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Prevalence and relationship of low bone mineral density in the development of juvenile idiopathic arthritis.

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Abstract

Objective: To assess the prevalence of low bone mineral density in Chinese patients, and to determine the potential risk factor in development of Juvenile Idiopathic Arthritis (JIA) among Chinese patients.
Materials and methods: A total of 120 JIA who routinely undergoing Dual X-ray Absorptiometry (DXA) scanning selected from Department of Pediatrics, Ren Ji Hospital, China between January 2014 to December 2016. Bone Mineral Density (BMD) was measured by DXA in all 120 patients. Lumbar Spine (LS) BMD of less than -1 and more than and equal to -2.5 score of BMD is defined as Osteopenia. Lumbar spine BMD of less than -2.5 score of BMD is defined as osteoporosis. Data on disease activity, QoL, BMI, age, gender, ethnicity, medication use, duration of medication use, clinical characteristics, and adolescence status were collected.
Result: Data of all 120 patients were analysed. In our study, 39% of subjects had osteopenia, whereas 21% subjects had osteoporosis. Of total, 20% of patients had low BMD. Our statistical analysis results showed a significant relationship between osteopenia and patients' age, diseases duration, treatment (corticosteroid) duration and dose of corticosteroid, were found to be highly correlated. Dose of corticosteroid (cumulative) dose and duration of diseases were found to be significantly related with LS osteopenia, whereas duration of disease positively related with LS osteoporosis.
Conclusion: Our results suggested that osteopenia and osteoporosis are common in Chinese patients with JIA. Dose of corticosteroid therapy and duration of diseases is mainly associated with JIA as it strongly linked with LS osteoporosis, LS osteopenia and low BMD.

Keywords: Osteoporosis, Osteopenia, Bone mineral density, Juvenile idiopathic arthritis.

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Introduction

Juvenile idiopathic arthritis is one the most common autoimmune disorder occurs in children of more than 16 y of age. It is considered as one of the most frequent chronic inflammatory diseases, it is characterized by the presence of autoantibodies. Epidemiological studies have projected that by 2025, more than 50% of the world's population aged 80 y or more will reside in Asia, with the number of annual hip fractures projected to exceed one million by 2030 [1].

Osteoporosis is a major cause of vertebral and non-vertebral fracture: over 1.5 million fractures per year are attributable to osteoporosis in the United States alone [2]. Clinical studies have focused primarily on postmenopausal osteoporosis in women [1]. Epidemiological studies have shown, however, that the prevalence of osteoporosis in men is higher than thought [2-4]. In addition, the mortality rate is higher in men than in women following an osteoporotic fracture [2-5] and low Bone Mineral Density (BMD) has been associated with increased all-cause mortality in men [6-8].

Osteoporosis is a significant public health problem which is gaining increased awareness in most developed countries. It eventually results in fractures of the spine, hip, forearm, and other bones not typically susceptible to fracture in young healthy individuals in the absence of significant trauma. Fractures of the hip result in substantial morbidity and mortality, as well as in substantial direct health care expenditures. The direct health care costs associated with fractures of the spine are less well characterized, but patients with multiple fractures clearly suffer increasing morbidity [9-11]. The objective of this study was to assess the prevalence and relationship of low bone mineral density in Chinese patients with JIA. The objective of this study was to assess the prevalence of low bone mineral density in Chinese patients, and to determine the potential risk factor in development of Juvenile Idiopathic Arthritis (JIA) among Chinese patients.

Materials and Methods

A total of 120 JIA who routinely undergoing Dual X-ray Absorptiometry (DXA) scanning selected from Department of Pediatrics, Ren Ji Hospital, China between January 2014 to December 2016. Bone Mineral Density (BMD) was measured by DXA in all 120 patients. Lumbar Spine (LS) BMD of less than -1 and more than and equal to -2.5 score of BMD is

defined as Osteopenia. Lumbar spine BMD of less than -2.5 score of BMD is defined as osteoporosis. Data on disease activity, QoL, BMI, age, gender, ethnicity, medication use, duration of medication use, clinical characteristics, and adolescence status were collected. We used computerized database of Ren Ji Hospital to collect required data to fulfil the objective of our study. Institutional ethics committee approval was obtained. Since, this was a retrospective, observational study, and patients whose medical records reviewed were not contacted, or are named in the study, thus the requirement for obtaining formal informed consent was waived by ethics committee. All BMD measurements will be performed using DXA (Hologic, Lunar, or Norland scanners). BMD will be measured at the baseline and endpoint. Standardized BMD (sBMD) data were the basis for any statistical analysis. The following standardization methodology was used.

