Evaluation of bone mineral density and vitamin D in patients with systemic lupus erythematosus and their relation to disease activity

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Background
Systemic lupus erythematosus (SLE) is a chronic autoimmune disorder that affects multiple systems and is associated with an inflammatory status. The aim of our study is to estimate the serum level of vitamin D and bone mineral density (BMD) in SLE patients and their relation to disease activity.

Patients and methods
Ninety SLE patients, fulfilling the updated American College of Rheumatology criteria 2012 and 60 age-matched and sex-matched controls were included in this study. The level of serum 25-hydroxyvitamin D (25(OH)D3) and dual-energy radiograph absorptiometry were done for patients and controls.

Results
There was significant difference between systemic lupus erythematosus disease activity index (SLEDAI) score and vitamin D (P<0.02). There were significant difference (P<0.01) between SLE and control with BMD of total lumbar (L1–L4) and total hip and highly significant difference (P<0.001) with neck of the femur, Ward's angle of the femur, trochanter of the femur, and the radius. There was significant difference (P<0.05) between SLE and control groups regarding T score of lumbar spine (L1–L4) (P<0.03), neck of the femur (P<0.01), and total hip bone (P<0.02). Our results showed that there was significant difference between SLEDAI score and T score of neck of the femur (P<0.02) and radius bone (P<0.012), while there was no significant difference between SLEDAI score and T score of total hip, lumbar spine (L1–L4), Ward's angle of the femur, and the trochanter of the femur.

Conclusion
Vitamin D deficiency and low BMD are common in SLE patients. There was significant difference between SLE patients and control group regarding vitamin D, BMD, and T score at different sites.

Keywords:
bone mineral density, disease activity score, systemic lupus erythematosus, vitamin D

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Introduction

Systemic lupus erythematosus (SLE) is a chronic autoimmune disorder affecting multiple systems and associated with an inflammatory status. The exact cause is unknown but may be due to interaction between genetic, ethnic, immunological, endocrine, environmental factors, and medications [1,2]. Osteoporosis is considered a common presentation in SLE patients although that there has been a great improvement in survival rate and quality of life of these patients [3]. There are multiple causes for bone loss which might be disease related or nondisease related, for example, age, white ethnicity, low BMI, and postmenopausal women. Disease-related causes are due to systemic inflammation which increases osteoclastic bone resorption and reduces osteoblastic bone formation [4–6]. Disease-related causes might be longer SLE disease duration, organ damage, markers of inflammation, renal failure, medications such as glucocorticoids, azathioprine, cyclophosphamide, and cyclosporine [7,8].

Furthermore, due to photosensitivity patients avoid sunshine exposure which has a role in the change of 7-dehydrocholesterol into previtamin D_3 in the skin, by the ultraviolet B radiation. This is considered the main source of vitamin D, though just a smaller amount is acquired from food [9], hence adding to diminished

bone mass [10]. The impact of vitamin D on dendritic cells is especially important in autoimmunity. Vitamin D causes inhibition of differentiation of T helper 1 lymphocytes, stimulation of T-regulatory cells, and reduction of the production of autoantibodies and the release of inflammatory mediators [11–13]. There are evidence that vitamin D has a role in SLE pathogenesis by suppressing the expression of 'interferon signature' [14].

Frequently pain caused by vitamin D deficiency might be ignored in these patients disregarding having multiple risk factors for its occurrence [15]. Hydroxychloroquine, which is a medication commonly used in SLE, is suspected to decrease vitamin D_2 conversion into the more biologically active vitamin D_3 [16]. SLE could cause bone loss through disease-related causes or medications. Disease-related causes are similar to vitamin D including reduced physical activity because of long-standing handicapping arthritis or myopathy, renal failure, endocrine dysfunctions, and the systemic effects of proinflammatory bone-resorbing cytokines [10].

So, the aim of our study is to estimate serum vitamin D and bone mineral density (BMD) in SLE patients and their relation to disease activity.

