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Obesity in Children and Adolescents: Effect on Bone Mineral Content and Density

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This study was carried out to determine the contribution of body fatness to Bone Mineral Content (BMC) and Density (BMD) in obese children and adolescents. Cross sectional sample of 90 schoolchildren with simple obesity (body mass index ≥95th percentile) and of age range 7.6-16 year participated in this study. Physical examination that included height, weight and pubertal stage assessment in addition to body fat% measurements were performed. Body Mass Index (BMI) was calculated. Regional BMC and BMD were measured by dual-energy X-ray absorptiometry (lumbar spine, proximal femur (neck, trochanter and Ward's triangle). The results indicated a significant effect of adiposity on BMC and BMD observed at all skeletal sites studied. Lumber spine BMC and BMD were greater in girls than boys with significant differences regarding BMC with $p<0.01$. Body fat % and BMI showed positive correlations with BMC and BMD of spine and hip measurements studied in both sexes. The presence of female sex can predict the increase in spine BMC ($p<0.01$), BMD ($p<0.001$), femur neck BMC ($p<0.001$) and trochanter BMD ($p<0.05$). The increase in age can predict the increase in spine BMC ($p<0.001$), BMD ($p<0.001$), trochanter BMC ($p<0.01$) and BMD ($p<0.01$). The progress in puberty stage can predict the increase in spine BMC ($p<0.01$) and BMD ($p<0.05$) and trochanter BMC ($p<0.001$) and BMD ($p<0.01$). While, height can not predict BMC or BMD of spine or hip measurements. In this population we concluded that, obesity assessed by BMI and body fat % was associated with increased vertebral bone content and density mainly spine and hip. The age, sex and puberty stage were consistent and independent predictors of BMC and BMD in obese children and adolescents. Future studies are needed to determine the effect of these differences on fracture risk and to determine whether the increases in spine and hip BMC are sustained into adulthood.

Key words: Children, obesity, bone mineral content, DXA

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INTRODUCTION

Osteoporosis is a growing health problem all over the world (Seeman, 2001). It is generally accepted that those who achieve a higher peak bone mass are less at risk of having an osteoporotic fracture later in life (Ma and Jones, 2003). Recent studies have shown that peak bone mass can be achieved by the early 20s and possibly even earlier in women (Salamone *et al*., 1996). It is therefore of interest to study the pattern of bone mineralization in children.

The effect of obesity on bone mass in children have yielded conflicting results, largely related to differing approaches to the assessment of two-dimensional projected DXA bone measures relative to age, bone size and body size. Some studies reported normal (Fischer *et al*., 2000, Hasanoglu *et al*., 2000) or increased Bone Mineral Content (BMC) in obese children (Mary *et al*., 2004), whereas others concluded that obese children have decreased bone mass relative to bone size and body weight (Goulding *et al*., 2000). The need for accurate assessment of the structural effects of obesity on bone mineral accretion is underscored by conflicting reports of the effects of increased fat mass and Body Mass Index (BMI) on fracture risk in childhood (Goulding *et al*., 1998, 2001; Skaggs *et al*., 2001; Ma and Jones, 2003). The objective of this study was to determine the contribution of body fatness to Bone Mineral Content (BMC) and Density (BMD) in obese children and adolescents.

MATERIALS AND METHODS

Ninety obese children of age range (7.6-16 year) were selected from Endocrinology Clinic in 6 October Medical Insurance Hospital. Those with organic causes of obesity were excluded, only those with simple obesity were included in this study. Exclusion was based on laboratory data (serum T3,T4, ACTH, etc.). Children were considered obese when they had Body Mass Index (BMI) ≥95th percentile according to the Egyptian Growth Charts (Al-Zanaty and Way, 2003). None of them had followed a weight reduction regimen prior to this study, nor had they received vitamin D or calcium supplements. Apart from their obesity they were in good general condition with normal sun light exposure and had no other known metabolic or endocrine disorders. All had normal serum creatinine, total protein and albumin. All subjects had a negative history for any disorders known to affect bone metabolism, including renal disease, liver disease, chronic diarrhea and gastric or bowel surgery. Children receiving a high dose of vitamins within 6 months of the study and those taking medications known to affect bone metabolism-such as antiepileptic drugs, rifampicin, cholestyramine, or chronic steroid therapy-were also excluded.

Measurements

Anthropometry and Tanner staging: Each child underwent a physical examination that included height, weight, body fat %, pubertal stage assessment.

