Original Article

Predictors of Reduced Bone Mineral Density in Juvenile Systemic Lupus Erythematosus.

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ABSTRACT

Introduction: One of the juvenile Systemic Lupus Erythematosus (j-SLE) consequences that lower patients' quality of life is low bone mineral density (BMD). By employing DXA (dual X-ray absorptiometry), BMD is evaluated. This study's objectives are to research BMD in SLE children and to describe the predicting factors.
Methods: A case control study included 30 SLE patients (the SLE group) (mean age, 14.8± 2.5 years; females, 83.3%) and 30 age and sex-matched, seemingly healthy children (the Control group). They had a thorough medical history and clinical examination, as well as laboratory tests, 25(OH) vitamin D levels, and BMD evaluation by DXA scan (scores at L2-L4). The information was presented as mean and standard deviation. The Pearson's correlation and the student t-test were used for statistical analysis. At a p value of 0.05, differences were deemed statistically significant.
Results: Low BMD was detected in the SLE group in comparison to the controls ($p<0.001$). Reduced BMD was detected in 46.6% of patients. Vitamin D level is lower in SLE group with statistically significant difference. On regression analysis; duration of disease, steroid use, and alkaline phosphatase were found to be independent variables that affected BMD.
Conclusion: SLE patients frequently have low BMD. A longer course of the illness, and higher overall glucocorticoid dose were powerful predictors of low BMD. The patients may be protected from the possibility of decreased BMD by DXA monitoring and the implementation of an appropriate therapy plan.

Key words: Bone mineral density; Systemic lupus erythematosus; dual X-ray absorptiometry

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INTRODUCTION

Juvenile Systemic lupus erythematous (j-SLE) is an uncommon but severe multisystemic disease with autoimmune/inflammatory base beginning before the age of 18. Having a relapsing and remitting nature, and causing anything from mild to potentially fatal disease, it is a highly complicated disease with substantial patient heterogeneity [1].

With a prevalence of 1.89-34.1 per 100,000 children, the estimated incidences of SLE vary from 0.36 to 2.5 per 100,000 children [2]. The peak age of onset is at 12.6 years [3]. Girls and young women are more likely to develop the condition (4.7–5.6:1), albeit the female preponderance is less obvious in children than it is in adults [4].

One of the most prevalent side effects of SLE is osteoporosis (OP) [5]. Increased knowledge of changes in bone metabolism and other variables that contribute to enhanced fracture risk and increased bone loss has been demonstrated in subgroups of individuals with certain systemic inflammatory connective tissue diseases throughout the past few decades [6].

According to studies, people with SLE are more likely to experience decreased bone mineral density [7]. Rates for osteopenia and OP in juvenile lupus were 37.5% and 20.3%, respectively [8]. The causes of bone loss in SLE are diverse and may include systemic inflammatory, hormonal, metabolic, and serological variables, as well as possible hereditary and drug-related factors [9, 10]. Currently, BMD examination by dual-energy X-ray absorptiometry (DXA) is considered the gold standard in clinical practice when it comes to OP diagnosis, including secondary reasons [11].

METHODS

Study design: This is a case control study, conducted in the pediatric nephrology unit and radiology department of Zagazig University hospitals over a period of 6 months. It included sixty children, divided in 2 groups:

Case group: included thirty SLE patients, aged up to 18 years, who were diagnosed, and followed up in pediatric nephrology unit and outpatient clinic. All patients fulfilled the American College of Rheumatology (ACR) revised criteria for SLE diagnosis [12].

Control group. This group comprised of 30 healthy children of comparable age and gender attending at outpatient clinics. Their ages ranged from 8 to 18 years. All were apparently healthy, with normal clinical examination. They had no history of chronic illness and were not taking any medications.

We excluded from our study patients who had used antiepileptics or anticoagulants within 6 months prior to enrollment. Patients with Parathyroid disorders, prolonged immobilization, chronic liver disease and malignant diseases were also excluded from the study.

All subjects in our study underwent:

1- Complete history taking including: Age, sex, onset of disease, course and relapses, initial clinical presentation, disease duration (from time of diagnosis until now), family history of autoimmune diseases, history of drug taking or blood transfusion, medications, frequency of flares, and activity in SLE patients measured by SLE Disease Activity Index (SLEDAI) [13].

2- Thorough clinical examination.