Patients and methods

A cross-sectional study was conducted at Assiut University Hospital from January 2018 to September 2018 on 90 SLE patients, fulfilling the updated American College of Rheumatology criteria 2012 [17]. The patients were selected from inpatients of Rheumatology and Rehabilitation Department and outpatients clinics. A total of 60 age-matched and sex-matched healthy individuals were also included in this study and served as the control group. All patients gave informed written consent and the study was approved by Ethics Medical Committee of xxxxx according to the guidelines of the Helsinki Declaration (IRB number: 17200361). Study was approved by Ethical Medical Committee of Assiut University Hospitals, Assiut, Egypt according to the guidelines of the Helsinki Declaration.

Exclusion criteria were patients aged less than 18 years and patients with diseases that alter bone metabolism (endocrinopathies, liver disease, end-stage renal disease, malignant hematopoietic diseases, bone tumors, and bone metabolism modifying treatments). We also excluded patients who had avascular necrosis of the hip, vertebral fractures caused by high-velocity injuries and diabetes.

Data collection

All SLE patients were subjected to full medical history including thorough clinical evaluation and examination including age, sex, BMI, disease duration, age of onset of disease, history of fever, fatigue, malar rash, photosensitivity, discoid rash oral ulcers, alopecia, arthritis, arthralgia, myositis, myalgia, pleuritis, pericarditis, vasculitis, thrombosis, seizures, psychosis, headache, convulsions, stroke, and other organ involvement. Also taken into consideration are duration and daily doses of medications including glucocorticoids, other medications used in the treatment of SLE (hydroxychloroquine, azathioprine, methotrexate, cyclophosphamide).

Disease activity of SLE patients was assessed by the systemic lupus erythematosus disease activity index (SLEDAI score). Categories were assessed as mild activity 0–10, moderate activity more than 10–20, and severe activity more than 20–30.

Laboratory investigations for lupus subjects included: erythrocyte sedimentation rate, creative protein, complete blood picture, kidney and liver function tests, urine analysis, 24 h proteins, antinuclear antibodies, anti-dsDNA, C3, C4.

Bone metabolites in the SLE group were assessed including total serum calcium, alkaline phosphatase, and phosphorus.

Measurements of serum level of total 25-hydroxyvitamin D level

The level of serum 25-hydroxyvitamin D (25(OH) D) level was quantitatively measured by enzyme-linked immunosorbent assay in serum (Epitope Diagnostics Inc., San Diego, California, USA) for all subjects included in SLE and control group as follows:

(1) Vitamin D severe deficiency if the serum level of 25(OH)D level is less than 10 ng/ml.
(2) Vitamin D insufficiency if the serum level of 25(OH)D level is between 10 and 30 ng/ml.
(3) Normal range of vitamin D if the serum level of 25(OH)D level is more than 30 ng/ml.

Assessment of bone mineral density for all subjects included in the systemic lupus erythematosus group

BMD (g/cm^2) was assessed both on the anteroposterior and lateral views of the total lumbar spine (vertebrae L1–L4), neck of the femur, Ward's angle of the femur, trochanter of the femur, total hip, and radius bone with dual-energy radiograph absorptiometry using a DPX-Alpha (Lunar-General Electric Device, Ge Medical Systems Lunar 3030 Ohmeda Madison Company, Wisconsin, USA, Model 7661). Bone mass was expressed using *T* score

According to WHO criteria [18]:
(1) Osteoporosis was defined as *T* score less than −2.5.
(2) Osteopenia defined as T score from − 1.5 to <2.5.
(3) Normal more than −1.0.

Statistical analysis

Data were collected and analyzed using the Statistical Package for the Social Sciences, version 20 (IBM Corp., Armonk, New York, USA). Continuous data were expressed in the form of mean ± SD or median (range), whereas nominal data were expressed in the form of frequency (%). χ^2 test was used to compare the nominal data of different groups in the study, whereas Student's *t* test was used to compare the mean of two different groups. Nonparametric Mann–Whitney test was used for quantitative variables which are not normally distributed. Pearson's correlation was done to test for linear relations between quantitative variables and if *r* more than 0.2 indicates nil correlation, 0.2: 0.4 indicates mild correlation, 0.4: 0.6 indicates moderate correlation, 0.6: 0.9 indicates strong correlation, and 1 indicates perfect correlation. *P* value was significant if less than 0.05.