Weight (kg) was measured to the nearest 0.5 kg while the child was wearing light clothing and no shoes, with the use of a standard clinical balance. Height (cm) to the nearest 0.1 was measured by using a wall-mounted stadiometer while the child standing with no shoes. Pubertal status was determined by physical examination and classified according to the method of Tanner (1998).

The BMI percentiles were used to classify subjects as follows: healthy weight, 5th-85th BMI percentiles; overweight, 85th-94th BMI percentiles; or obese, ≥ 95th BMI percentile (Krebs and Jacobson, 2003), only obese subjects were included. Body mass index was computed as weight/square height, where weight is expressed in kilograms and height inmeters.

Body fat % was measured using body fat monitor (Omron-BF 306-Germany made) measurements were done according to the manufacturer instructions.

Lumbar spine and hip DXA scans: Bone mass in the anterior-posterior lumbar spine (L_{2-4}) and in the proximal femur (neck, trochanter, Ward's triangle and total hip) were measured by using DXA [Luner model with prodegy (combination of pencil and fan beam), with pediatric software 3.8 g].

All subjects were measured on the same machine. The measurements were performed by using standard positioning techniques.

The DXA scans were analyzed to generate measures of vertebral and hip projected bone area (cm^2), BMC (g) and areal bone mineral density (BMD, g cm^{-2}). Lumbar spine and femur bone mineral density (BMD, g cm^{-2}), which was calculated as BMC/ bone area , was used as an estimate of volumetric BMD (Carter *et al*., 1992).

Statistics: Data were represented as mean±SD and compared using t-test for independent sample. Correlation was performed using Pearson correlation coefficient test. Multiple regression models were performed to predict factors affecting bone mineral content and density. Two tailed tests were considered and statistical significance was accepted for $p<0.05$. Analysis of data was done on IBM-PC microprocessor computer using SPSS software for windows version 8.

RESULTS

Subject characteristics: Subject characteristics are summarized in Table 1. The age, anthropometric measurements including weight, height and BMI in addition to measures of body fatness were not significantly different between boys and girls. The Tanner stage distributions and the proportion of children that were prepubertal differ between the 2 groups as girls are almost equally distributed while, 80% of boys did not reach menarche.

Comparison of bone measures between male and female subjects: The DXA results are summarized in Table 2. For lumbar spine measurements, girls had higher age matched and % z-score than boys. Also, for girls their bone mass exceed 100 of age matched %. Lumbar spine measurements including BMC and BMD, length were greater in girls than boys with significant differences regarding BMC with $p<0.01$. While bone area was greater in boys than girls.

Femur neck showed variable results BMC were greater in boys, while BMD and length were greater in girls but these differences were insignificant. All trochanter measurements (BMC-BMD and area) were greater in girls than boys but these differences were insignificant. For Ward's triangle BMC was significantly greater in boys than girls with $p<0.01$. While BMD was almost equal in both sexes.

Table 1: Characteristics of the obese subjects

	Females (n = 45)	Males (n = 45)
Age (year)	13.86±2.17	12.83±3.24
Tanner stage (n)		
1	18 (40%)	18 (40%)
2	-	9 (20%)
3	3 (20%)	9 (20%)
4	-	-
5	18 (40%)	9 (20%)
Weight (kg)	72.4±28.1	74.3±19.9
Height (cm)	146.8±12.8	152.3± 16.6
BMI	32.34±7.24	28.5±5.6
Body fat%	39.3±7.1	37.6±12.3

Table 2: Results of dual-energy X-ray absorptiometry scans in obese subjects

	Females (n = 45)	Males (n = 45)
Lumbar spine		
(%) age matched	106.6±7.4	88.1±17.9
z-score	0.22±0.24	-0.42±0.64
L2-4 area (cm^2)	35.9±6.9	37.5±5.57
L2-4 BMC (g)	31.5±12.9*	24.3±7.31
L2-4 BMD (g cm^{-2})	0.84±0.21	0.63±0.14
L2-4 length (cm)	8.8±1.2	8.6±1.02
Hip		
(%) age matched	100.56±10.99	95.32±16.56
z-score	2.2±0.44	-0.19±0.70
Femur neck area (cm^2)	4.14±0.86	4.85±1.11
Femur neck BMC (g)	3.55±1.3	4.01±1.14
Femur neck BMD (g cm^{-2})	0.83±0.16	0.81±0.12
Femur neck length (cm)	1.43±0.21	1.36±0.20
Trochanter area (cm^2)	9.3±3.7	8.6±3.6
Trochanter BMC (g)	7.1±3.8	5.9±1.9
Trochanter BMD (g cm^{-2})	0.72±0.11	0.70±0.12
Ward BMC (g)	0.74±0.14	1.9±2.3*
Ward BMD (g cm^{-2})	0.74±0.14	0.75±0.18

significant $p<0.01$

Table 3: Pearson correlation coefficient (r) between BMI, Body fat % and hip bone measurements

