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Original Investigation

Lumbar spine and proximal femur BMD values in Turkish girls and the effect of precocious puberty on BMD.

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Abstract

Previous studies have shown no impairment in bone mineral density in girls with precocious and early puberty. The aim of this study was to evaluate the effect of precocious puberty on BMD and to measure average bone mineral density in Turkish girls. Fourteen girls between the ages of 5-10 (7.57 ± 1.83 year) who had new diagnosed precocious and early puberty were included in this study. BMD was measured in the posterior-anterior projection at the lumbar spine and at the right hip using DEXA. Correlation analysis was performed among BMD in all sub-regions. According to age, new average BMD values of sub-regionals in lumbar spine and proximal femur were calculated by linear regression formula leading to an average value of the lumbar spine total BMD in normal population. According to new average ± SD BMD of all sub-regions, simulated new Z-scores of each girl in proximal femur and lumbar spine were calculated and statistically compared. We found significant Z-score correlation between proximal femur and lumbar spine (r=0.70 – 0.99). According to age, new average values of sub-regional BMD in lumbar vertebrae and proximal femoral sub-regions in Turkish girls were presented. Average spinal BMD values in Turkish girls were similar with western countries. We though that DEXA scan at lumbar spine, with the exception of some patients, may be enough for an accurate measurement in children.

Keywords: bone mineral density, precocious puberty, lumbar spine, femur, age

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Introduction

Diagnosis of central precocious puberty was made according to Tanner staging and pubertal LH response. Magnetic resonance imaging can be used to distinguish organic lesions of hypothalamic-pituitary [1].

Previous studies have shown no impairment in BMD in girls with precocious and early puberty [2-6].

Dual-energy x-ray absorptiometry (DEXA) is increasingly used to evaluate for bone loss in children. The Z score (SD score compared with persons of the same age) is more useful. T-score (SD score compared with young adults) for children is inappropriate to diagnose bone loss [7, 8].

The aim of this study was to evaluate the effect of precocious puberty on BMD and to measure average bone mineral density in Turkish girls.

Materials and Methods

Fourteen girls between the ages of 5-10 (7.57 ± 1.83 year) who had new diagnosed precocious and early puberty were included in this study, Our patients are at II/III Tanner stage. None of the children had a condition known or suspected to affect bone metabolism (a growth-affecting chronic disease, bone disease, histories of malignancy, radiotherapy or systemic corticosteroid treatment, mental retardation, physical disability). Body weight, height and body mass index values were recorded. The study subjects were divided into 2 groups: those less than 8 y of age and those 8 y of age or older. BMD was measured in the posterior-anterior projection at the lumbar spine and at the right hip using dual X-ray absorptiometry system (Hologic, QDR 4500, USA). All measurements were done by the same qualified technician. Correlation analysis was performed among BMD in all sub-regions. Linear regression curve, formulas and regression coefficients were obtained between lumbar spines total BMD and proximal femur BMD values in all sub-regions. According to age, new average BMD values of sub-regions in lumbar spine and proximal femur were calculated by linear regression formula leading to an average value of the lumbar spine total BMD in normal population. According to age, new calculated standard deviation values were obtained using linear regression curve and formulas from reference data of Hologic. Average BMD values in all sub-regions were very close to total lumbar spine. New average standard deviation values of total lumbar spine were considered as unique standard deviation value of all sub-regions.

Then, according to new average ± SD BMD of all sub-regions, simulated new Z-scores of each girl in proximal femur and lumbar spine were calculated and statistically compared.

Statistical analyses were carried out with the SPSS for Windows (10.0) statistical software. Data are presented as the mean ± standard deviation. One tailed Pearson test was used to correlation. Wilcoxon matched-pairs test and Friedman test were used to analyze differences of Z-scores. A $p<0.05$ was considered statistically significant.

Results

Descriptive analysis of girls was presented in Table 1.

Tablo 1. Descriptive analysis of girls

(n=14)	Mean± SD (year)	(min-max)
Age	**7.57 ± 1.83**	**(5.0 - 10.0)**
Body weight	**30.2 ± 9.8**	**(15.0 - 48.0)**
Height	**132.2 ± 1.4**	**(116.0 - 147.0)**

Z-scores of total lumbar spine was found into three groups: all girls (n=14), less than 8 y of age (n=5) and 8 y of age or older (n=9), (-0,24± 1,24; -0,14± 1,42 and -0,42± 0,97), respectively. Z-scores of total lumbar spine did not differ among groups ($p>0.05$).