Results

Ninety SLE patients and 60 age-matched and sex-matched controls were included in this study. Out of the 90 SLE patients; there were 78 (86.6%) women (only 12 of them were postmenopausal) and there were 12 men. As for the control group, it included 48 (80.0%) women (of which nine were postmenopausal) and 12 men. The mean age of the SLE group patients was 37.43 ± 7.82 years, which was nonsignificantly different from that of the control group (36.55 ± 5.920 years). As regards BMI of the SLE group 39 (43.3%) were underweight, 30 (33.3%) were normal, nine (10%) were overweight, and 12 (13.3%) were obese. However, there was no significant difference between both groups as regards age, sex, or BMI.

Table 1 shows the clinical, laboratory, and therapeutic characteristics of the SLE group.

Table 2 shows the comparison of the serum level of vitamin D in SLE and control groups. There was significantly lower mean value of serum vitamin D in the SLE group 22.99 ± 10.27 versus 32.06 ± 14.06 in the control group ($P < 0.01$). Moreover, there was a higher percentage of patients with deficient vitamin D in the SLE group (56.7%) versus 25.0% in the control group with highly significant difference ($P < 0.001$).

Our results showed no detected significant difference between vitamin D level and age, sex, BMI, disease duration, or medications used for the treatment of SLE including steroids, azathioprine, methotrexate, cyclophosphamide, and hydroxychloroquine ($P > 0.05$).

Fig. 1 shows the relationship between vitamin D level and the different clinical manifestations of the disease, whereas there was significant difference ($P < 0.05$) between the level of vitamin D and photosensitivity and seizures. However, there was no significant difference ($P < 0.05$) between the level of vitamin D and other clinical manifestations of the disease.

Table 1 Clinical, laboratory, and therapeutic characteristics of the systemic lupus erythematosus group

Item	SLE group (*n*=90)
Disease duration (years)	
Mean±SD	4.30±2.57
Range	0.5-9
≤1	12 (13.3)
>1 and ≤5	51 (56.7)
>5 and ≤10	27 (30.0)
>10	
SLEDAI score	16.10±7.35
Mild 0-10	18 (20)
Moderate >10-20	42 (46.7)
Severe >20-30	30 (33.3)
Presence of lupus nephritis	54 (60)
Medications	
Steroids	84 (93.3)
Duration of use (months)	36.55±4.89
Dose (mg/day)	32.03±20.62
Hydroxychloroquine	90 (100)
Azathioprine	90 (100)
Methotrexate	39 (43.3)
Cyclophosphamide	45 (50.0)
ESR (mm/h)	63.13±28.51
Creatinine clearance (mg/dl)	89.75±37.98
ANA	78 (86.7)
Anti-dsDNA	96.94±30.56
Serum calcium (mg/dl)	8.82±0.80
Serum phosphorus (mg/dl)	3.87±0.89
Alkaline phosphatase (IU/l)	22.06±12.05

Data are presented as mean±SD, range, or *n* (%). SLEDAI score, systemic lupus erythematosus disease activity index; ESR, erythrocyte sedimentation rate; ANA, antinuclear antibodies; anti-dsDNA, anti-double strands DNA antibody. Statistical significance is considered if *P*<0.05.

Table 2 Vitamin D level in systemic lupus erythematosus and control groups

Item	SLE group (*n*=90)	Control group (*n*=60)	*P*
Vitamin D (ng/ml)			
Mean±SD	22.99±10.27	32.06±14.06	<0.01*
Range	9.5-43.0	10.6-65.0	<0.001**
Deficient (<20 ng/ml)	51 (56.7)	15 (25.0)	
Insufficient (20-30 ng/ml)	12 (13.3)	15 (25.0)	
Normal (>30 ng/ml)	27 (30.0)	30 (50.0)	

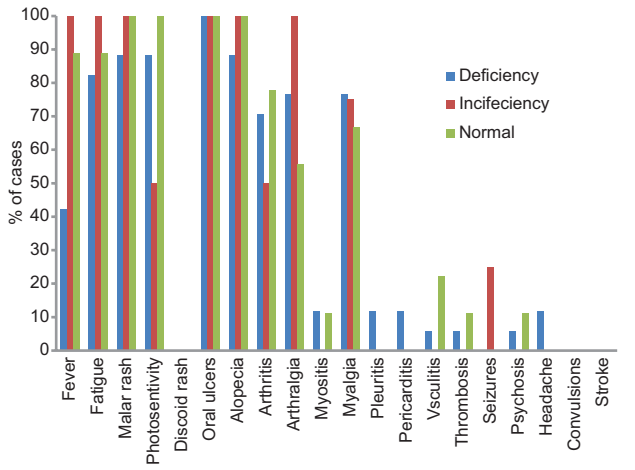
Data are presented as mean±SD, range, or *n* (%). SLE, systemic lupus erythematosus. Statistical significance is considered if *P*<0.05.