3- Laboratory investigations included complete blood count by Cell-Dyn 1700 cell counter, blood urea and serum creatinine by ROCHE-Integra 400, serum phosphate and serum Ca by COBAS 8000, liver profile, erythrocyte sedimentation rate, analysis of urine. Special investigations such as serum 25(OH) vitamin D using enzyme-linked immunosorbent assay (ELISA), alkaline phosphatase, and serum intact parathyroid hormone (PTH).

According to the American Academy of Pediatrics (AAP) / LWEPS's recommendations for the cut-off levels of vitamin D, vitamin D status was categorized **[14]:**

- 25(OH) D level of <15 ng/mL (<37.5 nmol/L) as deficiency,
- 25(OH) D level of 15– 20 ng/mL (37.5– 50 nmol/L) as insufficient
- 25(OH) D level of > 20 ng/mL (>50 nmol/L) as sufficient level.

4- Dual-energy X-ray absorptiometry (DXA) scan:

Dual energy X-ray absorptiometry measurements of BMD at L2-L4 of the lumbar spine were taken from SLE patients as well as from healthy controls that were matched for age and sex. Every patient performs a full-body scan while lying supine on the Lunar NT DXA machine's exploration table. Using a Smart Scan approach, the acquisition time is reduced while the anatomical landmarks are automatically detected, and the scan path is laid out. The GE Lunar NT DXA machine is a full-size pencil beam system that utilizes a narrow fan beam at an angle of 4.58 parallel to the body's long axis, peak energy of 80 kVp, current of 3 mA, and energies at 38 and 70 kVp produced by a K-edge filter. GE Healthcare Lunar enCORE 14.0 is used to evaluate each image. The analysis resulted in total and standard sub-regional measures for the following parameters: bone mineral content (BMC) in g, bone area (BA) in cm2, and bone mineral density (BMD), which was calculated as BMC/BA in g/cm^2. We present BMD as a Z score that is matched by age and gender. Lean soft tissue mass (LSTM) and total fat mass (FM) were also measured by the scanner, and a percentage of body mass was calculated. Body mass index Z-scores were employed to bypass any potential DXA technique constraints with the two-dimensional measurement of BMD and BMC in children, which is dependent on children's size and age. The analysis takes 12 to 14 minutes to complete **[15].**

Based on white women's bone density, the World Health Organization established the following categories in 1994 **[16]:**

- Normal bone: T-score of ≥ -1.0
- Osteopenia: T-score from-1 to -2.5.
- Osteoporosis: T-score < -2.5

The study was approved by the institutional review board (IRB). An informed written consent was taken from all parents at the time of recruiting. This study was carried out in accordance with the Declaration of Helsinki.

RESULTS

Demographic data of the study participants was summarized; 30 patients with SLE were included **(**25 females (83.3%) and 5 males (16.7%) with a ratio of 5:1), their ages ranged from 11.0 – 18.0 years, with a duration of 2 to 11 years since disease diagnosis. Control group was matched in sex and age, with no statistically significant difference between both groups **Table 1.**

Regarding vitamin D status in the study groups, there was a highly statistically significant difference

between both groups in vitamin D levels (p<0.001), being lower in SLE group. Sixty-three percent of patients were deficient, while 36.7% had insufficient level **Table 2**. There was statistically significant difference between SLE patients and control groups regarding bone density parameters by DXA. Osteopenia was detected in 43.3% and osteoporosis in 3.3% with total of 14 (46.6%) patients with low BMD **Table 3, Figure 1.**

There was no statistically significant difference in renal biopsy findings between patients with decreased and average BMD **Table 4**. There was a statistically significant association between BMD and age of onset and disease duration. Decreased BMD was associated with younger age of onset and longer disease duration **Table 5.** The association between BMD and Corticosteroids use has been studied. Longer duration and more methylprednisolone pulses were associated with lower BMD **Table 6.**

On studying the correlation between DXA results and recent laboratory findings of SLE group, we found that there was statistically significant +ve correlation with serum calcium and statistically significant -ve correlation with C4 and alkaline phosphatase **Table 7.** Regarding the association between BMD and disease activity**,** there was no statistically significant association between BMD and SLEAI of the studied patients **Table 8.**

