

Bone Mineral Density and Turnover in Non-Corticosteroid Treated African American Children with Juvenile Rheumatoid Arthritis

ANDREW J. HEAD, LINDA K. MYERS, MITCHELL A. WATSKY, MARK W. GREENWELL, KAREN D. BARROW, JEAN A. MICHELSON, and LAURA D. CARBONE

ABSTRACT. Objective. To determine bone mineral content (BMC), bone mineral density (BMD), Z scores, and markers of bone turnover in African American children with juvenile rheumatoid arthritis (JRA).

Methods. Eight children with JRA with no prior exposure to corticosteroids were evaluated. Lumbar spine (L1–L4) and total body and total hip BMC and BMD were determined using dual x-ray absorptiometry (DXA), and Z scores (BMD) were calculated. Serum samples of markers of bone turnover including pyridinoline (PYR), N-terminal propeptide of type I procollagen (PINP), osteocalcin (OC), and bone-specific alkaline phosphatase (BSAP) were measured.

Results. The mean Z score (BMD) at the lumbar spine (L1–L4) in patients with JRA was -1.2 ± 0.8 . Z scores for total body and total hip were within 1 standard deviation of normal compared with healthy historical controls matched for age, sex, and race.

Conclusion. BMD was normal for chronological age (defined as Z score ≥ 2.0) in African American children with JRA who had not previously been treated with corticosteroids. Further studies are needed on the effects of JRA on skeletal health in African American children. (J Rheumatol 2006;33:1001–3)

Key Indexing Terms:

JUVENILE RHEUMATOID ARTHRITIS
AFRICAN AMERICAN

BIOMARKERS
DUAL X-RAY ABSORPTIOMETRY

Low bone mineral content (BMC) and bone mineral density (BMD) are frequent findings in Caucasian children with rheumatic diseases, including juvenile rheumatoid arthritis (JRA)^{1–4}. JRA may also have longterm consequences on bone; one report suggested that the frequency of low bone mass is higher in adolescents with a history of early onset juvenile idiopathic arthritis⁵.

Racial differences in disease expression between African American and Caucasian children with JRA have been reported⁶. However, no study to date has examined the effects of

JRA on bone in African American children. We investigated areal BMC and BMD of the lumbar spine, total body and total hip, Z scores, and biomarkers of bone turnover in African American children with JRA.

MATERIALS AND METHODS

Patients were recruited from the pediatric rheumatology clinic at LeBonheur Children's Medical Center, Memphis, Tennessee. African American children < 18 years of age (age at diagnosis < 16 yrs) who met the American College of Rheumatology (ACR) criteria⁷ for the classification of pauciarticular, polyarticular, or systemic JRA were recruited. Patients were excluded for previous steroid treatment, weight > 250 pounds (113.6 kg), and pregnancy and/or lactation.

All patients had a physical examination performed by the same trained rheumatologist (AJH). Height, weight, Tanner staging, and tender and swollen joint counts were performed. Laboratory investigation included measurement of Westergren erythrocyte sedimentation rate (ESR) and measurement of bone biomarkers. Pyridinoline (PYR; Quidel Corp., San Diego, CA, USA), a marker of bone resorption, was measured in serum by ELISA. The N-terminal propeptide of type I procollagen (PINP) (DiaSorin, Stillwater, MN, USA), a marker of bone formation, was measured in the serum by radioimmunoassay. Additional markers of bone formation, including osteocalcin (OC) and bone-specific alkaline phosphatase (BSAP) were measured in serum by ELISA (Quidel). All specimens were measured in duplicate, and the mean value recorded. In our laboratory, the intraassay coefficients of variation (CV) for PYR, PINP, OC, and BSAP are 8.57%, 2.68%, 4.18%, and 3.83%, respectively.

Questionnaires were completed with assistance by an experienced nurse interviewing the child and parent. Demographic data, medical history, history of fracture, medications, menstrual history, family history of osteoporosis, smoking, and alcohol use were recorded. A Childhood Health Assessment Questionnaire (CHAQ) measured disability and pain.

From the Department of Medicine, Division of Rheumatology; Department of Pediatrics; Children's Foundation Research Center at LeBonheur Children's Medical Center; Department of Physiology-Biophysics; Department of Medicine, Division of Nephrology; and General Clinical Research Center, University of Tennessee Health Sciences Center, Memphis, Tennessee, USA.

Supported by a grant from the LeBonheur Foundation and supported in part by the National Institutes of Health, National Center for Research Resources, General Clinical Research Center Grant M01 RR00211.

A.J. Head, MD; K.D. Barrow, MS; L.D. Carbone, MD, MS, Department of Medicine, Division of Rheumatology; L.K. Myers, MD, Department of Pediatrics and Children's Foundation Research Center; M.A. Watsky, PhD, Department of Physiology-Biophysics; M.W. Greenwell, MD, Division of Nephrology; J.A. Michelson, MA, RD, General Clinical Research Center.

Address reprint requests to Dr. L. Carbone, University of Tennessee Health Science Center, Room G326, Coleman Building, 956 Court Avenue, Memphis, TN 38163. E-mail: lcarbone@utm.edu

Accepted for publication December 29, 2005.

