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Detection of joint involvement in patients with systemic lupus erythematosus using musculoskeletal ultrasound and its correlation with disease activity

Shahenaz Hamdi El genedi^{*} , Mohamed N. Salem, Mahmoud Farid, Thoraya Mohamed Ahmed and Hanan Ali Taha

Abstract

Background Musculoskeletal symptoms are common and could be the first presenting symptom in up to 50% of systemic lupus erythematosus patients, and they affect more than 95% of patients during the clinical course. The present study aimed to assess joint involvement in the wrists, hands, and knees of SLE patients using musculoskeletal ultrasonography and to correlate these findings with disease activity.

The study enrolled 40 Patients with SLE who were attending the Immunology outpatient clinic and internal medicine department of Beni-Suef University Hospital and 20 age and sex nearly matched healthy controls who have no rheumatological complaints. Participants had a comprehensive physical examination, series of laboratory tests, functional assessment by Health Assessment Questionnaire score, disease activity assessment of by European Consensus Lupus Activity score, and radiological examination by high-resolution Ultrasound machine called (LOGIC P 9) using a gray-scale US mode (13–18 MHz) with Power Doppler to detect joint synovitis, synovial hypertrophy, bone erosions and or tenosynovitis.

Results There was a statistically significant prevalence of US abnormality of knee joints in both asymptomatic and symptomatic cases versus controls contrary to the wrist and hand US abnormality. The presence of SLE increases the risk of US abnormalities in knee joints 28 times more than controls also increasing the age of the patient one year increase the probability of getting abnormal findings in the knee joint by 1.156 times. While the only independent variable that can affect US abnormal findings in the wrist joint is the increase in Systolic Blood Pressure 1 mmHg with 1.06 times.

Conclusion Musculoskeletal Ultrasound with applied Power Doppler is a good tool for the detection of early affection of joints either in symptomatic or asymptomatic SLE patients.

Keywords Lupus activity, Musculoskeletal, Arthritis, SLE, Synovitis, Ultrasound, Power Doppler

1 Background

Systemic lupus erythematosus (SLE) is a multi-systemic autoimmune disease with remissions and relapses that may simultaneously affect many organs [1]. In 95% of SLE patients, there is musculoskeletal involvement, which may be due to the disease itself or the medication used to treat it [2]. These symptoms include persistent

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or transitory stiffness and/or joint pain, which may or may not be accompanied by evidence of inflammation upon physical examination. It usually lacks clinical inflammatory signs and is symmetrical. Hand arthralgia without actual arthritic signs is a common complaint among SLE patients [3].

Joint involvement in SLE investigations has previously been described as (non-erosive, erosive, and non-deforming or deforming arthropathy). When evaluating rheumatic illnesses, joint ultrasonography is a reliable diagnostic method (such as PSA and RA). Evaluation of articular and peri-articular structures is also helpful [4]. Adding a Power Doppler signal to ultrasound (PDUS) allows for a sensitive evaluation of inflammatory changes in joints and hyperemia of soft tissues. This characteristic makes PDUS sensitive to finding abnormalities in joint tissue [5]. As a result, the majority of lupus arthritis patients frequently complain of non-deforming non-erosive (NDNE) arthritis. Even though all of these patients share some common inflammatory characteristics of arthritis, such as symmetry in the distribution of their small joints and morning stiffness, clinically evident synovitis is only present in a small percentage of them. Clinical synovitis and its relationships to disease activity markers have been the subject of many clinical trials [6]. The present study aimed to use musculoskeletal ultrasound to assess joint involvement in the wrists, hands, and knees of patients with systemic lupus erythematosus (SLE) and to correlate the results with disease activity.

2 Patients and methods

2.1 Aim of the study

Assessment of joint involvement in the wrists, hands, and knees of SLE patients using musculoskeletal ultrasonography and correlating the findings with disease activity.

2.2 Design and settings of the study

A case-control study was conducted at the Immunology outpatient clinic and the internal medicine department at Beni-Suef University Hospital.

2.3 Study population

The study was conducted on 40 SLE patients and twenty healthy age and sex nearly matched controls. Patients were classified into 2 groups (symptomatic group with arthritis, or arthralgia), and other (asymptomatic group for joint affection). Healthy controls had no personal or family history of autoimmune diseases and denied previous hand, wrist, or knee affection.