Table 3 Relationship between systemic lupus erythematosus disease activity index score and vitamin D

Item	SLEDAI score			*P*
	Mild (0-10) (*n*=18)	Moderate (>10-20) (*n*=42)	Severe (>20-30) (*n*=30)	
Vitamin D				
Deficient (<20 ng/ml)	9 (50.0)	24 (57.1)	18 (60.0)	<0.02*
Insufficient (20-30 ng/ml)	6 (33.3)	0	6 (20.0)	
Normal (>30 ng/ml)	3 (16.7)	18 (42.9)	6 (20.0)	

Data were presented as *n* (%). SLEDAI score, systemic lupus erythematosus disease activity index. Statistical significance is considered if *P*<0.05.

Figure 1



Relation between vitamin D level and clinical manifestations of the disease.

Table 3 shows the relationship between SLEDAI score and vitamin D where there was significant difference between them ($P < 0.02$). This indicates that with any significant increase in SLEDAI score, there is associated significant increase in the number of patients presented with vitamin D deficiency.

Table 4 shows the comparison between the mean value of BMD between the SLE and the control group. There were significance differences ($P < 0.01$) between SLE and control with BMD of total lumbar (L1–L4) and total hip and highly significant difference ($P < 0.001$) with neck of the femur, Ward's angle of the femur, trochanter of the femur, and radius.

There was significant difference ($P < 0.05$) between the SLE and control groups regarding the *T* score of lumbar spine (L1–L4) ($P < 0.03$), neck of the femur ($P < 0.01$), and total hip bone ($P < 0.02$).

Moreover, there was highly significant difference between the two groups regarding *T* score of Ward's angle of femur ($P < 0.006$), trochanter of the femur ($P < 0.007$), and the radius bone ($P = 0.005$).

Table 5 shows *T* score in SLE and control groups. There were significance difference ($P < 0.05$) between SLE and control groups with *T* score of total lumbar (L1–L4), neck of the femur and total hip and highly significant difference ($P < 0.001$) of Ward's angle of the femur, trochanter of the femur and radius. All cases (100%) in the control group were normal regarding the *T* score of neck of the femur, Ward's angle of the femur, trochanter of the femur, and total hip.

Our results showed that there was significant difference between SLEDAI score and *T* score of neck of the femur ($P < 0.02$) and the radius bone ($P < 0.012$) while there was no significant difference between SLEDAI score and *T* score of total hip, lumbar spine (L1–L4), Ward's angle of the femur, and the trochanter of the femur as shown in Table 6.

There was negative correlation between *T* score of total lumbar with vitamin D ($P < 0.05$). There was mild positive correlation between vitamin D and hemoglobin ($P < 0.05$, $r = 0.38$).

There were no correlation between vitamin D and SLEDAI with BMD of total hip, BMI of total lumbar L1–L4, BMD of Ward's angle of the femur, BMD of trochanter of the femur, and BMD of radius. Also, there was no correlation between each of vitamin D and SLEDAI score with *T* score of total hip, *T* score of total lumbar (L1–L4), *T* score of Ward's angle of the femur, *T* score of trochanter of the femur, and *T* score of radius.