Personal non-commercial use only. The Journal of Rheumatology Copyright © 2006. All rights reserved.

BMC (g) and area (cm²) were measured for the lumbar spine (L1–L4), total body, and total hip with dual-energy x-ray absorptiometry (DXA; Hologic Discovery: a fan-beam densitometer using low density software); BMD (g/cm²) was subsequently calculated for these areas. Z scores (relative to BMD) were calculated using the program provided by Dr. L. Bachrach, Stanford University School of Medicine⁸ (available from: <http://www-stat-class.stanford.edu/pediatric-bones/#applet>).

Continuous variables were analyzed using the Wilcoxon rank-sum test. All analyses were performed using SAS System for Windows (v 9.1; SAS Institute, Cary, NC, USA).

RESULTS

A total of 8 JRA patients (systemic n = 2, pauciarticular n = 1, polyarticular n = 5; male n = 3, female n = 5) are included in this report. Baseline characteristics including age, height, weight, Tanner stage, history of fractures, smoking history, and body mass index are shown in Table 1. The mean disease duration was 60.1 months, mean ESR was 23.3 ± 24.1 mm/h, mean CHAQ score was 0.8 ± 0.6, and the mean numbers of tender and swollen joints were 1.1 ± 0.6 and 2.5 ± 4.2, respectively. All patients were current users of nonsteroidal antiinflammatory drugs; one patient also reported current use of methotrexate (data not shown).

BMC, BMD, and Z scores (from BMD) of the JRA patients

Table 1. Characteristics of patients with juvenile rheumatoid arthritis (JRA) (n = 8).

Characteristic	Mean (SD) or N (%)
Male	3 (38)
Female	5 (63)
Age, yrs	14.0 (3.0)
Weight, kg	56.7 (17.0)
Height, cm	160.9 (13.5)
Tanner staging	
1	0 (0)
2	0 (0)
3	2 (25)
4	0 (0)
5	6 (75)
Type of JRA	
Systemic	2 (25)
Pauciarticular	1 (13)
Polyarticular	5 (62)
Disease duration, mo	60.1 (41.1)
Tender joint count	1.1 (0.6)
Swollen joint count	2.5 (4.2)
CHAQ-DI	0.8 (0.6)
Morning stiffness, min	16.3 (20.3)
Pain score, mm	50.5 (35.6)
MD global score, mm	23.8 (17.7)
ESR, mm/h	23.3 (24.1)
Fragility fracture	0 (0)
Traumatic fracture	1 (12.5)
Current smoking status	0 (0)
NSAID use	8 (100)

CHAQ-DI: Childhood Health Assessment Questionnaire Disability Index. NSAID: nonsteroidal antiinflammatory drugs; ESR: erythrocyte sedimentation rate.

are shown in Table 2. The mean Z score at the lumbar spine was -1.2 ± 0.8 in the JRA patients. Z scores (from BMD) at other skeletal sites, including total body and total hip, were within 1 standard deviation of the mean for age, sex, and race matched controls (Table 2).

Markers of bone turnover including PINP, OC, and BSAP (formation) and PYR (resorption) were measured. The mean and standard deviation values in these JRA patients were: PINP $622.4 \pm 451.7 \mu\text{g/l}$, OC $28.4 \pm 11.9 \text{ ng/ml}$, BSAP $113.0 \pm 69.4 \text{ U/l}$, and PYR $2.4 \pm 0.4 \text{ nmol/l}$. Because historical normative data for biomarkers specifically relative to African American children have not been reported, 3 race matched controls, mean age 11.1 ± 5.7 years, with no history of corticosteroid use or JRA, also donated blood for this analysis. PINP, OC, BSAP, and PYR did not differ significantly between the JRA patients and these controls (data not shown).

DISCUSSION

The major finding of our study is that African American children with JRA who have never been treated with corticosteroids have lumbar spine, total hip, and total body Z scores (from BMD) of ≥ -2 . This is significant, because guidelines set forth by the International Society for Clinical Densitometry (ISCD) suggest that in children only Z scores ≤ -2 should be considered low for chronological age⁹. Our findings suggest that BMD in African American children with JRA is within normal limits for chronological age.

Studies on BMC and BMD in children with JRA have largely been confined to Caucasian populations, and have not included large numbers of African Americans^{1-5,10}. In Caucasian children with JRA, lower BMD at the lumbar spine (in postpubertal girls)¹¹ and distal 1/3 radius¹², compared with controls, has been reported. To our knowledge, ours is the first report of BMD in exclusively African American children with JRA who have never been treated with corticosteroids.

Normative data on biomarkers in healthy children are limited; however, the mean values for all biomarkers measured in

Table 2. BMC, BMD, and Z scores (BMD) in patients with JRA (n = 8) by DXA.

