Turk J Med Sci
32 (2002) 43-48

Gülcan TÜRKER[1]
Kadir BABAOĞLU[1]
Demet GEDİKBAŞI[1]
Hakan DEMİR[2]
Fatma BERK[2],
Metin AYDOĞAN[1]
Şükrü HATUN[3]

Factors Affecting Bone Health in Children: A Preliminary Study in Kocaeli

Received: October 08, 2001

Departments of [1]Pediatrics, [2]Nuclear Medicine, [3]Pediatric Endocrinology Faculty of Medicine, Kocaeli University, Kocaeli-TURKEY

Abstract: Unhealthy bones in childhood are likely to be reflected as osteoporosis in the future. This study was planned to assess the bone health of children in the Kocaeli region and to determine the risk factors in terms of osteopenia. A total of 46 healthy children aged 6-16 years (21 girls and 25 boys, mean age: 8.74±2.56 years) were included in the study. A questionaire was used by the physicians to determine the sunlight exposure, dressing habits, calcium content of the diet, vitamin supplementation and daily physical activity. Bone mineral density was evaluated using dual-energy X-ray absorptiometry at L_2-L_4 levels of the lumbar spine, Ward's triangle and femur neck. Z-scores of bone mineral density were calculated. Serum calcium, phosphorus, alkaline phosphatase, ferritin levels and urinary calcium creatinine ratio were measured and an X-ray of the right wrist was taken. In 84% of the study group bone mineral density was lower than the expected values. Mean values of bone mineral density for the femur neck, L_2-L_4 level of lumbar spine and Ward's triangle were 0.64+0.11g/cm^2, 0.54+0.07 g/cm^2, and 0.55+0.10 g/cm^2, respectively. None of the children had hypoferritenemia, which has an adverse effect on matrix development. We only found a statistically significant correlation between bone mineral density, bone age and serum alkaline phosphatase levels. When the etiology of the decreased bone mineral density was evaluated, no correlation was found with dietary calcium intake physical activity, vitamin D supplementation, sunlight exposure, dressing habits and urinary calcium excretion.

Although none of the children was osteopenic (Z-score of BMD below – 2 SD), the majority had BMD values below those expected. We were unable to determine the etiology of the decreased BMD in this study. However, we suggest that air pollution might be an etiologic factor that must be studied in future in larger series. In addition, we think that weight-bearing activities and dietary calcium intake must be encouraged.

Key Words: Bone density, children, affecting factor, air pollution

Introduction

Peak bone mass is one of the main determinants of fractures and osteoporosis, which is generally a disease of aging adults. Bone formation and resorption continues throughout life with osteoblastic and osteoclastic activity. From infancy through early adulthood, up to about 30 years, the activity of bone formation predominates, resulting in a steady accumulation of bone mass. The bone mass is affected by several factors; calcium, vitamin D, phosphorus and protein content of the diet and their serum levels, environmental and genetic factors, hormonal factors like pubertal status, and physical activity (1,2). In this study, we assessed the bone mineral density and risk factors of osteopenia in a group of healthy children in Kocaeli.

Materials and Methods

Subjects: Forty-six healthy Turkish children aged 6-17 years (21 boys and 25 girls) were enrolled in the study. The children were healthy, had received no treatment with a known negative effect on the bone metabolism, and did not have a systemic disease impairing growth. The ethics committee of Kocaeli University Hospital approved the study protocol. Oral informed consent was obtained from the parents.

Methods: A questionnaire was completed on all subjects to determine premature birth, low birth weight, calcium content of the diet, vitamin D and polyvitamin use at infancy, physical activity in childhood, smoking, previous fractures and the onset of menarche. Calcium intake was determined by a detailed food frequency questionnaire about dairy products. Other questions were also asked to determine the sunlight exposure, dressing habits and holiday locations (seaside or village), and the educational and economic level of parents.

Calcium intake assessment: Calcium intake of the previous month was assessed by a 20-item food frequency questionnaire. Frequency of consumption was reported in 10 categories: rarely/never, 1 day/month, 1 day/2 weeks, 1 day/week, and 2, 3, 4, 5, 6, 7 days/week. Portion size was measured using household items (spoons, glasses, cups), to which standard weights were assigned. Use of food supplements, milk, yoghurt, orange juice and spinach was also assessed. Data on mean daily consumption of food products in grams were converted to calcium intake using local food composition tables. Then calcium intake was classified as 600 mg and 601-1000 mg.

