

Prevalence of Osteoporosis in 100 Iraqi Patients with Systemic Lupus Erythematosus: A Case Control Study

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Abstract

Back ground: In recent years, survival of patients with systemic lupus erythematosus (SLE) has raised significantly so long-term complications, as osteoporosis, are currently of major importance.

Objective: To assess the prevalence of osteoporosis in Iraqi patients with SLE.

Patients and Methods: This case control study was conducted on 100 SLE patients and 100 healthy controls matched in age, sex, and body mass index. Bone mineral density (BMD) obtained at the lumbar spine (L1-L4) and right and left femurs using dual energy X-ray absorptiometry (DXA) machine (Dexxum). Osteoporosis was diagnosed according to WHO guidelines criteria for diagnosis of osteoporosis and Z-scores was used in premenopausal women and men younger than 50 years.

Results: Mean age of SLE patients was 32.01±10.14 years and 32.46±6.29 years in the control group. Females represented 91% of patients and 92% of controls. The mean BMI of patients was 27.41±6.04 kg/m² compared to 28.8±5.26 kg/m² of controls. There was no statistical significant differences between both groups in demographic characteristics (P>0.05). BMD at lumbar spine was significantly lower in SLE patients than controls (82(82%) vs 61(61%), p< 0.001, OR (95%CI): 3.04(1.59-5.81). Of those patients with low BMD, 46% had osteoporosis. Additionally, BMD at total femur was significantly lower in SLE patients than controls (59 (59%) vs 24(24%), p<0.001, OR (95%CI): 4.56(2.48-8.37). Of those patients with low BMD at total femur, 15 (15%) had osteoporosis. Multiple logistic regression analysis showed non-significant association between low BMD in SLE patients and various baseline characteristics (P>0.05).

Conclusions: Prevalence of osteoporosis in Iraqi patients with SLE was 46% at lumbar spine and 15 % at total femur. This may suggest to do early screening for low BMD in patients with SLE for early diagnosis and appropriate treatment.

Keywords: SLE, Osteoporosis, Dual x-ray absorptiometry, Bone mineral density

1. Introduction

Systemic lupus erythematosus (SLE) is a worldwide autoimmune disease characterized by immunological hyperactivity and multi-system organ damage which primarily is a disease of young women [1,2]. Osteoporosis is a systemic, asymptomatic, skeletal disease characterized by decreased bone density and changes in bone microarchitecture that reduce bone strength and increase fragility that predispose the bone to fracture risk [3,4].

SLE patients has increased serum TNF- α , IL-1 and IL-6. Also, the high homocysteine concentration and high levels of LDL oxidation products present in these subjects due to the inflammation process can also contribute to osteoporosis.[5]Prevalence of osteoporosis in SLE patients was reported between 4% and 22% [6].

Up to our knowledge there is no previous study on prevalence of osteoporosis in SLE among Iraqi patients. This study was designed to assess the prevalence of osteoporosis in a sample of Iraqi SLE women and to evaluate risk factors if present.

2. Patients and Methods

2.1. Patients

This case control study was conducted on 100 patients with SLE who were seen at the Rheumatology Unit, Department of Medicine in Baghdad Teaching Hospital from November 2012 to September 2013. The diagnosis of SLE was made by rheumatologist according to Revised American College of Rheumatology (ACR) Classification Criteria for SLE [7]. For comparative purposes, 100 healthy controls were selected from healthy individuals.

Patients eligible for inclusion in the study had SLE without overlapping with other inflammatory arthritis or connective tissue diseases. Also they had no other chronic diseases.

Data taken included: age, sex, duration of SLE, disease activity index measured by SLEDAI [8], history of fragility fracture, family history of fragility fracture, daily dietary calcium intake, history of lacking exercise, history of smoking and alcohol drinking, medication history of steroid & cytotoxic drugs taken.

2.2. Methods

Body mass index was calculated according to following formula [9]: $BMI = \text{Body weight (kg)} / [\text{Body height(m)}]^2$ for patients and controls. Complete blood count (CBC), erythrocyte sedimentation rate (ESR), serum calcium, serum phosphorus, serum alkaline phosphatase and serum creatinine, and anti-ds-DNA were measured in patients. Urine examination was done for measurement of protein, white blood cells, red blood cells and cellular casts. X-ray of lumbar spine and both hips were done for patients and controls.