BMD values of sub-regions in lumbar vertebras and proximal femur were given in the Table 2. Increasing in BMD and standard deviation values with age was clearly observed.

Table 2. According to age group, BMD of sub-regions in lumbar spine and proximal femur (L1-4: lumbar vertebra's, Lt: total lumbar spine, Fn: femoral neck, Ftr: Femur trochanter, Fi: Femur intertrochanter, Ft: Femur total, Fw: Ward's region of femur)

	All girls (n=14)	**< 8 years old (n=5)**	**≥ 8 years old (n=9)**
	Mean± SD (g/cm^2)	**Mean± SD (g/cm^2)**	**Mean± SD (g/cm^2)**
1	0.540 ± 0.111	0.504 ± 0.075	0.560 ± 0.127
L2	0.613 ± 0.111	0.567 ± 0.068	0.638 ± 0.124
L3	0.645 ± 0.119	0.580 ± 0.069	0.682 ± 0.129
L4	0.628 ± 0.112	0.527 ± 0.029	0.684 ± 0.100
LT	0.610 ± 0.109	0.544 ± 0.047	0.646 ± 0.118
Fn	0.610 ± 0.087	0.582 ± 0.089	0.625 ± 0.088
Ftr	0.497 ± 0.092	0.472 ± 0.044	0.510 ± 0.110
Fi	0.714 ± 0.108	0.669 ± 0.070	0.738 ± 0.120
Ft	0.656 ± 0.095	0.622 ± 0.074	0.674 ± 0.104
Fw	0.615 ± 0.118	0.635 ± 0.12	0.604 ± 0.123

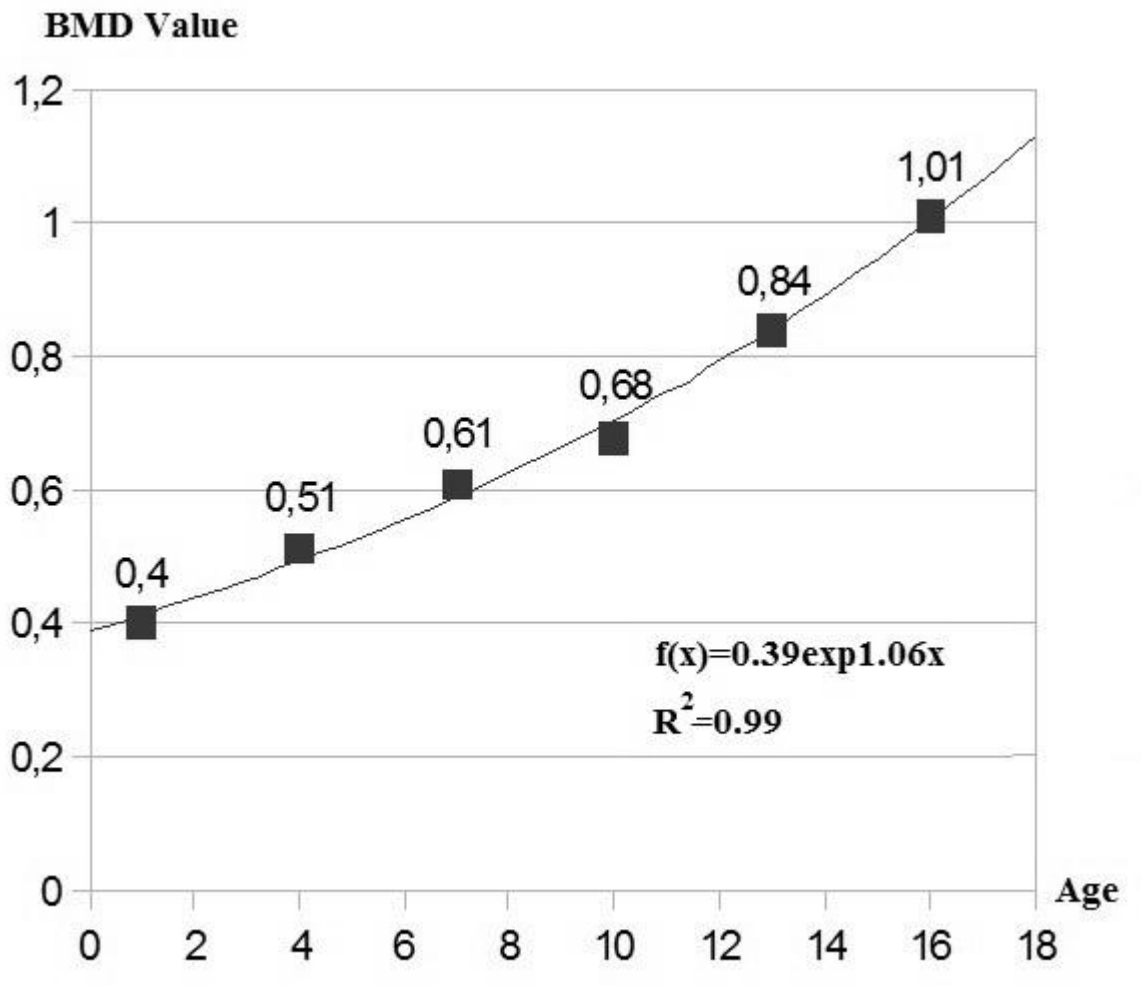
Cross-correlation analysis showed that BMD values of sub-regions in lumbar spine and proximal femur was positively correlated with total lumbar spine (r=0.701 – 0.989). The more correlated vertebras were the second and third vertebra in lumbar spine and the more correlated sub-regions in proximal femur were total and trochanteric sub-regions (Table 3).