Lumbar spine BMD

- For hologic instruments: sBMD (mg/cm^2)=1000 (1.091 × BMDHologic-0.016)
- For Lunar instruments: sBMD (mg/cm^2)=1000 (BMDLunar-0.0552)
- For Norland instruments: sBMD (mg/cm^2)=1000 (1.005 × BMDNorland+0.070)

Quantitative variable was presented as mean ± standard deviation. Categorical variables were presented as absolute number and/or percentage of subjects in each category, and were compared using Chi-square or fisher exact test (Univariate analysis). Pearson correlation coefficient was used to assess the relationship between osteopenia and osteoporosis with other variables (Multivariate analysis). In all cases, a $P<0.05$ was statistically significant among comparison groups. Data from each patient was coded and analysed using Graph Pad Prism statistical analysis software (version 6.0).

Results

Data of all 120 patients were analysed. Demography and patient characteristics of all patients were found similar, and presented in Table 1. In our study, 39% of subjects had osteopenia, whereas 21% subjects had osteoporosis. Of total, 20% of patients had low BMD.

Our study results suggested that there was correlation between osteopenia and patients' age during BMD measurements (using DXA), diseases duration, corticosteroid duration, dose of corticosteroid, history of kidney disorder and use of immune suppressant ($p<0.05$ for each) (Table 2). Similar trend was observed when relationship between osteoporosis and patients' age during BMD measurements (using DXA), duration of diseases, treatment (corticosteroid) duration, dose of corticosteroid, history of kidney disorder and use of immune suppressant was assessed (Table 2). In multivariate statistical analysis, we showed that patients' age during BMD measurements, diseases duration, treatment (corticosteroid) duration and dose of corticosteroid, were found to be highly correlated with osteopenia and lumbar spine osteoporosis ($p<0.05$ for each) (Table 2). Dose of corticosteroid (cumulative) dose was found to be significantly related with LS osteopenia, whereas duration of disease positively related with LS osteoporosis ($p<0.05$ for each) (Table 3). Also association between kidney disorder and LS osteoporosis were found to be statistically significant ($p<0.05$).

The parameters which were significantly associated with osteoporosis and osteopenia were undergoing further statistical analysis to confirm the reliability and validity of the statistical model which have been used to detect association. Our repeat analysis was found that dose of corticosteroid therapy (cumulative), duration of diseases which are the key predictor of LS osteoporosis and LS osteopenia ($p<0.05$ for each) (Table 3). Our results suggested that dose of corticosteroid therapy, and duration of diseases is strongly linked with LS osteoporosis and LS osteopenia ($p<0.05$ for each).

Discussion

Osteoporosis is a significant public health problem which is gaining increased awareness in most developed countries. It eventually results in fractures of the spine, hip, forearm, and other bones not typically susceptible to fracture in young healthy individuals in the absence of significant trauma.

To the best of our knowledge, this was the first investigation to evaluate prevalence and relationship of low bone mineral density in the development of juvenile idiopathic arthritis among Chinese individuals. In present study, we observed the involvement of osteopenia and osteoporosis was common in Chinese individuals with juvenile idiopathic arthritis, with prevalence of 39%, and 21%, respectively. Our finding is consistent with reports which suggested the positive relation between osteopenia and osteoporosis in development of juvenile idiopathic arthritis. In our study, we have not observed that the relationship between the dose of corticosteroids, duration of corticosteroid treatment with osteopenia and osteoporosis.