On analysis of linear regression of important parameters that can predict low BMD, longer disease duration (unstandarized β= 0.29, p <0.001), steroid use either duration (unstandarized β= 0.09, p <0.05), or number of pulses (unstandarized β= 0.03, p <0.043), and alkaline phosphatase (unstandarized β= 0.02, p <0.001), were significant independent predictors of reduced BMD in SLE patients **Table 9.**

Table 1: Demographic data of the study participants

Variables		SLE group (n=30)	Control group (n=30)	Test of sig.	p
Age (years):	X ± SD Range	14.8 ± 2.5 11.0 – 18.0	14.0 ± 2.3 10.0 – 18.0	t 1.29	0.20 NS
Sex:	Males Females	5 (16.7%) 25 (83.3%)	7 (23.3%) 23 (76.7%)	χ^2 0.42	0.52 NS
BMI (kg/m^2):	X ± SD Range	22.3 ± 1.9 18.0 – 26.0	21.5 ± 2.7 19.0 – 26.5	t 1.33	0.19 NS
Age of onset (years):	X ± SD Range	8.7 ± 2.3 4.0 – 12.0	N/A	**----**	----
Disease duration (years):	X ± SD Range	6.1 ± 2.7 2.0 – 11.0	N/A	**----**	----

X: Mean, SD: Standard deviation, t: Independent t test, χ^2: Chi square test, NS: non significant (P>0.05)

Table 2: Vitamin D levels in the study groups

Vitamin D levels	SLE group (n=30)		Control group (n=30)		χ^2	p
	No.	%	No.	%		
Deficient	19	63.3	0	0.0	33.39	**<0.001****
Insufficient	11	36.7	16	53.3		
Normal	0	0.0	14	46.7		

χ^2: Chi square test, **: Highly significant (P<0.001)

Table 3: DXA results and BMD in study groups

DXA		SLE group (n=30)	Control group (n=30)	Test of sig.	P
Lumbar spine	**X ± SD**	-0.65 ± 1.23	0.3 ± 0.1	**MW**	
	Median	-1.0	1.0	**4.22**	**<0.001****
	Range	-3.8 – 1.4	-0.9 – 1.4		
	Average	16 (53.3%)	25 (83.3%)	χ^2	
	Osteopenia	13 (43.3%)	5 (16.7%)	6.53	**0.04***
	Osteoprosis	1 (3.3%)	0 (0.0%)		

X: Mean, SD: Standard deviation, MW: Mann Whiteny test, χ^2: Chi square test, *:significant (P<0.05), **: Highly significant (P<0.001)

Table 4: Renal biopsy findings of the studied case group

Renal biopsy	BMD				χ^2	P
	Decreased (n=14)		Average (n=16)			
No biopsy	**No.**	**%**	**No.**	**%**		
Lupus nephritis class 1	5	35.7	3	18.7		
Lupus nephritis class 2	1	7.1	1	6.2		
Lupus nephritis class 3	4	28.5	8	50	4.3	0.4
Lupus nephritis class 4	1	7.1	2	12.5		
Lupus nephritis class 5	2	14.2	0	0		

χ^2: Chi square test

Table 5: Association between BMD and general characteristics of the studied patients

Variables		BMD		Test of sig.	p
		Decreased (n=14)	Average(n=16)		
Age (years):	X ± SD	13.8 ± 1.8	14.4 ± 2.8	T	0.4
	Range	11.0 – 17.0	11.0 – 18.0	0.8	NS
Sex:	Males	2 (14.3%)	3 (18.8%)	χ^2	0.9
	Females	12 (85.7%)	13 (81.2%)	Fisher	NS
BMI (kg/m^2):	X ± SD	21.7 ± 1.5	22.4 ± 1.9	T	0.3
	Range	19.5 – 24.1	18.0 – 25.7	1.0	NS
Age of onset (years):	X ± SD	9.0 ± 2.4	11.3 ± 2.4	T	**0.01***
	Range	4.0 – 12.0	7.0 – 15.0	2.7	
Disease duration (years):	X ± SD	4.8 ± 2.8	3.1 ± 3.4	MW	**0.03***
	Median	5.0	1.0	2.1	
	Range	1.0 – 11.0	1.0 – 11.0		
Frequency of relapse /2 years:	X ± SD	5.6 ± 3.7	4.4 ± 3.4	MW	0.3
	Median	6	4	1.0	NS
	Range	1 - 12	0 – 10		
Activity related to seasons:	Summer	3 (21.4%)	3 (18.8%)	χ^2	
	Winter	9 (64.3%)	6 (37.5%)	3.26	0.20
	No relation	2 (14.3%)	7 (43.8%)		NS

X: Mean, SD: Standard deviation, t: Independent t test, MW: Mann Whiteny test, χ^2: Chi square test, NS: non significant (P>0.05), *:significant (P<0.05).