Bone mineral density (BMD) obtained at the lumbar spine (L1-L4) and right and left femurs, using dual energy X-ray absorptiometry (DXA) machine (Dexxum). Osteoporosis was diagnosed according to WHO guidelines criteria for diagnosis of osteoporosis Z-scores should be used in premenopausal women, men younger than 50 years [15-18]. Osteoporosis: T score ≤ -2.5 standard deviations below the mean value of peak bone mass. Severe osteoporosis: T score ≤ -2.5 standard deviations below the mean value of peak bone mass plus the presence of at least one fracture. Osteopenia is a bone mineral density T score between -1 and -2.5 standard deviations below the mean value of peak bone mass. Normal bone density is a BMD less than 1 standard deviation below the mean value of peak bone mass. Z-scores of -2.0 or less is defined as BMD less than expected age and sex matched individuals.

Informed consent was obtained from each participant included in this study. Ethical approval was taken from the Ethics Committee of Medical Department, College of Medicine, Baghdad University.

2.3. Statistical analysis

Statistical software (SPSS V 18) was used for analysis. Descriptive statistics were presented as mean \pm standard deviation (SD) for continuous variables and as numbers and percentages (%) for categorical variables. Student's t test for independent 2 samples was used to compare means of continuous variables between patients and control groups. Chi square test was used to assess the significance of difference between categorical variables. Fisher's exact test was used alternatively when chi square couldn't be applied.

Odds ratio and the 95% confidence interval were calculated for categorical variables to estimate the risk value in between both groups. Multiple logistic regression analysis was performed using the low BMD level as dependent variable and the predictors were the age, female gender, disease duration, BMI, current smoking, positive exercise, daily dietary intake of calcium, disease activity, SLEDAI, PMHx of fracture, FHx of osteoporosis, Medications, ESR and Anti-dsDNA. Negative values of Beta (B) standardized coefficient indicated inverse correlation, positive values of B indicating direct correlation. Level of significance was set at $P < 0.05$ to be considered as significant difference or correlation.

3. Results

A total 100 SLE patients and 100 controls were enrolled in this study. The mean age of SLE patients was 32.01 ± 10.14 years and 32.46 ± 6.29 years in the control group. Females represented 91% of patients and 92% of controls. The mean BMI of patients was 27.41 ± 6.04 kg/m^2 compared to 28.8 ± 5.26 kg/m^2 of controls. There was no statistical significant differences between both groups in demographic ($P > 0.05$, Table 1).

In Table 2: BMD at spine was significantly lower in SLE patients compared to controls (82(82%) vs 61(61%), $p < 0.001$, OR (95%CI): 3.04(1.59-5.81). Of those patients with low BMD, 36% had osteopenia and 46% osteoporosis. In addition, BMD at total femur was significantly lower in SLE patients compared to controls (59 (59%) vs 24(24%), $p < 0.001$, OR (95%CI): 4.56(2.48-8.37). Of those patients with low BMD at total femur, 44 (44%) had osteopenia and 15 (15%) osteoporosis.

Multiple logistic regression analysis showed non-significant association between low BMD in SLE patients and various baseline characteristics ($P > 0.05$, Table 3).

Table 1. Demographic characteristics of 100 SLE patients and 100 controls

Variable	SLE (N=100)	Control (N=100)	P
Age (means \pm SD), years	32.01 \pm 10.14	32.46 \pm 6.29	0.71 [NS]
Female n.(%)	91 (91.0)	92 (92.0)	1.0 [NS]
BMI (mean \pm SD), kg/m^2	27.41 \pm 6.04	28.8 \pm 5.26	0.079 [NS]

[NS], $P > 0.05$ not significant; SD, standard deviation, BMI, body mass index; n, number.

Table 2: Bone mineral density measured by DXA in 100 SLE patients and 100 controls

BMD site	SLE patients =100	Controls=100	P	OR(95%CI)
Spine				
Normal n(%)	18 (18%)	40 (40%)	<0.001*	3.04(1.59-5.81)
Low n(%)	82(82%)	61(61%)		
Osteopenia n(%)	36 (36%)	43 (43%)		
Osteoporosis n(%)	46 (46%)	18 (18%)		
Total femur				
Normal n(%)	41(41%)	76 (76%)	<0.001*	4.56(2.48-8.37)
Low n(%)	59 (59%)	24(24%)		
Osteopenia n(%)	44 (44%)	22 (22%)		
Osteoporosis n(%)	15 (15%)	2 (2%)		

DXA, dual x-ray absorptiometry, SLE; systemic lupus erythematosus; OR, odd ratio; n, number; *p value significant.

