Osteopenia Is Common in Adult Male Patients with Active Juvenile Idiopathic Arthritis

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ABSTRACT. ***Objective.*** To assess the prevalence of osteopenia in Southeast Asian men with active juvenile idiopathic arthritis (JIA) and to identify predictors of reduced bone mineral density (BMD).

Methods. BMD of 30 men with active JIA and 23 healthy men was assessed by dual energy x-ray absorptiometry scans. Clinical variables that influence bone mass were also analyzed. T scores were calculated based on Caucasian normative data.

Results. Absolute BMD (g/cm^2) was significantly lower in men with active JIA compared to controls at all measured sites, i.e., lumbar spine ($p = 0.018$), hip ($p = 0.018$), and distal third of forearm ($p = 0.044$). More subjects in the JIA group had low BMD (T score ≤ -1.0) than controls at hip (22/30 vs 9/23; $p < 0.05$) and distal third of forearm (27/30 vs 10/23; $p < 0.001$), while at lumbar spine region the difference was not statistically significant (22/30 vs 13/23). A significant negative correlation of BMD was found with joint deformities, limitation of joint movement, Health Assessment Questionnaire score, and erythrocyte sedimentation rate. BMD at the hip and distal third of forearm was significantly lower in patients having arthritis at these sites. A positive correlation of BMD was found with body mass index.

Conclusion. A majority of Southeast Asian men with active JIA have reduced BMD. More patients in our cohort had low BMD compared to reports from Western countries. This finding may be attributed to use of Caucasian normative data, uncontrolled disease activity, severity of disease, poor nutritional status, or an ethnic variation. (J Rheumatol 2006;33:1642–5)

Key Indexing Terms:
JUVENILE RHEUMATOID ARTHRITIS OSTEOPOROSIS
BONE DENSITY CORTICOSTEROIDS SOUTHEAST ASIA

Osteoporosis is characterized by decreased bone mass and poor bone quality, thereby leading to reduced bone strength and increased fracture risk[1]. There is a universal decline in bone mineral density (BMD) in adults with advancing age due to increased bone resorption[2]. Peak bone mass attained at the end of adolescent growth therefore becomes a critical determinant in development of osteoporosis in adult life[3]. Young adults having higher peak bone mass are at a lower risk of developing osteoporosis in later life and vice versa. Skeletal maturation and peak bone mass are related to normal growth, and any adverse events during childhood, especially at puberty, have a negative influence on peak bone mass[4]. Reduced BMD has been reported by several studies in children and adolescents with juvenile idiopathic arthritis (JIA)[5-8]. Both disease and drugs (corticosteroids) have been incriminated as factors influencing BMD.

Data on magnitude and severity of this problem in adults with JIA are scarce and results variable[9-13]. Moreover no data are available from Southeast Asia due to limited availability of dual energy x-ray absorptiometry (DEXA) scans and nonavailability of normative BMD data. In addition, Indians have low calcium intake and high incidence of vitamin D deficiency, factors that can influence BMD[14,15]. We studied the prevalence of osteopenia in our cohort of adult patients with active JIA.

MATERIALS AND METHODS

Study design. This was a cross-sectional case controlled study. The study group comprised 30 men with active JIA consecutively attending the outpatient clinic at Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, a tertiary care referral hospital. In view of the small number of women with JIA, they were not included in the study. A rheumatologist (PA) examined all patients. Diagnosis and subtype classification of JIA was done as per International League of Associations for Rheumatology criteria[16]. Active JIA was defined as presence of active joint inflammation (swollen/tender joint), presence of systemic features, and/or elevated erythrocyte sedimentation rate (ESR) > 20 mm/h. Twenty-three healthy male hospital employees volunteered as controls. Informed consent was provided by all participants.

BMD measurements. BMD was determined by DEXA performed on the left hip, left distal third of forearm, and the lumbar spine (L1-L4) using a Hologic scanner. All measurements were done on the same machine. Since reference values are not available for normal Indian or Asian populations, Caucasian reference values were used for calculation of T scores. Participants were classified as having normal BMD (T score > –1 SD), osteopenia (T score between –2.5 and –1 SD), and osteoporosis (T-score < –2.5 SD) as per World Health Organization (WHO) criteria[17].