Our results showed that there was correlation between both the duration and doses of corticosteroids with other variables included in our SLE group. There were strong negative correlations between the duration of steroids used with BMD of the total hip bone ($P < 0.05$, $r = 0.83$), *T* score of Ward's angle of the femur ($P < 0.05$, $r = 0.74$), *T* score of the radius bone ($P < 0.05$, $r = 0.79$), between the doses of steroid used with BMD of total hip bone ($P < 0.05$, $r = 0.77$), and *T* score of lumbar spine (L1–L4) ($P < 0.05$, $r = 0.77$), while there were moderate negative correlations between the duration of steroid used with BMD of lumbar spine (L1–L4) ($P < 0.05$, $r = 0.48$), BMD of neck of the femur ($P < 0.05$, $r = 0.58$), BMD of the radius bone ($P < 0.05$, $r = 0.54$), *T* score of lumbar spine (L1–L4) ($P < 0.05$, $r = 0.58$), between the doses of steroid used with BMD of

Ward's angle of femur ($P < 0.05$, $r = 0.47$), BMD of trochanter of femur ($P < 0.05$, $r = 0.47$), and *T* score of lumbar spine (L1–L4) ($P < 0.05$, $r = 0.59$). Finally, there were mild negative correlations between the duration of steroid used with BMD of Ward's angle of femur ($P < 0.05$, $r = 0.37$), BMD of trochanter of the femur ($P < 0.05$, $r = 0.27$), *T* score of neck of the femur ($P < 0.05$, $r = 0.27$), between the doses of steroid used with *T* score of neck of the femur ($P < 0.05$, $r = 0.27$), T score of the radius bone ($P < 0.05$, $r = 0.27$).

Table 4 Bone mineral density in systemic lupus erythematosus and control groups

BMD	SLE group (*n*=90)	Control group (*n*=60)	*P*
Total lumber (L1-L4)			
Mean±SD	1.02±0.03	1.15±0.02	<0.01*
Range	0.23-1.34	0.84-1.32	
Neck of the femur			
Mean±SD	0.93±0.03	1.09±0.02	<0.003**
Range	0.32-1.43	0.92-1.28	
Ward's angle of the femur			
Mean±SD	0.818±0.04	1.02±0.02	<0.002**
Range	0.19-1.45	0.77-1.28	
Trochanter of femur			
Mean±SD	0.72±0.03	0.85±0.3	<0.002**
Range	0.14-1.19	0.30-1.0	
Total hip			
Mean±SD	0.73±0.18	0.85±0.13	<0.01*
Range	0.14-1.19	0.30-1.00	
Radius			
Mean±SD	0.43±0.02	0.52±0.01	<0.002**
Range	0.08-0.58	0.40-0.65	

Data are presented as mean±SD, range, or *n* (%). BMD, bone mineral density; SLE, systemic lupus erythematosus.

Table 5 *T* score in systemic lupus erythematosus and control groups

T score	SLE group (*n*=90)	Control group (*n*=60)	*P*
Total lumbar (L1-L4)	−1.24±0.24	−0.47±0.22	<0.03*
Osteoporosis	21 (23.3)	3 (5.0)	
Osteopenia	21 (23.3)	3 (5.0)	
Normal	48 (53.3)	54 (90.0)	
Neck of the femur	−0.353±0.31	0.675±0.17	<0.01*
Osteoporosis	3 (3.3)	0	
Osteopenia	21 (23.3)	0	
Normal	66 (73.3)	60 (100)	
Ward's angle of the femur	−0.70±0.36	0.69±0.21	<0.006**
Osteoporosis	12 (13.3)	0	
Osteopenia	30 (33.3)	0	
Normal	48 (53.3)	60 (100)	
Trochanter of femur	−0.65±0.32	0.52±0.15	<0.007**
Osteoporosis	6 (6.7)	0	
Osteopenia	33 (36.7)	0	
Normal	51 (56.7)	60 (100)	
Total hip	−0.73±0.53	0.25±0.02	<0.02*
Osteoporosis	24 (26.67)	0	
Osteopenia	24 (26.67)	0	
Normal	42 (46.67)	60 (100)	
Radius	−0.78±0.41	0.89±0.30	<0.005**
Osteoporosis	18 (20.0)	0	
Osteopenia	12 (13.3)	6 (10.0)	
Normal	60 (66.7)	54 (90.0)	

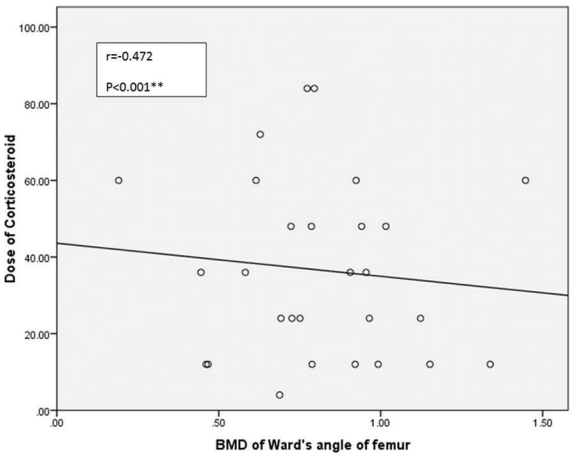
Data are presented as mean±SD, range, or *n* (%). SLE, systemic lupus erythematosus. Statistical significance is considered if *P*<0.05.