	Femur neck area	Femur neck area	Femur neck area	Femur neck area	Trochanter area	Trochanter BMD	Trochanter BMD	Ward's BMC	Ward's BMD
BMI	0.56**	0.71**	0.69**	0.71**	0.59**	0.78**	0.69**	0.37*	0.58**
Body fat (%)	0.56**	0.59**	0.45*	0.61**	0.37*	0.50**	0.63**	0.34	0.51**

**Significant $p<0.01$, *Significant $p<0.05$

Table 4: Pearson correlation coefficient (r) between BMI, Body fat % and spine bone (L2-4) measurements

	Spine area	Spine BMC	Spine BMD	Spine length
BMI	0.62**	0.82**	0.76**	0.77**
Body fat (%)	0.30	0.48**	0.55**	0.58**

**Significant $p<0.01$

Table 5: Multiple regression of spine bone mineral content (BMC g) in relation to other variables

	Coefficients *			
	Estimated partial regression coefficient (b_1)			
Prognostic variable	(b_1)	SE (b_1)	t	p-value
Age (years)	2.03	0.27	7.49	0.000
Sex (1 for males and 0 for females)	-7.96	0.91	-8.73	0.001
Puberty stage	2.14	0.76	2.80	0.006
Height (cm)	-2.19	0.05	-0.03	0.97
Spine bone area (cm^2)	1.01	0.18	5.40	0.000
Estimated intercept with estimated SE	-26.14	5.66		

*Dependent variable: Spine bone mineral content. R^2: 0.92, adjusted R^2: 0.91

Table 6: Multiple regression of Spine bone mineral density (BMD g cm^{-2}) in relation to other variables

	Coefficients *			
	Estimated partial regression coefficient (b_1)			
Prognostic variable	(b_1)	SE (b_1)	t	p-value
Age (years)	5.67	0.006	9.06	0.000
Sex (1 for males and 0 for females)	-0.18	0.02	-8.58	0.000
Puberty stage	4.27	0.018	2.42	0.017
Height (cm)	2.59	0.001	1.91	0.058
Spine bone area (cm^2)	-3.31	0.004	-0.76	0.44
Estimated intercept with estimated SE	-7.26	0.13		

*Dependent variable: Spine bone mineral density. R^2: 0.87, adjusted R^2: 0.86

Correlation between BMC and BMI and body fat %: There were no differences between girls and boys regarding the correlation between their obesity indices (BMI and body fat%) and BMC and BMD of spine and hip , so they were collected in a single group. Table 3 and 4 indicated the presence of significant positive correlation between obesity indices and almost all bone measurements studied.

Table 7: Multiple regression of Femur neck bone mineral content (BMC g) in relation to other variables

	Coefficients *			
	Estimated partial regression coefficient (b_1)			
Prognostic variable	(b_1)	SE (b_1)	t	p-value
Age (years)	-5.46	0.07	-0.76	0.44
Sex (1 for males and 0 for females)	-0.30	0.14	-2.10	0.03
Puberty stage	0.10	0.15	0.68	0.49
Height (cm)	7.57	0.01	0.62	0.53
Femur neck bone area (cm^2)	1.05	0.16	6.28	0.000
Estimated intercept with estimated SE	-1.55	1.40		

* Dependent variable: Femur neck bone mineral content. R^2: 0.83, adjusted R^2: 0.81

Table 8: Multiple regression of femur neck Bone Mineral Density (BMD gm cm^{-2}) in relation to other variables

	Coefficients *			
	Estimated partial regression coefficient (b_1)			
Prognostic variable	(b_1)	SE (b_1)	t	p-value
Age (years)	-1.022	0.015	-0.705	0.48
Sex (1 for males and 0 for females)	-5.60	0.029	-1.91	0.059
Puberty stage	3.360	0.032	1.04	0.30
Height (cm)	-2.22	0.002	-0.009	0.993
Femur neck bone area (cm^2)	7.33	0.03	2.13	0.03
Estimated intercept with estimated SE	0.57	0.28		

* Dependent variable: Femur neck bone mineral density. R^2: 0.36, adjusted R^2: 0.34

Table 9: Multiple regression of trochanter Bone Mineral Content (BMC g) in relation to other variables