Physical activity assessment: Physical activity included organized sports and recreational activities, such as walking, running, football, basketball, volleyball, swimming, skipping and cycling, and was measured in minutes per week. The questions were related to means of travel to and from school, usual level of activity at mid-morning and lunch time breaks, after school activities and participation in regular sporting activities including competitive sports. High activity was above 180 minutes per week, moderate activity was 120-180 minutes per week and low activity was 60-119 minutes per week.

Height was measured with a fixed stadiometer. Weight was measured without shoes on a standard clinical balance. Body mass index (BMI) was calculated as recommended (3). Percentile of weight and height was evaluated according to the method of the National Center for Health Statistics (NCHS) Growth Charts by Ross Laboratories (4). Skeletal maturation was assessed on the basis of roentgenograms of the right wrist according to the method of Greulich and Pyle (5).

Venous blood was drawn for serum alkaline phosphatase, calcium, phosphorous and ferritin analysis and urine was collected for the determination of the calcium and creatinine ratio.

Bone Mineral Density Assessment: Bone mineral density (BMD) (grams per cm^2) was measured in the a-p lumbar spine (L_2-L_4), femoral neck and Ward's triangle (Ward's tri) by DEXA (Norland XR-26 HS bone densitometer, with dynamic filtration, Norland Corp, Fort Atkinson, USA). The standard deviations of BMD were calculated using the Z-score. The Z-score was calculated according to normative values for the 2-20-year-old population studied by Zanchetta et al. (6). Osteopenia was defined here as a Z-score less than –2.0 standard deviation (6,7). The XR-26 was calibrated daily, 30 min after turning the apparatus on. Quality control was performed using two phantoms: a calculated and polyester anthropometric phantom for lumbar spine by the Norland Corp.

Evaluation of socio-economic level: The level of education and income of the parents, and the number of rooms in the house were asked. Socio-economic level was classified as levels 1-3. Parents with university, high school, and primary school education were considered to be level 3, level 2 and level 1 respectively.

Statistical Methods: The role of vitamin D supplementation and other factors influencing BMD was analyzed using a two-tailed Student's t-test, Mann-Whitney U-test and simple correlation analysis. $P<0.05$ and $p<0.01$ were considered significant. Socio-economic level was compared with BMD using variant analysis.

Results

The mean values and Z-score of BMD for lumbar spine, femoral neck and Ward's tri are shown in Table 1. The mean values of the Z-score for femur and L_2-L_4 were –0.45±0.54 SD and -0.41+0.44 SD, respectively. None of the children had a Z-score less than –2 SD (Table 1). The mean Z-score of L_2-L_4 and values of F BMD and W BMD were lower in boys. The lumbar Z-score was negative in 84% of the children's BMDs. There was no correlation between serum calcium, phosphorus and ferritin levels also no correlation was found with urinary calcium/creatinine ratio and values of BMD and the Z-score of the femur, lumbar and Ward's tri (Table 2). Serum ferritin, calcium and phosphorus levels were normal in all children in the study group.

The daily calcium intake of 87% of the children was 601-1000 mg. There were no significant differences in calcium intake between lumbar, femoral and Ward's tri BMD (Table 3). Eighty-seven percent of the children received vitamin D supplementation during infancy whereas 30% received it during childhood. Vitamin D supplementation during infancy and childhood is associated with higher femoral, lumbar and Ward's tri BMD (Table 4). None of the children smoked or had hypoferritenemia.

Table 1. Mean BMD serum P, ALP and Ca, ferritin levels, bone age, and urinary calcium creatinin ratio in boys and girls.

Study group	Total	Boys	Girls	p
Number	46	21	25	0.205
Age	8.74 ±2.56	8.21±1.78	9.18±3.04	0.205
F BMD g/cm^2	0.64 ±0.11	0.59±0.05	0.68±0.13	0.040*
L BMD g/cm^2	0.54±0.07	0.53±0.05	0.54±0.08	0.878
W BMD g/cm^2	0.55±0.10	0.51 ±0.05	0.58±0.12	0.042*
L Z-score	-0.41±0.44	-0.24±0.41	-0.55±0.42	0.018*
F Z-score	-0.45±0.11	-0.42±0.49	-0.47±0.59	0.765
P (mg/dl)	3.95±0.49	3.95±0.50	3.96±0.49	0.936
Ca (mg/dl)	9.44±0.59	9.42±0.62	9.46±0.58	0.797
ALP (IU/L)	244.19±121.70	225.05±80.81	259.17±146.10	0.380
Ferritin (ng/ml)	38.11±28.48	38.92±32.63	37.30±24.63	0.871
Urinary Ca/cr	2.60±6.02	3.63±7.72	1.26±2.41	0.361
Bone age (year)	7.97±2.66	7.61±1.83	8.30±3.25	0.425

*p<0.05 statistically significant

Table 2. Relation of bone mineral density with height, weight, bone age, serum calcium, serum phosphorus, and alkaline phosphatase level.