	Mean (SD)
BMC, g	
Total body	1891.1 (332.6)
Total hip	26.3 (6.5)
Lumbar spine (L1–L4)	43.1 (12.4)
BMD, g/cm ²	
Total body	0.995 (0.063)
Total hip	0.904 (0.142)
Lumbar spine (L1–L4)	0.828 (0.140)
Z scores (BMD)	
Total body	-0.2 (0.9)
Total hip	-0.6 (1.0)
Lumbar spine (L1–L4)	-1.2 (0.8)

BMC/D: bone mineral content/density.

our study including PINP, OC, BSAP, and PYR were within the normal ranges reported for these biomarkers in healthy children¹²⁻¹⁴. Because historical normative data for biomarkers specifically in African American children have not been reported, we also measured biomarkers in 3 race matched controls, mean age 11.1 ± 5.7 years, with no history of corticosteroid use or JRA, and found no significant differences between these controls and the JRA patients ($p > 0.05$ for PINP, OC, BSAP, and PYR, data not shown). In support of this, in Caucasian children with JRA, one report has suggested that bone turnover is normal⁴. In contrast, another report suggested that bone turnover may be lower in Caucasian children with JRA compared with healthy controls¹⁵.

Our study has several limitations. The sample size was relatively small, and we included patients with several different types of JRA and Tanner stages. Our study was not adequately powered to examine differences in bone metabolism markers between JRA subjects and 3 controls; however, we chose to include these controls because there is a lack of normative data on bone metabolism markers in African American children. Finally, our patients had low disease activity, and results may differ in populations with more severe disease activity.

Our study has several strengths as well. We are the first to study BMD and describe bone biomarkers in a population of all African American children with JRA. Further, our results are not confounded by corticosteroid use, which can affect BMD substantially.

Bone mineral density was normal for chronological age (defined as a Z score ≥ -2.0) in African American children with JRA who had not previously been treated with corticosteroids. However, further studies are needed to determine whether JRA has longterm implications for skeletal health in African American children.

ACKNOWLEDGMENT

We thank Victorina Pintea, MS, for her technical assistance in the biomarker analysis.

REFERENCES

1. Henderson CJ, Cawkwell GD, Specker BL, et al. Predictors of total body bone mineral density in non-corticosteroid-treated prepubertal children with juvenile rheumatoid arthritis. *Arthritis Rheum* 1997;40:1967-75.
2. Henderson CJ, Specker BL, Sierra RI, Campaigne BN, Lovell DJ. Total-body bone mineral content in non-corticosteroid-treated postpubertal females with juvenile rheumatoid arthritis: Frequency of osteopenia and contributing factors. *Arthritis Rheum* 2000;43:531-40.
3. Pepmueller PH, Cassidy JT, Allen SH, Hillman LS. Bone mineralization and bone mineral metabolism in children with juvenile rheumatoid arthritis. *Arthritis Rheum* 1996;39:746-57.
4. Polito C, Strano CG, Rea L, et al. Reduced bone mineral content and normal serum osteocalcin in non-steroid-treated patients with juvenile rheumatoid arthritis. *Ann Rheum Dis* 1995;54:193-6.
5. Lien G, Flato B, Haugen M, et al. Frequency of osteopenia in adolescents with early-onset juvenile idiopathic arthritis: A long-term outcome study of 105 patients. *Arthritis Rheum* 2003;48:2214-23.
6. Schwartz MM, Simpson P, Kerr KL, Jarvis JN. Juvenile rheumatoid arthritis in African Americans. *J Rheumatol* 1997;24:1826-9.
7. Cassidy JT, Levinson JE, Bass JC, et al. A study of classification criteria for a diagnosis of juvenile rheumatoid arthritis. *Arthritis Rheum* 1986;29:274-81.
8. Bachrach LK, Hastie T, Wang M-C, Narasimhan B, Marcus R. Bone mineral acquisition in healthy Asian, Hispanic, Black, and Caucasian youth: A longitudinal study. *J Clin Endocrinol Metab* 1999;84:4702-12.
9. Writing Group for the ISCD Position Development Conference. Position statement: executive summary. The Writing Group for the International Society for Clinical Densitometry (ISCD Position Development Conference). *J Clin Densitom* 2004;7:7-12.
10. McDonagh JE. Osteoporosis in juvenile idiopathic arthritis. *Curr Opin Rheumatol* 2001;13:399-404.
11. Hopp R, Degan J, Gallagher JC, Cassidy JT. Estimation of bone mineral density in children with juvenile rheumatoid arthritis. *J Rheumatol* 1991;18:1235-9.
12. Hillman L, Cassidy JT, Johnson L, Lee D, Allen SH. Vitamin D metabolism and bone mineralization in children with juvenile rheumatoid arthritis. *J Pediatr* 1994;124:910-6.
13. Tahtela R, Turpeinen M, Sorva R, Karonen SL. The aminoterminal propeptide of Type I procollagen: Evaluation of a commercial radioimmunoassay kit and values in healthy subjects. *Clin Biochem* 1997;30:35-40.
14. Sorva R, Anttila R, Siimes MA, Sorva A, Tahtela R, Turpeinen M. Serum markers of collagen metabolism and serum osteocalcin in relation to pubertal development in 57 boys at 14 years of age. *Pediatr Res* 1997;42:528-32.
15. Falcini F, Ermini M, Bagnoli F. Bone turnover is reduced in children with JRA. *J Endocrinol Invest* 1998;21:31-6.