Correlations between dose of steroids with BMD of Ward's angle of the femur is shown in Fig. 2, while correlation between duration of steroids and *T* score of total lumbar and trochanter of femur are shown in Figs. 3 and 4.

Discussion

Vitamin D is considered a liposoluble steroid hormone with an important role in calcium and phosphorus metabolism, and bone homeostasis [19,20]. There is a big variation in the prevalence of vitamin D deficiency in SLE patients ranging from 8 to 98% [21–25]. This variation might be due to age or fear of sunlight exposure [26]. Our study showed that vitamin D was deficient in 56.7%, insufficient in 13.3%, and normal in 30% of SLE patients with highly significant difference with controls. This might be due to that none of our patients had received vitamin D supplementation. These results are in accordance with some studies which found that the percentage of SLE patients who were 25(OH) D deficient or insufficient was between 65 and 77% [21,27,28]. Other studies done in Saudi Arabia, Norway, and Poland found that the frequency of 25(OH) D deficiencies among patients with SLE was 89.7, 82, and 71%, respectively [23–25]. A study done in Serbia found that all patients had low vitamin D levels: 32.6% patients with insufficiency and 67.4% of patients with deficiency [29].

Figure 2



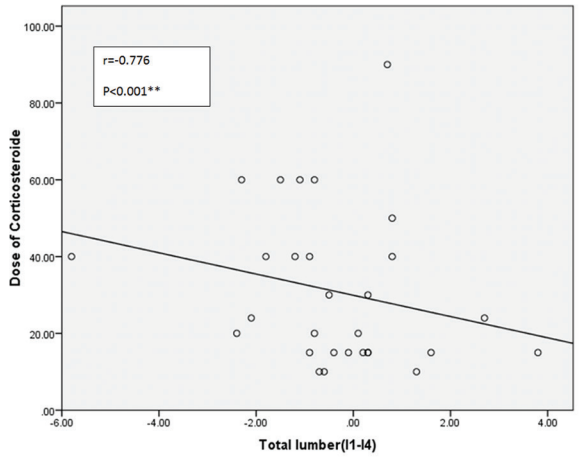
Correlation between dose of steroids and BMD of Ward's angle of femur in the SLE group. BMD, bone mineral density; SLE, systemic lupus erythematosus.

Table 6 Relationship between systemic lupus erythematosus disease activity index score and *T* score

T score	SELDAI score			*P*
	0-10 (*n*=18)	>10-20 (*n*=42)	>20-30 (*n*=30)	
Total lumber (L1-L4)				
Osteoporosis	3 (16.7)	3 (7.1)	15 (50.0)	0.159
Osteopenia	3 (16.7)	12 (28.6)	6 (20.0)	
Normal	12 (66.7)	27 (64.3)	9 (30.0)	
Neck of the femur				
Osteoporosis	0	0	3 (10.0)	<0.02*
Osteopenia	0	9 (21.4)	12 (40.0)	
Normal	18 (100)	33 (78.6)	15 (50.0)	
Ward's angle of the femur				
Osteoporosis	3 (16.7)	3 (7.1)	6 (20.0)	
Osteopenia	6 (33.3)	15 (35.7)	9 (30.0)	
Normal	9 (50.0)	24 (57.1)	15 (50.0)	
Trochanter of femur				
Osteoporosis	0	0	6 (20.0)	0.478 (NS)
Osteopenia	9 (50.0)	12 (28.6)	12 (40.0)	
Normal	9 (50.0)	30 (71.4)	12 (40.0)	
Total hip				
Osteoporosis	3 (16.7)	15 (35.71)	6 (20.0)	0.227
Osteopenia	6 (33.33)	9 (21.42)	9 (30.0)	
Normal	9 (50.0)	18 (42.85)	15 (50.0)	
Radius				
Osteoporosis	0	6 (14.3)	12 (40.0)	<0.012*
Osteopenia	9 (50.0)	0	3 (10.0)	
Normal	9 (50.0)	36 (85.7)	15 (50.0)	