Table 6: Association between BMD and Corticosteroids use in the studied patients

Variables		BMD		MW	P
		Decreased (n=14)	Average (n=16)		
Dose of prednisone at DXA study (mg/d):	X ± SD	27.5 ± 11.2	19.7 ± 17.5		
	Median	30.0	10.0	1.5	0.1
	Range	5.0 – 50.0	5.0 – 50.0		NS
Maximum prednisone dose (60 mg/d)		14 (100%)	16 (100%)	NA	NA
Duration of Maximum prednisone dose (y):	X ± SD	11.4 ± 6.2	2.9 ± 1.3		
	Median	9.0	2.0	4.5	**<0.001****
	Range	5.0 – 24.0	2.0 – 6.0		
Number of methylprednisolone pulses	X ± SD	29.4 ± 20.9	6.9 ± 3.0		
	Median	21.5	6	4.2	**<0.001****
	Range	9 – 66	3 – 12		

X: Mean, SD: Standard deviation, MW: Mann Whiteny test, NS: non significant (P>0.05), **: Highly significant (P<0.001)

Table 7. Correlation between DXA results and Recent laboratory findings of SLE group

Laboratory findings	DXA	
	r	P
C4	**-0.40**	**0.02 (*)**
C3	**-0.06**	**0.73**
ESR	0.03	0.82
Hb	-0.12	0.51
TLC	0.12	0.51
Platelets	0.14	0.44
Calcium	**0.36**	**0.04(*)**
Phosphate	0.15	0.41
PTH	0.26	0.23
Alkaline phosphatase	**-0.73**	**<0.001(**)**
Albumin	0.22	0.26
BUN	0.05	0.80
Creatinine	0.11	0.51
Vitamin D	0.27	0.19

r: Correlation coeffecinet , *: significant (P<0.05), **: Highly significant (P<0.001)

Table 8: Association between BMD and SLEAI of the studied patients

SLEAI	BMD				χ^2	P
	Decreased (n=14)		Average (n=16)			
Mild	**No.**	**%**	**No.**	**%**	2.68	0.26 NS
Moderate	6	42.9	11	68.8		
Severe	7	50.0	5	31.3		
	1	7.1	0	0.0		

Chi square test, NS: non significant (P>0.05)

Table 9: Linear regression analysis for significant predictors of BMD among SLE group

Parameter	Unstandardized Coefficients		Standardized Coefficients	T	P
	β	Std.Error	β		
Age of onset	0.06	0.07	0.12	0.79	0.440
Duration of disease	**-0.29**	**0.06**	**-0.71**	**-4.71**	**<0.001****
Duration of steroid	**-0.09**	**0.04**	**0.43**	**2.06**	**0.05***
methylprednisolone pulses	**-0.03**	**0.01**	**-0.39**	**2.15**	**0.043***
C4	-0.001	0.02	-0.008	-0.07	0.945
Calcium	0.09	0.20	-0.05	0.43	0.672
Alkaline phosphatase	**-0.02**	**0.004**	**-0.65**	**-3.74**	**0.001***

**: Highly significant (P<0.001), *: significant (P<0.05)

Figure 1: A full-body scan appearing on the screen of a computer linked to a DXA scanner.

DISCUSSION

Osteoporosis, a frequent clinical issue in inflammatory illnesses, is a skeletal disorder marked by decreased bone density and degeneration of bone microarchitecture, which ultimately leads to increased bone fragility and a high risk for fragility fractures. Numerous studies have shown that SLE patients have low BMD, and that accelerated bone loss is more common in SLE patients than in the general population [7].

Inflammation, glucocorticoid use, vitamin D deficiency, and conventional risk factors such as sex and age all put patients with SLE at risk for diminished bone density. Better prevention and treatment methods are required for morbidity problems like osteoporosis because SLE survival has increased due to better therapies [17]. Our study was done to evaluate BMD (frequency of reduced bone mass and osteoporosis) in SLE patients, in addition to studying possible risk factors for reduced BMD.