Table 3. Cross-correlation analysis between BMD values of sub-regions in lumbar spine and proximal femur (r: Pearson correlation, L1-4: lumbar vertebra's, Lt: total lumbar spine, Fn: femoral neck, Ftr: Femur trochanter, Fi: Femur intertrochanter, Ft: Femur total, Fw: Ward's region of femur).

		All girls (n=14)	**< 8 years old (n=5)**	**≥ 8 years old (n=9)**
L1-Lt	r	0,949	0,911	0,911
	p	0,000	0,016	0,016
L2-Lt	r	0,976	0,981	0,981
	p	0,000	0,002	0,002
L3-Lt	r	0,989	0,948	0,948
	p	0,000	0,007	0,007
L4-Lt	r	0,921	0,228	0,228
	p	0,000	0,356	0,356
Fn-Lt	r	0,701	0,791	0,791
	p	0,003	0,056	0,056
Ftr-Lt	r	0,776	0,854	0,854
	p	0,001	0,033	0,033
Fi-Lt	r	0,895	0,811	0,811
	p	0,000	0,048	0,048
Ft-Lt	r	0,846	0,821	0,821
	p	0,000	0,044	0,044
Fw-Lt	r	0,453	0,843	0,843
	p	0,052	0,037	0,037

According to age, average BMD values in Hologic reference database was presented in figure 1.

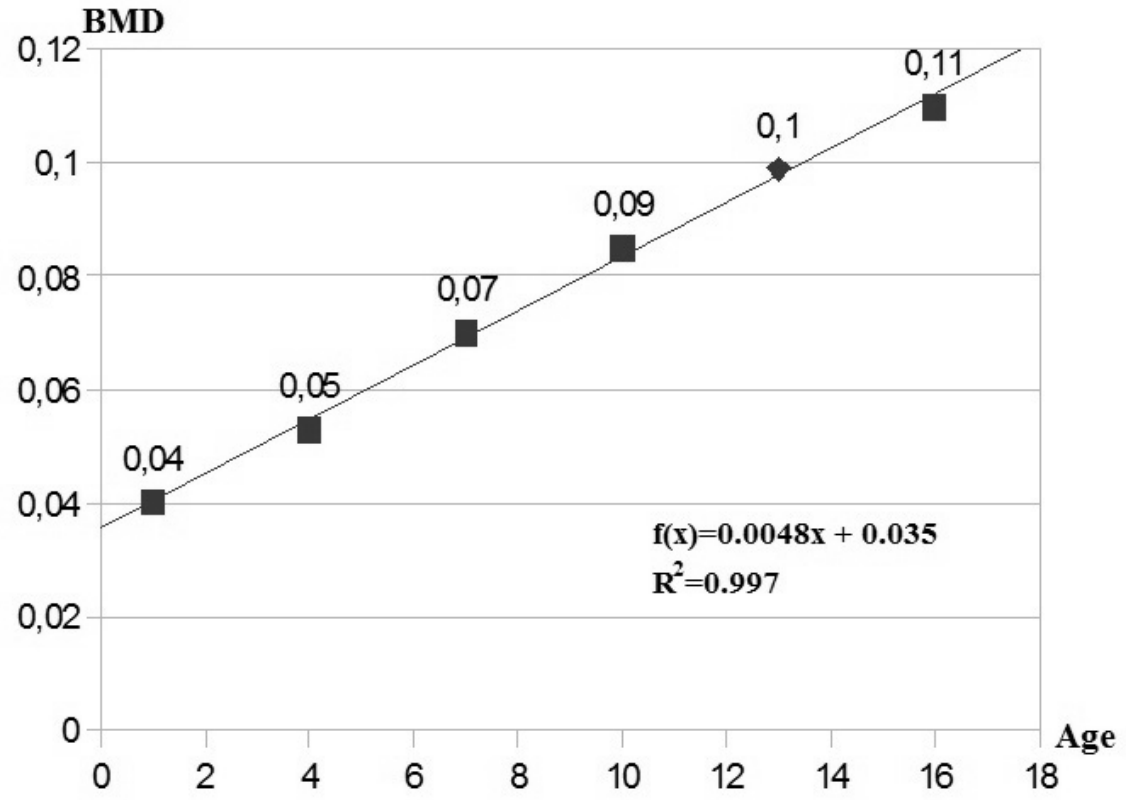
Figure 1. Exponential relationship between age and BMD was found in Hologic reference database



