the independent variables revealed no significant effect (Table 4).

Discussion

Previous studies reported the prevalence of vitamin D insufficiency < 50 nmol/L to be 80-100% among Saudi women [9-12]. Most studies included adults of reproductive age group and/or post-menopausal women. Only a few studied the younger age group, and these included children and of both sexes; the present study included exclusively adolescent girls. The prevalence of vitamin D insufficiency < 50 nmol/L was 89% among the adolescents in this study. This rate is higher than that reported in other countries which varied between 30-50% [13-16] Interestingly, this is similar to that reported by Al-Othman *et al.* of 331 Saudi boys and girls aged 6-17 years, with all of them having less than desirable vitamin D level (< 30 nmol/L) [17] and a more recent study by Al-Daghri *et al.* [18] of 493 girls with mean age of 14.8 years with 90% of them with 25 OH D of < 50 nmol/L. One-third of the adolescents of this study had 25 OH vitamin D < 25 nmol/L, and this is comparable to that of Al-Dagri *et al.* of 40% of girls that had 25 OH vitamin D of < 25 nmol/L [19].

Although most adolescents (98%), in this study had less than desirable 25 OH vitamin D (< 75 nmol/L) using IOM criteria, this was not associated with abnormalities of other bone health indices. Could the Saudi adolescents have a higher threshold before a significant biochemical disturbances result from a low vitamin D? A question that needs to be addressed with future longitudinal cohort studies beginning at adolescent's age through and into the menopausal and postmenopausal periods.

Al-Saleh *et al.* reported a similar observation of a normal serum PTH and calcium and 1,25 dihydroxy-vitamin D of all age groups of Saudi subjects (including 22 children and 56 adults of both sexes), with an established low serum 25 OH vitamin D (< 50 nmol/l). It was suggested that local cutoffs should be set that will be of clinical significance to identify those at risk of difficult end points like secondary hyperparathyroidism and bone-related diseases [20]

Although 1,25 dihydroxy-vitamin D is dependent on availability of 25 OH D, its level is also dependent on the activity of 1 alpha hydroxylase which is regulated by: PTH, Ca, and phosphate and fibroblast growth factor 23 (FGF23). Could genetic or other factors at a molecular microenvironment modify the response to low 25 OH vitamin D through 1- alpha hydroxylase, PTH, or calcium and phosphate? Future studies are needed.

Conclusion

This study revealed that vitamin D insufficiency is almost universal in the adolescent age group of Saudi girls, although other bone health parameters were not affected including the bone formation marker: osteocalcin. Could different genetic factors or other microenvironment molecules have effect on the physiology of bone health of Saudi females? Future studies are needed.

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Table 3. — *Correlations between osteocalcin, 25 OH vitamin D, and bone profile of adolescents.*

		Osteocalcin	25OH-vitD	Ca	alkPO4	PO4	PT
Osteocalcin	Pearson correlation	1	-0.087	0.204**	-0.131	-0.153*	-0.011
	Sig. (2-tailed)		0.167	0.002	0.055	0.023	0.856
25OHvitD	Pearson correlation	-0.087	1	0.340**	-0.167*	0.316**	-0.187**
	Sig. (2-tailed)	0.167		0.000	0.014	0.000	0.003
Ca	Pearson correlation	0.204**	0.340**	1	-0.458**	0.188**	-0.612**
	Sig. (2-tailed)	0.002	0.000		0.000	0.004	0.0000
AlkPO4	Pearson correlation	-0.131	-0.167*	-0.458**	1	-0.027	0.396**
	Sig. (2-tailed)	0.055	0.014	0.000		0.685	0.000
PO4	Pearson correlation	-0.153*	0.316**	0.188**	-0.027	1	-0.067
	Sig. (2-tailed)	0.023	0.000	0.004	0.685		.0318
PT	Pearson correlation	-0.011	-0.187**	-0.612**	0.396**	-0.067	1
	Sig. (2-tailed)	.0856	.0003	0.000	.000	0.318	

***Correlation is significant at the 0.01 level (two-tailed). *Correlation is significant at the 0.05 level (two-tailed).*

Table 4. — *Correlation of osteocalcin with the independent variables (age, BMI, exercise, sun exposure, diet rich in calcium), and bone profile.*

Coefficients				
			95% Confidence Interval for B	
Model		Sig.	Lower bound	Upper bound
1	(Constant)	0.294	-213.487	75.101
	Age	0.192	-3.816	0.924
	BMI	0.069	-1.358	0.066
	Exercise/ hours-day	0.706	-5.425	7.590
	Sun exp.days*	0.655	-2.785	1.868
	Sun.exp.duration.in.hrs**	0.558	-6.155	10.478
	Calcium servings/day	0.992	-2.067	2.087
	Serum OH-vit D	0.759	-0.417	0.318
	Serum Ca	0.097	-12.670	120.748
	Serum alkPO4	0.655	-.038	0.057
	Serum PO4	0.062	-19.081	0.615
	Serum PT	0.193	-1.084	4.461

[a]*Dependent variable: osteocalcin. *sun exposure days per week. **Sun exposure duration in hours.*

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