Thirty SLE patients were enrolled in the current study, with 25 females (83.3%) and 5 males (16.7%) with female predominance. Our findings were comparable to those of a study conducted in 2014 by Peracchi et al, on 30 Caucasians, with a mean age of 13.7 years, which indicated that 83.3% of SLE patients were females [18]. The majority of juvenile SLE studies have shown high female-to-male ratios (3-5:1) [19], which are almost identical to the ratios found in our study (5:1). The female-to-male ratio in our study, however, was significantly lower than that of previous Egyptian study (12:1) done on 52 SLE patients (aged 11.9+/-2.6 years) [20].

In our study, there was a statistically significant difference in vitamin D level between SLE group and control group, being lower in the first group. We found that 63.3 % of SLE group was vitamin D deficient, while 36.7 % had insufficient levels. In contrast to control group, 53% detected to have vitamin D insufficiency and 46% had sufficient levels. Our results agreed an adult study done by Islam et al. [21]. It is not specific for SLE, as it has been consistently reported in many other autoimmune diseases like rheumatoid arthritis [22]. Reduced renal function, avoiding sun exposure, and the use of glucocorticoids could be explanations for decreased vitamin D levels [23].

Only a few studies had looked at how common osteopenia and osteoporosis were in children with SLE. According to the findings of DXA scan, the present study showed a substantial difference between lupus patients and healthy children of the same age and sex. Compared to healthy children of the same age and sex, children with SLE exhibited decreased BMD. This was consistent with previous study done on adult patients with SLE. It was concluded that bone loss in SLE is varied and is likely a complex process that may result from the illness itself or by therapy [24].

The range of DXA at the lumber spine was lower in SLE group in comparison to control group with statistically significant difference between both. According to our findings in lumbar spine, 43.3% of patients were osteopenic, while 3.3% of them had osteoporosis in comparison to only 16% of control group who were osteopenic. According to cross-sectional researches, the prevalence of osteopenia ranges from 11 to 62% (lumbar) [25] and 6 to 74% (hip) [26] while that of osteoporosis is between 4 and 42% (lumbar) [27] and 3 to 42% (hip) [26] which included an older

age group of patients**.** The wide variation in prevalence between studies is probably caused by factors such as ethnicity, age, sex, and different study approaches [27, 7].

The present study found a strong relationship between bone density, as evaluated by DXA, and both the age at disease onset and the duration of the disease. Younger age at disease onset and longer disease duration were linked to decreased bone density at the femoral neck. Similar findings were reported by Sinigaglia et al., who showed a substantial difference in the length of treatment, particularly steroid treatment, among treated lupus patients with abnormal DXA scan results [28]. According to Compeyrot-Lacassagne et al. osteopenia is prevalent in juvenile SLE and is more directly linked to extended disease duration than steroid dosage [8].

In terms of steroid use, there was a statistically significant relationship between BMD and corticosteroid usage among the patients who were studied, particularly the number of methylprednisolone pulses and maximum steroid dose, which is consistent with Jung et al., who explained that an excess of glucocorticoids is what causes a severe form of secondary osteoporosis [29]. Steroids can reduce BMD through induction of osteoblasts and osteocytes apoptosis, at the same time osteoblasts inhibition mainly in trabecular bone, in addition to enhancement of calcium excretion and reduction of calcium absorption, suggesting a decoupling of bone formation and destruction [7, 30]. Contrarily El-Hady et al. found no correlation between the length of treatment or steroid dosage and poor BMD as shown in abnormal findings of DXA scan [24]. The reason for different results may be the use of different steroid protocols.

A chronic inflammatory response seen in patients with SLE may be an additional factor contributing to decrease BMD, as many of pro-inflammatory cytokines like TNF and IL-6 were found to be increased in SLE. These cytokines can induce bone loss by promotion of stimulation of osteoclasts differentiation, therefore persistent disease activity aid in rapid progression of bone loss [31]. However, we couldn't prove an impact of disease activity (SLEDAI) on the decline in BMD. Previous studies agreed with our findings [24, 32]. The measures used to assess disease activity are most likely only measured at a single point in time, which is the likely cause.