	F BMD g/cm^2	L BMD g/cm^2	W BMD g/cm^2
Age	0.526**	0.375*	0.524**
Height	0.770**	0.640**	0.608**
Weight	0.663**	0.584**	0.486**
Serum Ca (mg/dl)	0.038	-0.01	0.136
Serum P (mg/dl)	0.123	0.006	0.082
Serum ALP (IU/L)	0.391	0.217	0.210
Serum ferritin (ng/dl)	-0.135	-0.111	-0.016
Urinary Ca/Cr	-0.135	-0.187	-0.052
Bone age (month)	0.654**	0.477**	0.532**

* p<0.05 statistically significant
**p<0.01 statistically significant

Table 3. BMD and calcium intake.

	Calcium intake daily		P
	600 mg	601- 1000 mg	
Number	6	40	
F BMD g/cm^2	0.58+0.10	0.64+0.11	0.159*
L BMD g/cm^2	0.53+0.06	0.54+0.07	0.828
W BMD g/cm^2	0.54+0.12	0.55+0.10	0.588

*P< 0.5 statistically significant

Table 4. BMD and vitamin D supplementation in infancy and childhood.

	Vitamin D supplementation infancy			Vitamin D supplementation childhood		
	Yes	No	p	Yes	No	p
Number	39	7		14	31	
F BMD g/cm g/cm^2	0.65±0.11	0.54±0.03	0.008**	0.69±0.10	0.62±0.10	0.019*
L BMD g/cm g/cm^2	0.55±0.07	0.47±0.01	0.005**	0.57±0.05	0.52±0.07	0.017*
W BMD g/cm g/cm^2	0.56±0.10	0.45±0.05	0.010*	0.59±0.09	0.53±0.10	0.047*

*p<0.05 statistically significant
**p<0.01 statistically significant

Physical activity had no significant positive correlation with BMD in the children. Eighty-five percent of the children had moderate activity whereas 15% had low activity. None of the children participitated in regular sporting activities, including competitive sports (Table 5).

Socio-economic level had no association with BMD (Table 6). The percentage of covered style of clothing was 13%. Eighty-five percent of the children lived in houses with enough sun exposure; 51% went to the seaside on holiday. However, these factors did not have a correlation with BMD (p>0.5).

Discussion

In this study, the determinants of BMD were evaluated in 46 healthy children in the Kocaeli region. The mean values of Z-scores for femur and L_2-L_4 were not below –2 SD for any of the children. Girls had higher femur and Ward's triangle BMDs than did boys. BMDs for femur and lumbar spine and Ward's triangle had a significant positive correlation with alkaline phosphatase activity (p<0.05).

Table 5. Physical activity and BMD of femur, lumbar spine and Ward's tri.

	Physical activity		p
	low	moderate	
Number	28	18	
F BMD g/cm^2	0.62±0.10	0.67±0.11	0.244
L BMD g/cm^2	0.53±0.08	0.54±0.05	0.096
W BMD g/cm^2	0.54±0.10	0.56±0.10	0.360

p< 0.05 statistically significant

Determinants of BMD in healthy persons include genetic and ethnic factors, hormonal status, dietary calcium intake, physical activity, and weight. Genetic determinants of BMD can be modified by nutrition, physical activity, sunlight exposure and life style (1,2). We found a lower bone density in the Kocaeli region with negative Z-scores in 84% of the study group but no osteopenia, and moderate physical activity, lower bone age, and 601-1000 mg calcium intake.

BMDs for the lumbar spine were lower than the values obtained from previous studies in Turkish children by Hasanoglu et al. and Tanyer et al. with BMD values of 0.655+0.175 g/cm^2 and BMD 0.72+0.02 g/cm^2 respectivly (8,9). Also our values for the BMD of the lumbar spine were lower than those in a study by Glastre et al. in 135 healthy Caucasian children using dual energy X-ray absorptiometry (Hologic QDR 1000) (10). In Glastre et al.'s study, mean BMD was between 0.625±0.068 g/cm^2 at 1-10 y and 0.891±0.123 g/cm^2 at 10-15 y (10). These values were higher than ours. They found no significant difference between boys and girls (10). The lumbar BMD values determine by Boot et al. ranged between 0.656±0.07 g/cm^2 and 1.058±0.10 g/cm^2 for boys; and 0.708±0.08 g/cm^2 and 1.21±0.15 g/cm^2 for girls at 6-16 y (11). BMD values of children in Kocaeli were lower than those given by Boot et al. (11). Our BMD values for Ward's triangle were similar to those published by Zamora et al. with 0.638±0.007 g/cm^2 (12). Similar to the literature, our values had significant differences between girls and boys. The mean femoral and Ward's tri BMD of girls was found to be higher than that of boys, similar to the results of studies by Tanyer et al., Hasanoglu et al. and Faulkner et al. (8-9,13).