2.4 Inclusion criteria

- All patients were between the ages of (and 20_60) years.
- All patients fulfilled the Systemic Lupus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) criteria.

2.5 Exclusion criteria

- Patients aged less than 20 years or more than 60 years.
- Patients are known to have other autoimmune or rheumatological diseases, diabetes mellitus, or arthritis related to the hepatitis C virus.

2.6 Sample size

The sample size was calculated using G*Power 3.1.9.4 calculator. The smallest required sample size was 40 SLE patients and 20 controls.

t tests—means: difference between two independent means (two groups)

Analysis:	A priori: compute the required sample size	
Input:	Tail(s)	=Two
	Effect size d	=0.79
	α err prob	=0.05
	Power (1-β err prob)	=0.80
	Allocation ratio N2/N1	=2/1
Output:	No centrality parameter δ	=2.8846721
	Critical t	=2.0017175
	Df	=58
	Sample size group 1	=20
	Sample size group 2	=40
	Total sample size	=60
	Actual power	=0.8096594

2.7 Study methods

2.7.1 All patients were subjected to the following:

- Full history taking including past and recent medical history.
- Demographic data including age and sex
- Full physical examination including comprehensive musculoskeletal examination.

- Functional assessment by using the health assessment questionnaire (HAQ-DI) score (validated Arabic version).
- Disease activity score of the disease by using the ECALM score (European Consensus Lupus Activity Measurement) for SLE.
- Radiological examination: High-resolution US machine was used called (LOGIC P 9) using a gray-scale US mode (13–18 MHz) (Fig. 1), by an expert rheumatologist on all patients and controls PD evaluation was performed with a PD frequency of 10 MHz, gain 50% and low wall filter. For each US evaluation, an adequate amount of warm gel was used, and compression with the probe was avoided, to accurately evaluate synovial vascularization. We examine hand, wrist, and knee joints by the US. Both longitudinal and transverse scans are performed by slightly moving the transducer from radial to ulnar and from proximal to distal sides on the dorsal aspect to enable maximum coverage of the anatomical surface areas. Joint effusion and/or synovial hypertrophy were used to define joint synovitis. The Outcome Measures in RA Clinical Trials offered criteria of SH as hypochoic intra-articular tissue that was non-displaceable, weakly compressible, and may or may not present a PD signal (OMERACT). We evaluated synovial vascularization by using PD analysis. A cortical flaw or break in the surface of the bone was referred to as bone erosion and was visible in both the transverse and longitudinal scans. Tenosynovitis was described as hypochoic or anechoic thickening tissue that was seen in two perpendicular planes, with or without fluid within the tendon sheath. To

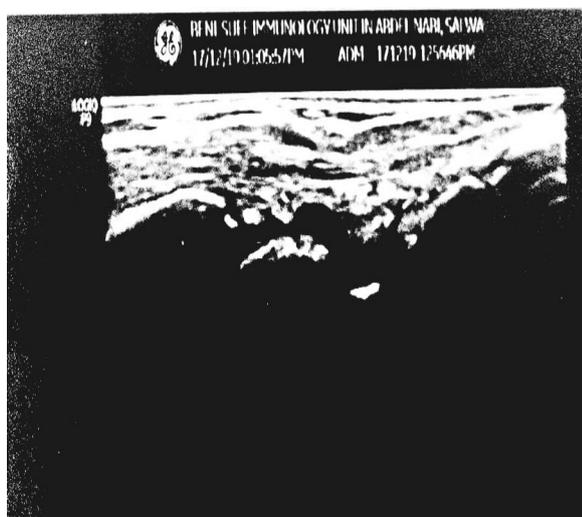


Fig. 1 Right wrist joint erosions

evaluate the vascularity of joints and tendons, PD was used. 34 joints, including the 5 proximal interphalangeal (PIPs), 5 distal interphalangeal (DIPs) 5 metacarpophalangeal (MCPs) in wrists and knees bilaterally, were investigated. GSUS was used for the US findings. The corresponding tendons surrounding the joints were examined.