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Accepted for publication March 28, 2006.

Laboratory and functional assessments. ESR was measured using the Westergren method. Serum levels of total proteins, albumin, alkaline phosphatase, creatinine, calcium, and phosphate, and urinary calcium excretion corrected for creatinine were measured in all patients with JIA. Functional status of all patients was assessed by Health Assessment Questionnaire (HAQ). Daily calcium intake was estimated by 3 days' dietary recall method[18]. The entire dietary intake for 3 days was recorded; in addition, patients were queried about calcium-containing diets. History was taken for medication use, past or present steroid use, sun exposure, history of prior fractures, bony pains, tobacco or alcohol use, and physical activity.

Data analysis. Intergroup comparison for continuous variables between the 2 groups was calculated by unpaired t test; qualitative variables were assessed using chi-squared and Fisher's exact tests. BMD of patients with left wrist, left hip, or lumbar spine involvement was compared with patients without involvement of these sites using Mann-Whitney U test. Chi-squared test was used to compare BMD between different types of arthritis. Pearson's correlation analysis was performed to identify factors affecting BMD in patients with JIA.

RESULTS

Demographic characteristics of patients with JIA were comparable to controls except mean age, which was significantly lower in patients with JIA (22.6 ± 5.12 vs 27.35 ± 4.04 yrs; p = 0.001). Body mass index (BMI) of patients with JIA was 19.79 ± 3.73 kg/m^2 and 15/30 patients had BMI below the normal recommended value of 19 kg/m^2. However, there was no difference in BMI between patients and controls (Table 1).

Among the 30 patients with JIA, 13 had enthesitis related arthritis, 4 had systemic onset disease, 6 had rheumatoid factor (RF) negative polyarticular, 2 had RF-positive polyarticular disease, one had extended oligoarticular disease, and 4 had persistent oligoarticular disease indicating that a majority of patients had a widespread systemic inflammatory disease course. The mean age of onset was 11.37 ± 2.67 years and the mean disease duration was 11.27 ± 5.39 years.

The median active joint count was 1 (range 0–6). Patients with systemic disease had systemic features like fever and organomegaly. The mean ESR was 31.9 ± 20.4 and 20 of the 30 patients had ESR > 20. A majority of patients had no significant functional limitation as indicated by mean HAQ score of 0.4 ± 0.6. Fifteen of 30 patients had a HAQ score of 0; 11 had a HAQ score < 1; 3 had a HAQ score between 1 and 2; and only one patient had a HAQ score > 2.

Joint deformities were present in 5 patients. Sun exposure was adequate, but the mean calcium intake (773.67 ± 284.84 mg/day) was below the recommended dietary allowance. A majority of patients (19, 63.3%) were not doing regular physiotherapy and only 11 patients were doing active physiotherapy > 30 minutes more than twice a week. History of steroid intake was present in 17 (56.7%) patients; of those, 2 patients were currently receiving steroids (prednisolone 10–15 mg/day for 24 mo and 10 mg/day for 3 mo). Data were not available for the duration of steroid treatment in 2 patients, while for the other 15 patients the median duration of steroid treatment was 12 months (range 0.5–48). Cumulative prednisolone dose per patient in steroid users was 3.7 g (0.27–12.0 g). There was no history of pathologic fractures.

Table 1. Demographic characteristics of patients with active JIA and controls. Results are expressed as mean ± standard deviation.

Variable	Cases	Controls	p
No.	30	23	
Mean age, yrs	22.6 ± 5.12	27.35 ± 4.04	< 0.001
Mean height, cm	166.9 ± 7.58	167.38 ± 8.06	NS
Mean weight, kg	55.6 ± 13.68	59.91 ± 7.01	NS
BMI	19.79 ± 3.73	21.35 ± 1.78	NS

BMI: body mass index; NS: not significant.

BMD was significantly lower in the JIA group compared to controls at all measured sites, i.e., lumbar spine (0.89 ± 0.131 vs 0.97 ± 0.089 gm/cm^2; p = 0.018), hip (0.82 ± 0.134 vs 0.91 ± 0.126 gm/cm^2; p = 0.018), and distal third of forearm (0.566 gm ± 0.071 vs 0.61 ± 0.081 gm/cm^2; p = 0.044) (Figure 1).