	Coefficients *			
	Estimated partial regression coefficient (b_1)			
Prognostic variable	(b_1)	SE (b_1)	t	p-value
Age (years)	0.41	0.11	3.51	0.001
Sex (1 for males and 0 for females)	-0.61	0.31	-1.93	0.056
Puberty stage	0.98	0.26	3.71	0.000
Height (cm)	-2.09	0.02	-0.83	0.40
Trochanter bone area (cm^2)	0.91	0.09	9.27	0.000
Estimated intercept with estimated SE	-1.09	2.35		

* Dependent variable: Trochanter bone mineral content. R^2: 0.87, adjusted R^2: 0.86

Multiple regressions of spine and hip bone measurements with different variables: The presence of female sex can predict the increase in spine BMC ($p<0.01$), BMD ($p<0.001$),femur neck BMC ($p<0.05$) and trochanter BMD($p<0.05$) as indicated in Table (5 to 10).

The increase in age can predict the increase in spine BMC ($p<0.001$), BMD ($p<0.001$), trochanter BMC ($p<0.01$) and BMD ($p<0.01$) as indicated in Table (5 to 10).

Table 10: Multiple regression of Trochanter bone mineral density (BMD in g cm^{-2}) in relation to other variables

	Coefficients *			
	Estimated partial regression coefficient (b_1)			
Prognostic variable	(b_1)	SE (b_1)	t	p-value
Age (years)	2.86	0.009	3.04	0.003
Sex (1 for males and 0 for females)	-6.62	0.025	-2.60	0.011
Puberty stage	7.04	0.02	3.29	0.001
Height (cm)	4.31	0.002	2.122	0.037
Trochanter bone area (cm^2)	-4.42	0.008	-0.55	0.58
Estimated intercept with estimated SE	-4.98	0.91		

* Dependent Variable: Trochanter bone mineral density. R^2:0.37 , adjusted R^2: 0.34

The progress in puberty stage can predict the increase in spine BMC ($p<0.01$) and BMD ($p<0.05$) and trochanter BMC ($p<0.001$) and BMD ($p<0.01$) as indicated in Table 5-10. While, height can not predict BMC vor BMD of spine or hip measurements.

DISCUSSION

The present results indicated that obesity in children and adolescents is accompanied by increased regional and perhaps total bone measurements (the latter was not tested in this study , but it can be deduced). In contrast with our findings, other investigators have reported normal (Manzoni *et al*., 1996) or decreased (Goulding and (2000) whole-body BMC and bone area relative to body size. Again, this relates to the choice of body size covariates. Manzoni *et al*. (1996) reported no differences in whole-body bone measures between obese children and nonobese control subjects after adjustment for height, weight, lean mass and fat mass. Goulding *et al*. (2000) reported lower whole-body bone area and BMC relative to body weight in obese children.

There are several possible mechanisms for increased bone mass in childhood obesity. Hormonal influences, such as increased circulating leptin concentrations or increased conversion of and rostenedione to estrogen, may play a role (Klein *et al*., 1998; Thomas and Burguera, 2002).

Leptin acts as a growth factor on the chondrocytes of skeletal growth centers via insulin-like growth factor I receptor expression and thereby potentially contributes to the increased linear growth and skeletal mass observed in childhood obesity (Maor *et al*., 2002). During puberty, estrogen promotes accrual of bone mass on the cortical endosteal surface and in trabecular bone. Also, both androgens and estrogens stimulate calcium absorption and retention and result in a net positive flow of calcium into bone, which contributes to bone accumulation (Schoenau *et al*., 2001).

In addition, this study confirmed the well-recognized contribution of variables such as age, pubertal stage and sex on BMC and BMD in children and adolescents (Annemieke *et al*., 1997; Molgaard *et al*., 1998; Asma *et al*., 2004). During childhood and adolescence as age increases it is logic to have increase in BMC and BMD due to subsequent growth and secretion of growth hormone.

During puberty, growth hormone as well as sex steroid levels increase and both have a positive influence on BMD and contributes to bone accumulation (Frank, 1995; Gilsanz *et al*., 1998). The influence of puberty on BMD was higher in girls than in boys. Animals studies showed a more important role of estrogen than of androgen in mineralization of the skeleton (Frank, 1995). Estrogen is an important determinant of BMD in girls during puberty.