Table 3: Multiple logistic regression analysis for association of low BMD in 100 SLE patients and baseline characteristics

Predictor	B	p	OR (95%CI)
Age	-0.030-	0.47	0.971 (0.89-1.05)
Female gender	0.561	0.73	1.753 (0.07-43.01)
Disease duration	0.108	0.17	1.114 (0.95-1.30)
BMI	-0.003-	0.96	0.997 (0.89-1.11)
Current smoking	-0.544-	0.71	0.58 (0.03-10.02)
Positive Exercise	1.146	0.29	3.14 (0.38-26.04)
Daily dietary Calcium intake	1.094	0.38	2.98 (0.25-35.13)
Disease activity +ve	1.550	0.14	4.71 (0.58-37.80)
SLEDAI	0.098	0.13	1.10 (0.97-1.25)
PMHx fracture	0.333	0.76	1.39 (0.16-12.20)
FHx of OP	-23.798-	0.99	0.0 (0.0)
Drugs			
Corticosteroid use (ever)	-19.253-	1.0	0.0
Current prednisone dosage	0.046	0.14	1.04 (0.98-1.11)
Methylprednisolone (ever)	-1.019-	0.48	0.36 (0.02-5.98)

Anti-malarial (current)	-1.475-	0.22	0.23 (0.02-2.43)
Methotrexate (current)	-0.645-	0.35	0.53 (0.14-1.99)
MMF (current)	1.103	0.33	3.01 (0.33-27.19)
CYC (ever)	-0.319-	0.78	0.73 (0.08-7.03)
AZT (ever)	-1.22	0.14	0.30 (0.06-1.46)
Lab			
ESR	0.013	0.20	1.01 (0.99- 1.03)
Anti-dsDNA	0.320	0.68	1.38 (0.31- 6.15)

SLEDAI, systemic lupus erythematosus disease activity index; MMF, mycophenolate mofetile; CYC, cyclophosphamide; AZT, azathioprine; ds-DNA; double stranded deoxyribonucleic acid; BMI, body mass index, PMHX, past medical history; FHx, family history; ESR, erythrocyte sedimentation rate; anti-ds-DNA, anti ds-DNA; double stranded deoxyribonucleic acid

4. Discussion

Up to our knowledge this is the first case control study that assessed prevalence of osteoporosis in Iraqi patients with SLE and its risk factors. Interestingly, osteoporosis in lumbar spine was significantly more frequent in patients' group than controls (46% vs 18%). Additionally, osteoporosis in the total hip was significantly more in patients compared to controls (15 % vs 2%).

The increased prevalence of osteoporosis in SLE patients may be potentially linked to inflammatory mediators such as IL-6, IL-1, and TNF- α that can promote bone resorption [10]. In addition, there may be other factors predisposing to lower BMD, such as premature menopause, menstrual irregularity, sun avoidance leading to reduced vitamin D, reduced physical activity, amenorrhea in SLE patients, and corticosteroids [11]. Recently, the systemic effect of proinflammatory bone-resorbing cytokines has been considered a disease-dependent mechanism for osteoporosis that is independent of other risk factors [12].

Previous studies have reported variable figures for prevalence of osteoporosis in SLE. Uaratanawrong et al [13] demonstrated that prevalence of osteoporosis was 48% at lumbar spine (LS) and 3% at femoral neck. Other authors reported prevalence of osteoporosis was 1% to 23% [14, 15] among SLE patients.

Possible explanation for this differences may be related to racial differences and more inadequate vitamin D in our patients due to sun avoidance.

In this study, osteopenia observed in SLE patients was 36% at LS and 44 % at total hip which is within the range of other studies ((25–50%) [16, 17].

In the current study, multiple logistic regression analysis for predictors of low BMD in SLE patients showed non-significant relationship between the factors taken and low BMD. There was non-significant relationship between corticosteroids (CS) use and BMD which was unexpected finding. This may be explained by the smaller number of patients and limited follow up duration in our study. Previous studies reported controversial findings. Li et al [7] reported no association between BMD and CS dose or duration of treatment in Hong Kong Chinese. Other studies [18,19] reported no relationship between CS intake and BMD and suggested that SLE disease per se lead to the low BMD.

In contrast, Uaratanawong et al [13] showed a relationship between cumulative CS dose and LS BMD in Thai SLE patients. Also Jacob et al [11] reported significant low BMD was associated with CS use.

Additionally, we did not find a significant relationship between SLE disease activity measured by the SLEDAI and dietary calcium intake with low BMD. Possibly due to good control of disease activity and dietary calcium intake. Similar finding was showed by Jacobs et al study [20].

This study has some limitations: first, small sample size and short period time of the study. Second, we did not measure serum vitamin D in our patients for ethical reasons and unavailability in our hospital at that time. Despite these limitations, our findings call the importance of attention to early detection and treatment of the high prevalence of osteoporosis in SLE patients which is a well-recognized major public health problem associated with high morbidity, mortality, and health care cost.

5. Conclusions

Prevalence of osteoporosis in a sample of Iraqi patients with SLE compared to controls at LS and at total hip was increased. There was non-significant relationship between factors taken and low BMD. Larger prospective study may be needed to confirm the finding in this study and early follow up of SLE patients by DXA for early diagnosis and appropriate treatment of osteoporosis.

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