At the lumbar spine, 22 (73.3%) patients with JIA had low BMD (T score < –1.00), of which 8 (26.7%) were osteoporotic (T score < –2.5) per WHO criteria[19] using Caucasian normative data. At the hip, 22 (73%) had low BMD, of which 7 (23.3%) were osteoporotic, while 27 (90%) had low BMD at distal third of forearm, of which 12 (40%) were osteoporotic (Table 2).

A positive correlation of BMD was found with BMI. There was no significant correlation between calcium intake or disease duration with BMD values. A negative correlation was found with joint deformities, limitation of joint movement, HAQ score, and ESR value. BMD of the hip had a significant positive correlation with BMD of the spine as well as BMD of the distal third of forearm, while the correlation between spine and distal third of forearm was not significant (Table 3).

Patients having hip joint disease (n = 11) had significantly lower BMD at the hip (p = 0.001) and lumbar spine (p = 0.018) compared to patients without hip joint involvement (n = 19). Similarly, patients having wrist disease (n = 5) had significantly lower BMD at distal third of forearm (p = 0.001)

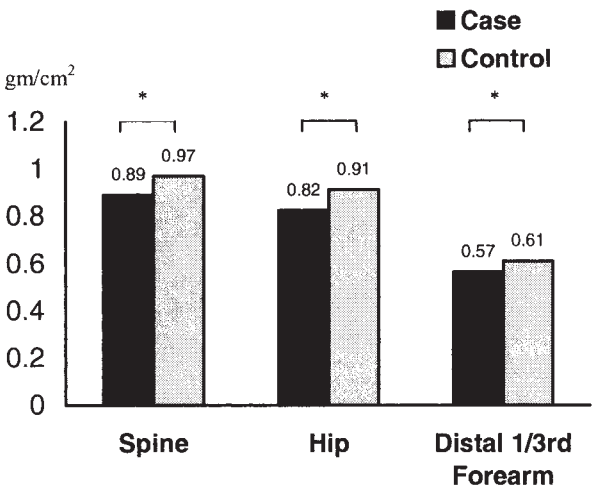

Figure 1. Mean BMD (g/cm^2) of controls (n = 23) and patients with JIA (n = 30). *p < 0.05.

Table 2. Distribution of BMD classified per WHO definitions for osteoporosis (T score < –2.5), osteopenia (T score < –1.00 and ≥ –2.5), and normal (T score ≥ –1.0) compared to Caucasian normative data. Overall there was no difference in BMD at the lumbar spine in patients or controls but the prevalence of osteoporosis was higher in patients ($p < 0.05$) compared to controls.

	Cases, n (%)	Controls, n (%)	p
Lumbar spine			
Osteoporosis	8 (26.7)	1 (4.3)	NS
Osteopenia	14 (46.7)	12 (52.2)	
Normal	8 (26.7)	10 (43.5)	
Hip			
Osteoporosis	7 (23.3)	4 (17.4)	< 0.05
Osteopenia	15 (50)	5 (21.7)	
Normal	8 (26.7)	14 (60.9)	
Distal third of forearm			
Osteoporosis	12 (40)	1 (4.3)	< 0.001
Osteopenia	15 (50)	9 (39.1)	
Normal	3 (10)	13 (56.5)	

Table 3. Factors having significant correlation with BMD at different sites. Values indicate Pearson's correlation coefficient.

	BMD Hip	BMD Spine	BMD Distal Forearm
Joint deformity	-0.174	0.095	-0.592†
Joint limitation	-0.377*	-0.143	-0.644††
BMI	0.571†	0.535†	0.30
HAQ	-0.468**	0.362*	-0.204
ESR	-0.374*	-0.306	-0.0.163
BMD spine	0.755††	—	0.229
BMD distal third of forearm	0.393*	0.229	—
BMD hip	—	0.755††	0.393*

* $p < 0.05$, ** $p < 0.01$, † $p < 0.005$, †† $p < 0.001$.

compared to patients not having wrist joint involvement (n = 25). There was no significant difference in BMD of patients with (n = 7) or without (n = 23) lumbar spine involvement. BMD was not significantly different among patients when comparing JIA subtype, steroid intake, and physiotherapy.