- Laboratory investigations: The erythrocyte sedimentation rate (ESR); semi-quantitative C-reactive protein (CRP) (positive if >6 mg/L); C3 and C4 (normal C3 12–49 U/ml, C4 63–192 U/ml); CBC; anti-nuclear antibody (ANA) (positive if >1.2 U/ml); anti-ds DNA antibody (positive if >20 U/ml); urinary albumin/creatinine ratio; serum creatinine and rheumatoid factor (RF) measured by latex fixation test (positive if >8 IU/ml) to exclude RA.

2.8 Statistical analysis

Analysis of data was performed using SPSS v. 22 (Statistical Package for Social science) for Windows, description of variables was presented for quantitative variables as mean \pm standard deviation (SD), while for qualitative variables as numbers (No.) and percentage (%). Comparison between quantitative variables was carried out by independent sample t-test and one-way ANOVA test for normally distributed variables while nonparametric Mann–Whitney test and Kruskal–Wallis test were used for quantitative variables which are not normally distributed. Comparison between categorical data was done using the Chi-square test. Pearson correlation was used to test the correlation between different quantitative variables. Regression was used to examine the predictor factors that may affect the disease activity. The odds ratio (OR) with its 95% confidence interval (CI) was used for risk estimation. The significance of the results was assessed in the form of a *P* value that was differentiated into: (non-significant when the *P* value >0.05 , significant when the *P* value ≤ 0.05 , and highly significant when the *P* value ≤ 0.001).

3 Results

The present study was conducted on forty SLE patients who were attending the Immunology outpatient clinic and internal medicine department of Beni Suef University Hospital. The forty SLE cases were classified into two groups symptomatic arthritis or arthralgia group 26 (65%) and asymptomatic group 14 (35%). The SLE patients were predominantly females 34 (85%). The mean age was (30.9 ± 8.2) , the mean duration of disease was 5.5 ± 4.2 (4.5 y) years, the mean BMI was (26.95 ± 4.534) , and the mean systolic blood pressure was (127 ± 16.7)

Table 1 Demographic and clinical characteristics of SLE patients

Variable	SLE patients	
	Frequency (No. = 40)	Percentage (%)
<i>Sex</i>		
Female	34	85.0
Male	6	15.0
Age in years, Mean \pm SD	30.9 \pm 8.2	
Disease Duration (years), Mean \pm SD	5.5 \pm 4.2	
BMI, Mean \pm SD	26.95 \pm 4.534	
<i>Joint involvement</i>		
Number of tender joints, Mean \pm SD	5.1 \pm 4.7	
Number of swollen joints, Mean \pm SD	1.9 \pm 2	
Clinical arthritis	24	60.0
Deformity (Jaccoud arthropathy)	6	15.0
<i>Arthritis</i>		
Asymptomatic	14	35.0
Symptomatic	26	65.0
Cutaneous manifestations	30	75.0
Raynaud's	2	5.0
Neurological manifestations	8	20.0
Cardiac manifestations	18	45.0
Pulmonary manifestations	10	25.0
Nephritis	32	80.0
<i>Classes of renal biopsy</i>		
Indicated but the patient refused	6 (15%)	15.0
Not indicated	18 (45%)	45.0
Class III LN	4 (10%)	10
Class IV LN	6 (15%)	15
Class V LN	6	15
ECLAM score, Mean \pm SD	5.2 \pm 2.5	
HAQ score, Mean \pm SD	0.51 \pm 0.3	
<i>Medications</i>		
Pulse IV steroids	22	55.0
IV Cyclophosphamide (CYC)	18	45.0
Prednisolone (oral steroids)	40	100.0
MMF	6	15.0
AZA	10	25.0
HCQ	38	95.0

BMI body mass index; HAQ health assessment questionnaire; CYC Cyclophosphamide; AZA Azathioprine; HCQ Hydroxychloroquine, MMF Mycophenolate mofetil

and diastolic blood pressure (83.5 \pm 19.1) mmHg (Table 1).

While as regards the control group of twenty normal persons, they were predominantly females 16 (80%) also, and 4 males (20%). The mean age was (34.7 \pm 9.9),

the mean BMI was (28.00 \pm 6.974), and the mean systolic blood pressure was (120 \pm 11.2) and diastolic blood pressure (was 76.5 \pm 10) mmHg. So, there was no statistically significant difference between cases and controls regarding their age, sex, BMI, systolic, diastolic blood pressure, and the presence of symptomatic arthritis (P value > 0.05).