It has been noted that there was no statistical significant relation between diseases activity score with osteopenia and osteoporosis. Our study results suggested that there was relationship between osteopenia and patients' age during BMD measurements, diseases duration, treatment (corticosteroid) duration, dose of corticosteroid, and history of kidney disorder. Similar trend was observed when relationship between osteoporosis and patients' age during BMD measurements, diseases duration, treatment (corticosteroid) duration, dose of corticosteroid, and history of kidney disorder was assessed. Further, in multivariate statistical analysis, we observed that there was statistical significant association between LS BMD and hip BMD with osteopenia and osteoporosis. Our statistical analysis results showed that patients' age during BMD measurements, diseases duration, treatment (corticosteroid) duration and dose of corticosteroid, were found to be highly correlated osteopenia and osteoporosis. Dose of corticosteroid (cumulative) dose was found to be significantly related with LS osteopenia, whereas duration of disease positively related

with LS osteoporosis. Also association between kidney disorder and LS osteoporosis were found to be statistically significant. The parameters which were significantly associated with osteoporosis and osteopenia were undergoing further statistical analysis to confirm the reliability and validity of the statistical model which have been used to detect association. Our repeat analysis was found that low bone mineral density was associated with development of JIA (Table 3). Also other variables which significantly affect the outcome were dose of corticosteroid therapy (cumulative), duration of diseases which are the key predictor of LS osteoporosis, LS osteopenia and BMD. Our results suggested that dose of corticosteroid therapy, and duration of diseases is strongly linked with LS osteoporosis, LS osteopenia and low BMD.

Table 1. *Demography and clinical characteristics.*

	Total juvenile idiopathic arthritis (N=120)	**Subjects with osteopenia (N=60)**	**Subjects with osteoporosis (N=30)**	**Subjects with Hip MBD less than 80% (N=30)**
Age at baseline (y), Mean (SD)	14.09 (3.95)	15.81 (4.22)	14.27 (4.28)	14.64 (11.01)
Race (%)				
White	0	0	0	0
Other	0	0	0	0
Asian-Chinese	100	100	100	100
BMI at baseline (kg/m^2), Mean (SD)	23.21 (3.38)	23.94 (3.50)	22.59 (3.16)	24.39 (4.55)
Disease duration (years), Mean (SD)	4.16 (1.37)	4.31 (1.17)	5.05 (1.24)	4.65 (0.36)
Previous vertebral fracture at baseline (%)	62.4	56	58.3	63.6
Previous non-vertebral fracture at baseline (%)	47.2	49.5	45.8	45.5
Previous osteoporosis medication at baseline (%)	1.8	4.6	0	0
Medicines used (%)				
Mycofenolate	34	36	37	35
Cyclosporine	3	4	6	9
Azathioprine	52	63	71	66
NSAID	21	22	27	24
Duration of treatment, y (SD)				
Mycofenolate	2 (0.3)	2.3 (0.4)	2.3 (0.6)	1.5 (0.4)
Cyclosporine	1.2 (0.6)	1.8 (0.5)	1.2 (0.3)	1.3 (0.3)
Azathioprine	1.7 (0.4)	1.9 (0.9)	1.6 (0.7)	1.52 (0.8)
NSAID	2.3 (0.2)	1.2 (0.4)	1.4 (0.2)	1.42 (0.32)

Table 2. *Univariate analysis of outcome measures and correlation coefficients between key variables.*

Outcome	**P values**		**Pearson's correlation coefficients**		
	Subjects with osteopenia (N=60)	**Subjects with osteoporosis (N=30)**	**Outcome**	**Correlation coefficients**	**P value**
Age at the time of BMD measurement	0.0042	0.0042	Age during BMD measurement/duration disease	0.36	0.0023
Duration of diseases	0.0032	0.0021	Age during BMD measurement/Corticosteroid use	0.39	0.001
Corticosteroid use duration	0.012	0.02	Duration of disease/ Corticosteroid use	0.96	0.00043
Dose of corticosteroids (cumulative)	0.012	0.0022	-	-	-

Table 3. *Multivariate analysis between key variables.*

Outcome	P value	Final analysis
		Point estimates (95% CI)
LS BMD correlation *vs.* total corticosteroid dose	<0.05	1.24 (1.02-1.43)
LS BMD correlation *vs.* duration of disease	<0.05	1.20 (1.12-1.33)
Hip BMD correlation *vs.* total corticosteroid dose	<0.05	1.23 (1.32-1.23)
BMD correlation *vs.* duration of disease	<0.05	1.17 (1.32-1.43)

Conclusion

Our results suggested that osteopenia and osteoporosis are common in Chinese patients with JIA. Dose of corticosteroid therapy and duration of diseases is mainly associated with JIA as it strongly linked with LS osteoporosis, LS osteopenia and low BMD.

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Statement of Competing Interests

Authors' declare no conflict of interest.

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