Table 6. Socio-economic level and BMD of femur, lumbar spine and Ward's tri.

	SEL 1	SEL 2	SEL 3	P SEL 1-SEL 2	P SEL 1-SEL 3
Number	7	28	6	>0.05	>0.05
F BMD g/cm^2	0.64+0.11	0.62+0.06	0.58+0.06	>0.05	>0.05
L BMD g/cm^2	0.52+0.06	0.53+0.04	0.52+0.02	>0.05	>0.05
W BMD g/cm^2	0.53+0.09	0.54+0.10	0.54+0.10	>0.05	>0.05

p<0.05 statistically significant

The most significant correlation was found between bone ages and femoral bone density, whereas Tanyer et al; Glastre et al. and Trouerbach et al. found a positive correlation between bone age and lumbar BMD (9,10,14).

Calcium, magnesium, phosphorus and iron are essential for many functions, such as mineralization of bones, serving as cofactors to many enzyme systems, sustaining muscle and nerve excitation, and, in the case of iron, maintaining the oxygen carrying capacity of the blood (15). Calcium supplementation during skeletal formation increases peak bone mass and may prevent osteoporosis (1,15,16). Daily calcium intake in our study was not low and was higher than that in Tanyer et al.'s study group with 426.56±232.79 mg/day (9). Vitamin D supplementation during infancy and prepubertal age is associated with higher bone mineral mass (17). Children in the study group were supplemented during infancy but not during childhood. Bone mineral density had a positive correlation with ferritin (18). Serum ferritin levels were normal in this study. The positive determinant of BMD was vitamin D supplementation during infancy. On the other hand, we found that weight-bearing physical activities in children were insufficient.

Physical activity stimulates mechanoreceptors. Nitric oxide has been shown to act as a mediator of cytokines in the mechanoreceptor of bone tissue (19). Physical activity increases bone density mainly in children, adolescents and to a minor extent in adults. Weight-bearing activities, such as walking, jumping, and playing basketball and volleyball, have a greater effect than nonweight-bearing activities, such as cycling and swimming (11,20). Children in our study have moderate activity but they do not participate in weight-bearing activities.

Although the daily calcium intake and physcial activity of our study group were similar to those in other studies in Turkish children, BMD values were found lower in our study (8,9).

Smoking is related to decreased bone mass and increased risk of osteoporotic fractures (21). None of children smoked or had hypoferritenemia, which has an adverse effect on matrix development.

There are petroleum refinery and dye factories in the Kocaeli region, which is one of the major industrial areas in Turkey. Petroleum refineries produce heavy metals such as vanadium and cadmium, and organic and inorganic chemicals. Vanadate-induced nitric oxide production has been shown to act as a mediator of cytokines in osteoblast in cell culture, although high doses are toxic to these cells (19). Cadmium exposure induces bone resorption in vitro and in vivo that can lead to low bone mass and increased incidence of fracture (22). Vanadium compounds are insulin and growth factor-mimetic compounds of osteoblast in cell culture, although high doses are toxic to these cells (20). Serum bone-type alkaline phosphatase activity in women living in a cadmium-polluted area is increased (23). Alkaline phosphtase activity increased in our study but there was no association with lower BMD.

Decreased BMD and increased alkaline phosphtase activity in our study might be attributed to air pollution in Kocaeli. We should investigate air pollution in relation to bone density and encourage weight-bearing activities and more calcium intake and vitamin D supplementation after infancy.

Correspondence author:

Gülcan TÜRKER

C-41 Blok, No: 11, Yahyakaptan,

41001 İzmit, Kocaeli-TURKEY

Abbreviations

ALP:	alkaline phosphatase
F BMD:	Femur neck bone mineral density
L BMD:	Lumbar spine 2- lumbar spine 4 bone mineral density
W BMD:	Ward's Tri bone mineral density
SEL 1:	Socio-economic level 1 (low)
SEL 2:	Socio-economic level 2 (moderate)
SEL 3:	Socio-economic level 3 (high)
F Z-score:	Femure neck Z-score
L Z-score:	Lumbar spine L2-L4 level Z-score

References

1 Matkovic V. Nutrition, genetics and skeletal development. J Am Coll Nutr 15:556-69, 1996.

2. Prince RL. Diet and the prevention of osteoporotic fractures. New Engl J Med 337:701-2, 1997.

3. Schwartz ID, Bercu BB: Normal growth and development. Clinical Pediatric Endocrinology (Ed.In Hung Wellington) Mosby-Year Book, Inc. 1992, pp: 13-42.