Comparable to El-Hady et al. [24]**,** our investigation revealed no significant correlation between DXA scan parameters and serum phosphorus. Higher serum levels of phosphate and lower hip BMD, according to Figueiredo et al. are independent bone parameters **[33]**. Our research revealed a significant substantial association between alkaline phosphate and DXA scans at the femoral neck. Alkaline phosphatase was the only bone mineral indicator that had an obvious effect on BMD [34]**.**

The current study showed no statistically significant relationship between intact PTH and DXA scan values in lupus patients. In line with the findings of Goubraim et al., who found that intact PTH levels did not correlate with any BMD measures [35]. In contrast, other adult studies revealed a significant correlation between DXA scan parameters and parathormone level in lupus patients who had just been diagnosed [36, 24]**.** These findings differ

because of the longer duration of disease and older age of patients in these studies.

For proper skeleton mineralization, it is essential to consume the recommended amounts of calcium and vitamin D. Low calcium levels and vitamin D deficiency can affect BMD [31]. However, there was no correlation between vitamin D level and DXA scan parameters in our study. Our findings didn't match with earlier researches on adult lupus patients, which established a strong negative correlation between vitamin D levels and scores of BMD [37]. Despite unproven efficacy, calcium and vitamin D supplementation are recommended for all patients who undergo long-term use of steroids.

On linear regression analysis of various predictors of low BMD, we detected that longer disease duration with prolonged steroid use and high alkaline phosphatase were the most important factors for development of reduced BMD in children with SLE.

The limited sample size and different ethnic background could be the cause of the apparent lack of a meaningful relationship between low BMD and some factors, as vitamin D level and SLE activity.

RECOMMENDATIONS

A follow up with DXA scan in children with lupus is needed for early diagnosis of low BMD. Also, it is better to try other therapeutic protocols using lower doses of steroids and using steroid sparing drugs to decrease their side effects on BMD.

LIMITATIONS

Being a single center study with small sample size may exhibit some limitations to our study.

CONCLUSION

We found that BMD is reduced in SLE children compared to healthy controls. Low vitamin D is common in SLE children. Low BMD is associated with longer disease duration, and steroid use, but no association could be detected with disease activity or vitamin D level. Further studies are needed on larger sample sizes for more confirmed correlation

ABBREVIATIONS

AAP	American Academy of Pediatrics
ACR	American College of Rheumatology
BMD	Bone mineral density
DXA	Dual-energy X-ray absorptiometry
j-SLE	Juvenile-Systemic lupus erythematous
SLEDAI	SLE Disease Activity Index
PTH	parathyroid hormone

REFERENCES

1- Hedrich CM, Smith EMD, Beresford MW. Juvenile-onset systemic lupus erythematosus (jSLE) Pathophysiological concepts and treatment options. Best Practice & Research Clinical Rheumatology. 2017; 31(4):488-504.

2- Rees F, Doherty M, Grainge M, Davenport G, Lanyon P, Zhang W. The incidence and prevalence of systemic lupus erythematosus in

the UK, 1999-2012. Annals of the rheumatic diseases. 2016; 75(1):136-41.

3- Watson L, Leone V, Pilkington C, Tullus K, Rangaraj S, McDonagh JE. UK Juvenile-Onset Systemic Lupus Erythematosus Study Group. Disease activity, severity, and damage in the UK Juvenile-Onset Systemic Lupus Erythematosus Cohort. Arthritis Rheum. 2012 Jul; 64(7):2356-65. Doi: 10.1002/art.34410. PMID: 22294381.

4- Ambrose N, Morgan TA, Galloway J, Ionnoau Y, Beresford MW, Isenberg DA; UK JSLE Study Group. Differences in disease phenotype and severity in SLE across age groups. Lupus. 2016 Dec; 25(14):1542-1550. Doi: 10.1177/0961203316644333. Epub 2016 May 4. PMID: 27147622; PMCID: PMC5089221.

5- Orsolini G, Bultink IEM, and Adami G. Bone health, an often forgotten comorbidity in systemic lupus erythematosus: a comment on the new recommendations. Ann Rheum Dis. 2020; 79(11): e150.

6- Bultink IEM. Bone Disease in Connective Tissue Disease/Systemic Lupus Erythematosus. Calcified Tissue International. 2018; 102(5):575-91.

7- Sun YN, Feng XY, He L, Zeng LX, Hao ZM, Lv XH, Pu D. Prevalence and possible risk factors of low bone mineral density in untreated female patients with systemic lupus erythematosus. Biomed Res Int. 2015; 510514. Doi: 10.1155/2015/510514. Epub 2015 Feb 11. PMID: 25738154; PMCID: PMC4337055.