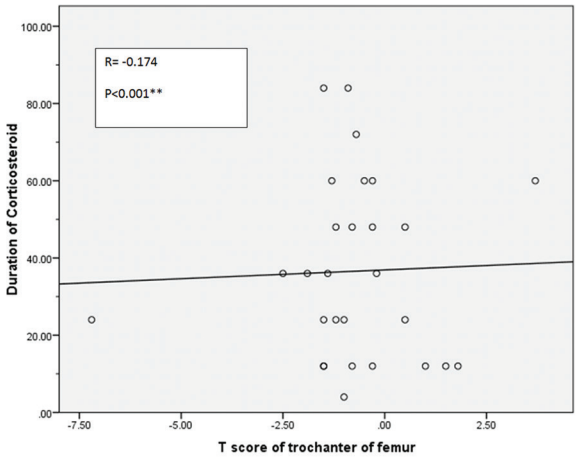
Data are presented *n* (%). SLEDAI score: systemic lupus erythematosus disease activity index. Statistical significance is considered if *P*<0.05.

Figure 3



Correlation between dose of steroids and *T* score of total lumbar (L1–L4) in the SLE group. SLE, systemic lupus erythematosus.

Figure 4



Correlation between duration of steroids and *T* score of trochanter of femur in the SLE group. SLE, systemic lupus erythematosus.

Abaza *et al.* conducted a study on Egyptian patients and reported that the prevalence of vitamin D insufficiency was 73% and deficiency in 23% [30]. Another study also on Egyptian patients by Abou-Raya *et al.*[31] reported that the prevalence of deficient vitamin D serum levels among patients with SLE was 69%.

Some authors reported much low rates in Canada (18%), Hong Kong (27%), United States (20%), and Spain (15%) [27,28,32,33].

An investigation on the recently diagnosed SLE patients reported that vitamin D deficiency is considered a possible risk factor for development of the disease. This short disease duration in that study suggested that vitamin D deficiency could be a cause rather than a consequence. Because of these investigations looking at a potential role for vitamin D in the prevention and/or treatment of SLE diagnosed SLE patients suggested that vitamin D deficiency is considered a possible risk factor for development of

the disease. This short disease duration in that study suggested that vitamin D deficiency could have a role in the etiopathogenesis of SLE[28].

Our study showed that the mean serum concentration of vitamin D was 22.99 ± 10.27. This is similar to Kamen *et al.*[21] who reported that mean serum 25(OH) D concentration was 21.6 ng/ml in SLE patients. A study done on Egyptian patients reported that the mean of vitamin D was 17.6 ± 6.9 with highly significant difference with controls [30]. On the other hand another two studies found that the mean serum concentration was 11.9 [29,34].

As regards the relation between vitamin D and SLEDAI score our study showed significant difference between them ($P < 0.02$). This is in accordance with other cross-sectional studies [9,30,32,35–41]. This might be due to the inhibitory effect of vitamin D on T helper 1 immunity and autoantibodies production [42]. On the other hand, other authors reported absence of correlation between 25(OH)D level and disease activity scores [27,28,43–46].

We found no significant correlation between disease duration and vitamin D deficiency. This is in accordance with other authors [27–30,33,47]. This might be explained by the fact that vitamin D status is affected more by disease activity and by applied therapy, rather than disease duration [29]. A study conducted in Saudi Arabia reported that there was significant correlation between disease duration and vitamin D deficiency [48].

Our results showed no detected significant difference between vitamin D level and medications used for the treatment of SLE including corticosteroids, azathioprine, methotrexate, cyclophosphamide, and hydroxychloroquine ($P > 0.05$). Some authors found correlation between vitamin D and corticosteroids [30,40,49–51].