4. Hamill PV, Drizd TA, Johnson CL, et al: Physical growth: National center for Health Statistics Percentiles. Am J Clin Nutr 32: 607, 1979.

5. Greulich WW, Pyle SI. Radiographic Atlas of Skeletal Development of the Hand and Wrist. Stanford University Press, Stanford, California. 2nd Edition 1959.

6. Zanchetta JR, Plotkin H, Filgueria MLA. Bone mass in children: normative values for the 2-20 year-old population. Bone 16: 3935-95, 1995.

7. Leonard MB, Propert KJ, Zemel BS, Stallings VA, Feldman HI. Discrepancies in pediatric bone mineral density reference data: potential for misdiagnosis of osteopenia. J Pediatr 135: 182-88, 1999.

8. Hasanoglu A, Bideci A, Cinaz P, Tumer L, Unal S. Bone mineral density in childhood obesity. J Pediatr Endocrinol Metab 13: 307-11, 2000.

9. Tanyer G, Topcu M, Sıklar Z, Dallar Y, Yorgancıoglu R. Evaluation of bone mineral density in normal children aged 2-16 years. J Clin Sciences and Doctor 4: 733-42, 1998.

10. Glastre C, Braillon P, David L, Cochat P, Meunier PJ, Delmas DP. Measurment of bone mineral content of the lumbar spine by dual energy x-ray absorptiometry in normal children: Correlation with growth parameters. J Clin Endocrinol Metab 70: 1330-33, 1990.

11. Boot A M, De Ridder MAJ, Pols HAP, Krenning EP, De Muinck Keizer-Schrama SMPF. Bone Mineral Density in children and adolescents: Relation to puberty, calcium intake, and physical activity. J Clin Endocrinol Metab 82: 57-62, 1997.

12. Zamora SA, Rizzoli R, Belli DC, Slosman Do, Bonjour JP. Vitamin D supplementation during infancy is associated with higher bone mineral mass in prepubertal girls. J Clin Endocrinol Metab 84: 4541-4, 1999.

13. Faulkner RA, Bailey DA, Drinkwater DT, McKay HA, Arnold C, Wilkinson AA. Bone densitometry in Canadian children 8-17 years of age. Calcif Tissue Int 59: 344-51, 1996.

14. Trouerbach WT, Man SA, Gommers D, Zwamborn AW, Grobbee DE. Determinants of bone mineral content in childhood. Bone and Mineral 13: 55-67, 1991.

15. Clarkson PM, Haymes EM. Exercise and mineral status of athletes: calcium, magnesium, phosphorus, and iron. Med Sci Sports Exerc 27: 831-43, 1995.

16. American Academy of Pediatrics. Calcium requirements of infants, children, and adolescents (RE9904). Pediatrics 104. 1151-57, 1999.

17. Ferrari SI, Rizzoli R, Slosman DO, Bonjour JP. Do dietary calcium and age explain the controversy surrounding the relationship between bone mineral density and vitamin D receptor gene polymorphisms? J Bone Mineral Res 13: 363-370, 1998.

18. Fogelholm M. Vitamins, minerals and supplementation in soccer. J Sports Sci 12: s 23-7,1994.

19. Cortizo AM, Caporossi M,Lettieri G, Etcheverry SB. Vanadate-induced nitric oxide production: role in osteoblast growth and differentiation. Eur J Pharmacol 400: 279-85, 2000.

20. Slemenda CW, Miller JJ, Hui SL, Reister TK, Johnston CC. Role of physical activity in the skeletal mass in children. J Bone Miner Res 6:1227-33, 1991.

21. Ortego-Centeno N, Munoz-Torres M, Jodar E, Hernandez-Quero J, Jurado-Duce A, de la Hiquera Torres-Puchol J. Effect of tobacco consumption on bone mineral density in healthy young males. Calcif Tissue Int 60: 496-500, 1997.

22. Wilson AK, Bhattacharyya MH. Effect of cadmium on bone: an in vivo model for the early response. Toxicol Appl Pharmacol 145: 68-73, 1997.

23. Tsuritani I, Honda R, Ishizaki M, Yamada Y, Aoshima K, Kasuya M. Serum bone-type alkaline phosphatase activity in women living in a cadmium-polluted area. Toxicol Lett 71: 209-16, 1994.