8- Compeyrot-Lacassagne S, Tyrrel PN, Atenafu G, Doria AS, Stephens D, et al. Prevalence and etiology of low bone mineral density in juvenile systemic lupus erythematosus. Arthritis Rheum. 2007; 56: 1966-1973.

9- Casabella A, Paolino S, Alessandri E, et al. Evaluation of bone quality by trabecular bone score (TBS) in systemic lupus erythematosus patients. Ann Rheum Dis. 2019:78(Suppl 2): 945–6. Doi:10.1136/annrheumdis-2019eular.6753**.**

10- Mendoza-Pinto C, Rojas-Villarraga A, Molano-González N, et al. Bonemineral density and vertebral fractures in patients with systemic lupus erythematosus: A systematic review and meta-regression. PLoS ONE. (2018) 13: e0196113. Doi: 10.1371/journal.pone.0196113.

11- El Maghraoui A and Roux C**.** DXA scanning in clinical practice. QJM. 2008; 101:605–17. Doi: 10.1093/qjmed/hcn022**.**

12- Hochberg MC. Updating the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheum 1997; 40:1725.

13- Lam GKV, Petri M. Assessment of systemic lupus erythematosus. *Clin Exp Rheumatol.* 2005; 23: S120–32.

14- Misra M, Pacaud D, Petryk A, Collett-Solberg PF, Kappy M; Drug and Therapeutics Committee of the Lawson Wilkins Pediatric Endocrine Society. Vitamin D deficiency in children and its management: review of current knowledge and recommendations. Pediatrics. 2008 Aug; 122(2):398-417. Doi: 10.1542/peds.2007-1894. PMID: 18676559**.**

15- Carey JJ, Delaney MF, Love TE, Cromer BA, Miller PD, Richmond BJ, Manilla-McIntosh M, Lewis SA, Thomas CL, Licata AA. Dual-energy X-ray absorptiometry diagnostic discordance between Z-scores and T-scores in young adults. J Clin Densitom. 2009 Jan-Mar; 12 (1):11-6. PMID: 19195620. Doi: 10.1016/j.jocd.2008.11.001.

16- Kanis JA, Seeman E, Johnell O, Rizzoli R, Delmas P; Committee of Scientific Advisors, International Osteoporosis Foundation. The perspective of the International Osteoporosis Foundation on the official positions of the International Society for Clinical Densitometry. Osteoporos Int. 2005 May; 16 (5):456-9**.**

17- Peracchi OA, Terreri MT, Munekata RV, Len CA, Sarni RO, Lazaretti-Castro M, Hilário MO. Low serum concentrations of 25-hydroxyvitamin D in children and adolescents with systemic lupus erythematosus. Braz J Med Biol Res. 2014 Aug; 47(8):721-6. Doi: 10.1590/1414-431x20143948. Epub 2014 Jul 29. PMID: 25055165; PMCID: PMC4165300.

18- Khoo JJ, Pee S, Thevarajah B, Yap YC, Chin CK**.** Lupus nephritis in children in Malaysia. J Paediatr Child Health. 2005 Jan-Feb; 41(1-2):31-5. PMID: 15670221. Doi: 10.1111/j.1440-1754.2005.00532.x.

19- Bakr A**.** Epidemiology treatment and outcome of childhood systemic lupus erythematosus in Egypt. Pediatr Nephrol. 2005 Aug; 20(8):1081-6. Epub 2005 Jun 7. PMID: 15940546. Doi: 10.1007/s00467-005-1900-2.

20- Islam MA, Khandker SS, Alam SS, Kotyla P, Hassan R. Vitamin D status in patients with systemic lupus erythematosus (SLE): A systematic review and meta-analysis. Autoimmunity Reviews. 2019; 18(11):102392.

21- Salman-Monte TC, Torrente-Segarra V, Vega-Vidal AL, Corzo P, Castro-Dominguez F, Ojeda F, et al. Bone mineral density and vitamin D status in systemic lupus erythematosus (SLE): A systematic review. Autoimmun Rev. 2017; 16:1155–9**.**

22- Edens C, Robinson AB**.** Systemic lupus erythematosus, bone health, and osteoporosis. Curr Opin Endocrinol Diabetes Obes. 215; 22:422-431.