A limitation of this study is that bone age, an important predictor of skeletal maturity and bone mass, was not assessed. In children, the increments in BMC are in large part influenced by growth and size. They are also influenced by the amount of soft tissues surrounding bone, another variable that significantly changes with growth. Although the use of computerized tomography to measure bone mass would circumvent these problems, DXA remains the most convenient technique used to assess bone mass in children because of the short scan time and low radiation dose required. Although it has been suggested that the use of DXA-derived BMC, without any size correction, is a superior approach for evaluating bone mass (Kroger *et al*., 1992), this notion is controversial (Leonard *et al*., 1999) and was not the usual procedure used in the pediatric studies published to date (Smith *et al*., 2002).

The skeleton is a composite of many tube-like (e.g., limbs) and broad (e.g., pelvis) structures that vary in depth and thickness. Therefore, bone area is a poor measure of the volume of bone over which the BMC is distributed. DXA bone area is a function of subject height and bone width. In a child with broad bones for height, assessment of BMC for bone area will result in the comparison of that child with a significantly taller child of comparable bone area and this difference in BMC and bone area will reflect differences in bone length rather than width (Fewtrell, 2003). So, we used BMD in g cm^{-2} (BMC/BMA) in addition to BMC as the primary outcome measures to express bone mass in the growing skeleton.

A technical limitation of DXA is related to the potential for projection error in the assessment of bone measures in children specially the spine as the standard software for the analysis of the lumbar spine frequently fails to detect a complete bone map in children (Smith *et al*., 2002). The present study using Luner model with prodegy (combination of pencil and fan beam), in addition to presence of pediatric software, minimized this problem.

During childhood and adolescence, bone mineral accretion results in sex- and maturation-specific increases in cortical dimensions and trabecular density (Molgaard *et al*., 1998). As emphasized in the recent NIH Consensus Statement report on osteoporosis, the bone mass attained during growth is a critical determinant of the risk of osteoporosis later in life (NIH, 2000). Persons with higher peak bone mass after adolescence have a greater protective advantage when the inexorable declines in bone mass that are associated with increasing age take their toll. Peak bone mass is strongly influenced by genetic factors, but the full genetic potential for bone mass is attained only if nutrition, physical activity, and other lifestyle factors are optimized (Salamone *et al*., 1996).

Where as the increase of bone mineral content seems to be beneficial and lowers the risk of osteoporosis. Some studies consider it a dangerous risk for bone fractures. A study of bone biomechanics in adult male rats with dietarily induced obesity showed significantly greater bone strength in the obese rats than in the controls (Brahmabhatt *et al*., 1998). The cross-sectional geometry and ultimate fracture load of the femur were higher in the obese rats than in the controls.

Ultimately, the clinical significance of altered bone mineral accrual lies in the occurrence of fractures. Studies on the effect of fat mass and BMI on fracture risk have yielded conflicting results (Cooper *et al*., 2002; Cummings *et al*., 1993). It was proposed that the increased BMC in childhood obesity results in increased bone strength but that this increase is not sufficient to overcome the significantly greater forces generated when an obese child falls on an outstretched arm (Skaggs *et al*., 2001). This can be explained by the increased biomechanical loading due to increased body weight and increased lean muscle mechanical forces that may also have contributed to the increased bone dimensions and mass observed in the obese subjects. Increased loading of long bones produces the greatest mechanical stresses on the subperiosteal surface and stimulates bone formation by subperiosteal expansion (Frost, 1987). For example, loading in the playing arm in racquet sports induces significant increases in bone dimensions and mass (Haapasalo *et al*., 2000).

The effect of weight gain on bone loading has been examined in adults. A longitudinal study in postmenopausal women showed that women who gained weight experienced a significant increase in hip cortical section modulus through periosteal expansion (Beck *et al*., 2001). A QCT study in healthy children

suggested that weight bearing and mechanical stresses are important determinants of cortical bone mass, whereas trabecular bone density is influenced by hormonal factors associated with sexual development (Mora *et al*., 1994).

Sex differences in fat distribution (subcutaneous or visceral) (Arfai *et al*., 2002) may have differing effects on regional elevation of the skeleton. In this study, this was not clear as there were no significant increases in all regional bone measurements in girls compared to bone measurements in boys, except for the spine ,where girls had significant higher BMC. This may be attributed to the distribution of age in the studied group as most of them were prepubertal (80% of the boys and 60% of the girls) with no enough hormonal influence on fat distribution.

In conclusion, this study provided strong evidence that obesity assessed by BMI and body fat % was associated with increased vertebral bone content and density mainly spine and hip. The age, sex and puberty stage were consistent and independent predictors of BMC and BMD in obese children and adolescents. Future studies are needed to determine the effect of these differences on fracture risk and to determine whether the increases in spine and hip BMC are sustained into adulthood.

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