The SLE cases had predominant cutaneous manifestations in 30 (75%). There was less incidence of other manifestations such as nephritis in 32 (80%), cardiac manifestations in 18 (45%), pulmonary manifestations in 10 (25%), neurological manifestations in 8 (20%), and Raynaud's in 2 (5%). There were 32 (80%) patients who had LUPUS nephritis detected in clinical and laboratory with the presence of proteinuria with mean urinary albumin/creatinine ratio 1252.4 \pm 1681.4, active urinary sediment, and/or elevated kidney functions. Six of them refused to take a renal biopsy and received a trial of immunosuppressive drugs for further follow-up. Ten of them had microalbuminuria less than 500 mg/dl or had an inadequate renal biopsy for histopathological readings 0.16 patients had documented renal biopsies; six patients had class V LN, six patients had class IV LN and four patients had class III LN. Almost all the studied patients were on HCQ (95%) as a main therapy for all SLE patients unless there was contraindication and low dose oral prednisolone of less than 10 mg daily, 55% had received pulse steroids during the disease to control flares, 45% had received IV CYC as an induction therapy mainly in lupus nephritis or neuropsychiatric manifestations, 25% were on AZA as maintenance therapy and well-tolerated drug, and only 15% were on MMF as a maintenance therapy mainly for LN or pulmonary symptoms due to its high cost as shown in (Table 1). Joint involvement in SLE patients was present in twenty-four patients (60%). They had clinically detected arthritis or arthralgia. The mean number of tender joints was 5.1 \pm 4.7. The mean number of swollen joints was 1.9 \pm 2. Clinically correctable and reversible deformity (Jaccoud arthropathy) appeared in 6 (15%) patients. The disease activity parameters were measured by ECLAM score with mean measures of 5.2 \pm 2.5, and mean HAQ 0.51 \pm 0.3, (Table 1).

The Laboratory characteristics of SLE patients are shown in (Table 2) which illustrated that all patients were positive ANA, 95% were positive dsDNA, high incidence of anemia mainly anemia of chronic illness with mean HB 10.3 \pm 2.5 (gm) and only 2 (5%) patients had AIH (auto-immune hemolytic anemia) with Coombs test positivity. The mean ESR in 1st hour was 50.6 \pm 31.9 which was moderately elevated intermittently during the disease. The mean CRP was 20 \pm 48 (positive If \geq 6 mg/dl). Serum Complement (C3 and C4) were consumed in many cases,

Table 2 Laboratory Data of SLE patients

Parameters	SLE group (No. = 40)
HB g/dl, (Mean ± SD)	10.3 ± 2.5
TLC (× 10 ³), (Mean ± SD)	5.6 ± 1.9
PLT (× 10 ³), (Mean ± SD)	256.5 ± 98.9
ESR (mm/h), (Mean ± SD)	50.6 ± 31.9
CRP mg/dl, (Mean ± SD)	20 ± 48
Creatinine mg/dl, (Mean ± SD)	1.1 ± 0.7
Urinary A/C ratio, (Mean ± SD)	1252.4 ± 1681.4
C3 mg/dl, (Mean ± SD)	68.4 ± 49.6
C4 mg/dl, (Mean ± SD)	8.4 ± 7.9
ANA, No. (%)	40 (100%)
dsDNA, No. (%)	38 (95%)
AIH, No. (%)	2 (5%)

A/C ratio albumin/creatinine ratio; AIH autoimmune hemolytic anemia; ANA antinuclear antibody; anti dsDNA anti-double-stranded DNA antibody; C3 C3 complement fraction; C4 C4 complement fraction; CRP C-reactive protein; ESR erythrocyte sedimentation rate

especially those who had LN activity with mean measures C3 (68.4 ± 49.6) and C4 (8.4 ± 7.9).

Patients and controls underwent bilateral musculoskeletal US examination with PD evaluation of the hand, wrist, and knees. US examinations were performed according to EULAR guidelines for musculoskeletal US in rheumatology [7], the following joints were scanned bilaterally on the dorsal and volar sides to detect any abnormalities such as synovitis, erosions, effusions, osteophytes according to definitions provided by the Outcome Measures in RA Clinical Trials (OMERACT) Special Interest Group for

Musculoskeletal US in Rheumatology [8]. Synovial vascularization was assessed with PD evaluation.