Exponential relationship between age and BMD of total lumbar spine was found in reference database (R^2 =0.99) and exponential regression formula was presented in this figure.

According to age, standard deviation value of average BMD in total lumbar spine was increased in Hologic reference database. Linear regression formula and curve between standard deviation and age was presented in figure 2 (R^2 =1).

Figure 2. Linear regression formula and curve between standard deviation and age in Hologic reference database.



According to age, new average values of sub-regional BMD in lumbar vertebrae and proximal femoral sub-regions were calculated by linear regression formula leading to an average value of the lumbar spine total BMD in normal population (Table 4 and 5).

Table 4. New average values of sub-regional BMD in lumbar vertebrae and proximal femoral sub-regions were calculated according to age (L1-4: lumbar vertebra's, Lt: total lumbar spine, Ft: Femur total, Ftr: Femur trochanter).

Age	Lt mean	L1 mean	L2 mean	L3 mean	L4 mean	Ft mean	Ftr mean	SD of all sub-regions
1	0.412	0.328	0.408	0.427	0.408	0.452	0.283	0.040
2	0.438	0.355	0.434	0.455	0.436	0.478	0.310	0.045
3	0.464	0.384	0.462	0.485	0.466	0.506	0.339	0.050
4	0.493	0.415	0.491	0.516	0.497	0.535	0.370	0.055
5	0.523	0.447	0.523	0.550	0.531	0.566	0.402	0.059
6	0.555	0.482	0.556	0.585	0.567	0.599	0.437	0.064
7	0.589	0.518	0.591	0.623	0.604	0.634	0.474	0.069
8	0.625	0.557	0.629	0.662	0.644	0.672	0.513	0.074
9	0.663	0.598	0.668	0.705	0.687	0.711	0.554	0.079
10	0.703	0.642	0.710	0.749	0.732	0.753	0.598	0.083
11	0.746	0.688	0.755	0.797	0.780	0.797	0.644	0.088
12	0.792	0.737	0.803	0.847	0.831	0.844	0.694	0.093
13	0.841	0.789	0.853	0.901	0.885	0.894	0.746	0.098
14	0.892	0.845	0.906	0.958	0.942	0.947	0.802	0.103
15	0.946	0.904	0.963	1.018	1.003	1.004	0.861	0.107
16	1.004	0.966	1.023	1.082	1.067	1.063	0.924	0.11

Table 5. Regression analysis of BMD between total lumbar spine and other regions. (L1-4: lumbar vertebra's, Lt: total lumbar spine, Ft: Femur total, Ftr: Femur trochanter).

	Linear regression formula	**R^2**
L1-Lt	f(x)=0.928x + 0.108	0.9
L2-Lt	f(x)=0.962x + 0.020	0.95
L3-Lt	f(x)=0.904x + 0.026	0.98
L4-Lt	f(x)=0.998x + 0.046	0.85
Ft-Lt	f(x)=0.969x - 0.026	0.72
Ft-Lt	f(x)=0.924x + 0.151	0.6

Then, according to new average ± SD BMD of all sub-regions, simulated new Z-scores of each girl in proximal femur and lumbar spine were presented in Table 6.