Steroids might result in altered metabolism of vitamin D. It was reported that 25(OH) D_3 has been reduced in patients with rheumatoid arthritis treated with corticosteroids [52]. Some authors found that patients on antimalarial treatment had higher levels of vitamin D [28,51]. This was explained by the fact that hydroxychloroquine inhibits t1α-hydroxylation of 25(OH) D, thus decreasing the levels of the most active form of vitamin D [53]. Other authors found no correlation between vitamin D and hydroxychloroquine [29,54].

Our results showed that there were significance differences ($P < 0.01$) between SLE and controls with BMD of total lumbar (L1–L4) and total hip and highly significant difference ($P < 0.001$) with neck of the femur, Ward's angle of the femur, trochanter of the femur, and radius. This is similar to other authors who have reported a low BMD in SLE patients with significant difference compared with controls [7,10,55–57].

There were significance differences ($P < 0.05$) between SLE and control groups with *T* score of total lumbar (L1–L4), neck of the femur and total hip and highly significant difference ($P < 0.001$) of Ward's angle of the femur, trochanter of the femur, and radius. Osteopenia is seen at trochanter of femur (36.7%), Ward's angle of femur (33.3%), total hip (26.67%), neck of femur (23.3%), and total lumbar (23.3%), while osteoporosis was more seen at total hip (26.67%), total lumbar (23.3%), and radius (20%).

Mori *et al.*[58] reported that *T* score below −2.5 was higher at lateral lumbar spine compared with anteroposterior spine, total hip, and femoral neck. This was also reported by other authors [59–61].

We found osteoporosis at all sites, we assessed *T* score reaching up to 26.67%. A much lower percentage (up to 8.9%) was found in a study in Spain [56], China [62], United Kingdom [57], and Malaysia [36]. Also a higher percentage was found by other authors reaching up to 36% [62–65].

While we found osteopenia and osteoporosis at the femur and hip more than the total lumbar others reported that osteopenia and osteoporosis were found more at the lumbar spine compared with the hip [5,62,64–67]. The reasons for this discrepancy are unclear but may be due to variations in the type of bone architecture comprising these two anatomic sites [68].

Our results showed that there was significant difference between SLEDAI score and *T* score of neck of the femur ($P < 0.02$) and radius bone ($P < 0.012$), while there was no significant difference between SLEDAI score and *T* score of total hip, lumbar spine (L1–L4), Ward's angle of the femur, and the trochanter of the femur. This is in accordance with Lee *et al.* [69], Zhang *et al.* [70], and Barbulescu *et al.* [66]. This might be due to the inflammatory status and its effect on the bone. On the other hand, García-Carrasco *et al.*[2] and Sinigaglia *et al.*[10] and others [56,62,71,72] found no significant correlation between disease activity and BMD. The reason probably is that indexes used to evaluate disease activity are only measured at one point in time and different disease durations.

Glucocorticoids are considered the cornerstone for treatment of SLE patients and improve survival rate, quality of life, and also promote osteoporosis by inhibiting osteoblasts, especially in sites rich in

trabecular bone, as the lumbar spine [73]. Our results showed that there was negative correlation (strong, moderate, or mild) between dose or duration of corticosteroids with all aspects of BMD or *T* score. This is consistent with a study by Sun *et al*. [62], who reported a significant negative correlation between low BMD at the lumbar spine and at total hip. These findings were also consistent with two large population studies in Indian and Canadian populations [74,75]. A study by Jacobs *et al*.[8] reported a correlation between bone loss and use of corticosteroids in a 6-year follow-up of SLE patients. A study performed recently on patients with SLE in United States, treated with low-dose glucocorticoids with low disease activity had normal bone density [37]. Several studies, including large or small cohorts, reported no effect of corticosteroid therapy on bone loss in patients with SLE [8,76].

We found no significant correlation between disease duration and BMD. This is inconsistent with studies performed in China, Spain, and the United States, who found no correlation of disease duration and BMD [56,62,75]. On the other hand Mori *et al*.[58] reported negative correlation between disease duration and BMD in a group of patients not treated with bisphosphonate, but in the other group who was treated with bisphosphonate these negative correlations were not present.

Conclusion

Vitamin D deficiency and low BMD are common in SLE patients. There was significant difference between SLE patients and control group regarding vitamin D, BMD, and *T* score at different sites. There was significant correlation of serum vitamin D, *T* score, and BMD with SLEDAI at most sites.

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Conflicts of interest

There are no conflicts of interest.

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