23- El-Hady H, Abd-El Aziz Kora M, Soliman S, Ragheb A, Zahran E. Study of bone mineral density in patients with systemic lupus erythematosus. Menoufia Medical Journal. 2014; 27(3):556-61.

24- Bhattoa HP, Bettembuk P, Balogh A, Szegedi G, Kiss E. Bone mineral density in women with systemic lupus erythematosus. Clin Rheumatol. 2002; 21(2):135-41. Doi: 10.1007/s10067-002-8272-9. PMID: 12086164

25- Mok CC, Mak A, Ma KM. Bone mineral density in postmenopausal Chinese patients with systemic lupus erythematosus. Lupus. 2005; 14 (2):106-12. PMID: 15751814. Doi: 10.1191/0961203305lu2039oa.

26- Bultink IE**.** Osteoporosis and fractures in systemic lupus erythematosus. Arthritis Care Res (Hoboken). 2012; 64(1):2-8. Doi: 10.1002/acr.20568. PMID: 22213721

27- Sinigaglia L, Varenna M, Binelli L, Zucchi F, Ghiringhelli D, et al. Bone mass in systemic lupus erythematosus. Clin Exp Rheumatol. 2000; 18: S27-S34.

28- Jung JY, Choi ST, Park SH, Kwon SR, Kim HA, Kim SS, et al. Prevalence of osteoporosis in patients with systemic lupus erythematosus: A multicenter comparative study of the World Health Organization and fracture risk assessment tool criteria. Osteoporosis and sarcopenia. 2020; 6(4):173-8.

29- Haris A, Szabó A, Lányi É, Mucsi I, Polner K**.** Acute and long-term effects of corticosteroid therapy on bone metabolism in patients with kidney diseases. Clin Nephrol.2012; 78:17-23.

30- Wiad Lek. Peculiarities of bone mineral density in women of different reproductive age with systemic lupus erythematosus.2021; 74(2):303-309.

31- García-Carrasco M, Mendoza-Pinto C, Escarcega RO, Jimenez-Hernandez M, Morales IE, et al. Osteoporosis in patients with systemic lupus erythematosus. IMAJ. 2009; 11:486-491.

32- Figueiredo CP, Rajamann NM, Loes JB, Caparbo VF, Jakayame L, et al. Serum phosphate and hip bone mineral density as additional factors for high vascular calcification scores in a community-dwelling: the São Paulo Ageing & Health Study (SPAH). Bone. 2013; 52: 354-359.

33- Marwaha RK, Sripathy G. Vitamin D & bone mineral density of healthy school children in northern India. Indian J Med Res. 2008; 127:239-244.

34- Goubraim R, Kabbaj N, Salihoun M, Ghaoui Z, Nya M, et al. Metabolic bone disease in viral cirrhosis: a prospective study. ISRN Hepatology. 2013; 2013.

35- Kota S, Jammula S, Meher L, Modi K. Correlation of vitamin D, bone mineral density and parathyroid hormone levels in adults with low bone density. IJO. 2013; 47: 402-407.

36- Caraba A, Munteanu A**,** Crișan V. Bone Mineral Density in Patients with Systemic Lupus Erythematosus. J Orthop Ther: JORT. 2018; 1111. DOI: 10.29011/2575- 8241. 00111.

37- Caraba A, Munteanu A, Crișan V. Bone Mineral Density in Patients with Systemic Lupus Erythematosus. J Orthop Ther: JORT. 2018; 1111. DOI: 10.29011/2575- 8241. 00111.

AUTHORS' CONTRIBUTIONS

The submitted manuscript is the work of the author and co-author.
All authors have contributed to authorship, have read and approved the manuscript.
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Acquisition of data: FA, HT.
Analysis and/or interpretation of data: M I.
Drafting the manuscript: FA, M ES
Revising the manuscript critically for important intellectual content: FA, M NA
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STATEMENTS

Ethics approval and consent to participate

This study protocol and the consents were approved and deemed sufficient by the Ethical Committee of Zagazig University (ZU#10709) and informed written consent was obtained in every case from their legal guardians.

Consent for publication

The contents and material of the manuscript have not been previously reported at any length or are being considered for publishing elsewhere.

Availability of data and material

"Not applicable"

Conflict of interest

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