DISCUSSION

Our study shows that a majority of men with active JIA have significantly lower BMD than controls. Articular involvement at wrist and hip regions correlated with low BMD at these sites, indicating a role for local factors in bone mineralization. In addition, markers of disease activity and severity had a negative correlation with BMD, indicating the influence of systemic factors.

The mean age of patients with JIA was significantly lower than controls. However, this is unlikely to have influenced the results, as BMD at all 3 sites measured had no significant correlation with age. Most patients were in the 20–30 years age group and only one patient was above 35 years of age. Hence age-related decline in BMD was not expected in most patients.

Previous studies[9-13] have also found reduced BMD in adults with JIA. However, the frequency of osteopenia in those studies has varied from 28% to 50% at the lumbar spine and between 32% and 53% at the femoral neck, compared to 73.3% at both lumbar spine and left hip in our cohort[9-13]. Several factors could be responsible for this difference. All our patients had active arthritis at the time of evaluation. Haugen, *et al*[12] showed that BMD was significantly lower in patients with JIA with persistent disease activity, whereas patients having achieved remission had BMD comparable to healthy controls. Also, previous studies[10,12] have shown current disease-related inflammatory variables are related to reduced BMD. In previous studies the pauciarticular form of arthritis formed the major subgroup[9-13], in contrast to our study in which only 13.3% patients had persistent oligoarticular disease, indicating higher inflammatory activity in our cohort. Also, the mean BMI of patients with JIA was 19.79 ± 3.73 and 50% had BMI below the normal limit of 19 kg/m^2. As BMI had a significant correlation with BMD at all 3 sites measured, poor nutritional status of our patients with JIA could be another factor. Ethnicity has been proposed as a risk factor in the development of osteopenia, and studies have shown that a healthy Indian population has low bone mass[19,20]. This is also reflected in our data, as a significant proportion of our healthy controls had lower T scores compared to Caucasian references. Finally, since normative BMD data are not available for an Indian population, T scores were calculated using Caucasian reference values, which would overestimate the prevalence of osteopenia. Since this is the first study on the prevalence of osteopenia in adults with active JIA from Southeast Asia, it might be possible that JIA patients of Asian descent are more predisposed to the development of osteopenia. Normative data from our population is required to ascertain the true effect of active JIA on BMD.

Among the various factors correlated with BMD was the presence of joint deformities, limitation of normal range of joint movements, HAQ scores, and ESR, while no correlation was found with calcium intake, history of steroid treatment, type of arthritis, and active physiotherapy. Previous studies[4-8] have shown that in children with JIA reduced physical activity, insufficient dietary intake of vitamin D and calcium, steroid treatment, and disease severity and activity are risk factors for reduced BMD. In adults, however, current disease-related inflammatory markers, physical disability, severity of disease, and disease activity appear to be more important. It has been suggested that the pathogenic mechanism of osteopenia is different in children with JIA compared to adults[10]. In children, evidence for reduced bone turnover has been found, while in adults there is evidence of increased bone turnover and resorption[4,10,12]. Age-related differences in clinical predictors of osteopenia in patients with JIA are therefore likely.

It has been shown that children with JIA have reduced bone mineralization, resulting in decreased peak bone mass. This leads to lower bone mass reserves, thereby resulting in higher risk for osteopenia and fractures in adult life[3]. The finding of reduced BMD in adults with active JIA supports this. However, current evidence is restricted to a few cross-sectional case controlled studies, and a longitudinal study is required from disease onset through adulthood to analyze the prevalence and risk factors associated with the development of this complication.

Our results indicate that adult patients with active JIA have significantly reduced BMD compared to healthy controls. Both cortical appendicular skeleton and axial trabecular bone are affected. Among major risk factors are ongoing disease activity, joint deformity, poor nutritional status, and functional limitation. Better control of disease activity is required to minimize the risk of this complication.

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