Table 6. Simulated new Z-scores of sub-regions in all girls

ROI	**Mean± SD**	**(min-max)**
Lt (n=14)	-0.241±1.244	(-1.700 - 2.700)
L1 (n=14)	0.014±1.567	(-2.284 - 2.864)
L2 (n=14)	0.004±1.447	(-1.892- 2.532)
L3 (n=14)	-0.018±1.440	(-2.084- 2.899)
L4 (n=14)	-0.051±1.025	(-1.530- 2.405)
Ft (n=14)	-0.177±1.301	(-2.027- 2.441)
Ftr (n=14)	-0.527±1.348	(-2.595- 1.169)

Mean values of Z -scores in these sub-regions were around zero. Simulated new Z-scores of these sub-regions were compared using Friedman test and were not found difference statistically (p=740).

Discussion

In the previous study, Significant Z-score correlation in 339 pediatric patients was found between proximal femur and lumbar spine (r = 0.73, P = 0.0001) [9]. Our results were similar with literature.

Gafni et al re-interpreted of DEXA scans in 34 children who had low BMD based on DEXA scan and reported that more than half of the patients actually had a normal BMD. According to error frequency, use of T-score (62%) was the most error. Choice of wrong reference database (21%) and drawing of incorrect bone map (21%) were others [7].

Only use of age-specific reference data may not be appropriate in children. Pubertal stage, bone age, height age, body composition and ethnicity should be considered to accurate interpretation of Z-score in children [9]. Although increased skeletal size and delayed puberty can lead to apparent low BMD and untreated precocious puberty can lead to high BMD. Several correction methods have been proposed for these variability's in bone size and pubertal stage [7, 10]. These methods are not commonly used in routine evaluation.

After DEXA scan, automatic bone map drawing software usually can not detect bone edge correctly. The bone map should be adjusted manually by technician [7]. Additionally we sometimes saw that neck axis in proximal femur was not correctly detected by automatic software.

Arikowski reported that prepubertal BMD values in boys are similar with girls in Finland [8]. Similar result was reported by Fonseca et al in Brazilian children [11]. We calculated standardized BMD values for lumbar spine from out results and previous studies. According to prepubertal age, we saw that average BMD values in lumbar spine did not differ among Turkey, Brasil and Finland.

According to World health organization criteria, patients with a T-score of < -2.5 was taken as osteoporotic and those between < -1 and -2.5 was taken as osteopenic in adults. T-score of BMD for children is inappropriate to diagnose bone loss. Z-scores in four additional sub-regions in lumbar spine are possible to calculate using our methods in fourteen girls. Bone mapping was easy. Correlations among sub-regions in lumbar spine were high. Some patients who had vertebral pathologies, metallic implants, or applied spinal surgery or radiotherapy raised spine operations may need to look at another area of the body for BMD measurement.

Z-scores of total and trochanteric sub-regions in femur proximal should be used in these girls. On the other condition, DEXA scan at lumbar spine may be enough for an accurate measurement in children.

Previous studies have shown no impairment in BMD in girls with precocious and early puberty [2-6]. Assa et al reported that girls with central idiopathic precocious puberty have lower BMD. During the first year of therapy with gonadotropin-releasing hormone agonist, BMD show a normalization trend [12]. Another study observed that BMD was significantly lower at discontinuation of treatment and increased to control values after gonadal activity resumption [1]. According to stage of precocious puberty, with the findings of the literature, four phases may be defined as at the beginning of the early signs, under treatment, discontinuation of treatment and untreated girls. BMD is normal at the beginning of the early signs of puberty and increased in untreated patients by the effect of sex steroids. BMD can be slightly decreased or normal under treatment with gonadotropin-releasing hormone (GnRH) agonist. The rapid increase in BMD can be seen discontinuation of treatment. Early or precocious puberty should be treated with GnRH agonist to prevent permanent short stature. Because of the beginning of the early signs, normal Z-scores in lumbar spine and proximal femur values can be calculated at the beginning of the early signs of precocious puberty.

Conclusion

We found significant Z-score correlation between proximal femur and lumbar spine (r=0.701 – 0.989). According to age, new average values of sub-regional BMD in lumbar vertebrae and proximal femoral sub-regions in Turkish girls were presented. Average spinal BMD values in Turkish girls were similar with western countries. We though that DEXA scan at lumbar spine, with the exception of some patients, may be enough for an accurate measurement in children.

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