Among the SLE group, abnormal US was found in wrist joints in 14 (35%) among SLE group versus 4 (20.0%) among the control group in the form of carpal tunnel syndrome or mild effusion without erosions or evidence of synovitis by applying PD. As regards the SLE patients, there was synovitis in 6 (15%), erosion in 6 (15%), CTs in 4 (10%), and effusion in 4 (10%), but there was no statistically significant difference between the symptomatic SLE patients, asymptomatic SLE patients and controls regarding the wrist joint manifestations by the US (*P* value > 0.05), (Table 3).

Furthermore, abnormal US findings in knee joints were detected in 26 (65%) patients. It included joint effusion in (40%) of symptomatic lupus patients versus (0.0%) in asymptomatic lupus patients and (10.0%) in the control group. And this finding was the only statistically significant one in the knee US (*P* value = 0.001). Other findings included osteophytes in 10 (5%), erosions in 4 (10%), subcutaneous edema in 4 (10%), and no synovitis, (Table 3) & (Figs. 1, 2, 3, 4).

Regarding the relation between the grades of renal affection in the SLE group and the presence of abnormal findings in the US in knee and wrist joints, the present study revealed that there was no statistically significant relationship between the different classes of renal affection in the SLE group and the presence of abnormal findings in the US in the knee and wrist joints (*P* value > 0.05).

The current study demonstrated that the presence of SLE significantly increases the probability of getting abnormal findings in the knee joint in the US by 28.5

Table 3 Characteristics and Sonographic findings of SLE subgroups (Symptomatic and Asymptomatic) and Control group

Variable	Symptomatic SLE (No. = 16)	Asymptomatic SLE (No. = 24)	Control Group (No. = 30)	<i>P</i> value
Age	30.9 ± 9.1	30.7 ± 6.6	34.7 ± 9.9	0.99
Female/Male	22/4 (55%) / (10%)	12/22 (30%) / (5%)	16/4 (80%) / (20%)	0.02
BMI	28.7 ± 4	23.7 ± 3.7	28.00 ± 6.974	0.001
Overall wrist joint US abnormality	12 (30%)	2 (5%)	4 (20%)	0.03
Synovitis	6 (15%)	0 (0%)	0 (0%)	0.05
Erosion	4 (10%)	2 (5%)	0 (0%)	0.06
Carpal tunnel S	4 (10%)	0 (0%)	4 (20%)	0.55
Effusion	4 (10%)	0 (0%)	2 (10%)	0.55
Overall knee joint US abnormality	22 (55%)	4 (10%)	4 (20%) 16 (80%)	0.001
Synovitis	0 (0%)	0 (0%)	0 (0%)	
Osteophytes	2 (5%)	0 (0%)	0 (0%)	0.60
Erosion	2 (5%)	2 (5%)	0 (0%)	0.51
Effusion	16 (40%)	0 (0%)	4 (20%)	0.001
SC edema	2 (5%)	2 (5%)	0 (0%)	0.51

US ultrasound; SC subcutaneous

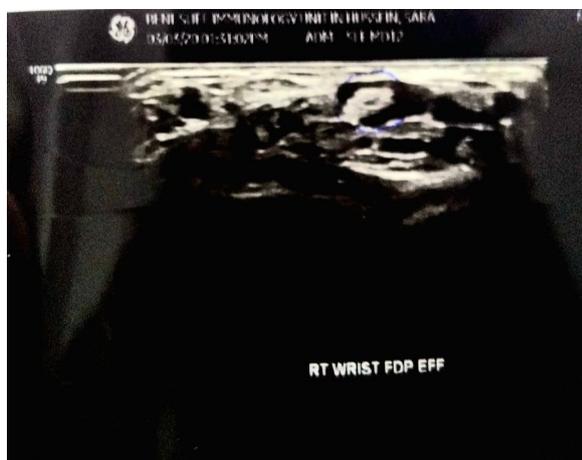


Fig. 2 Hand flexor middle tendons tenosynovitis

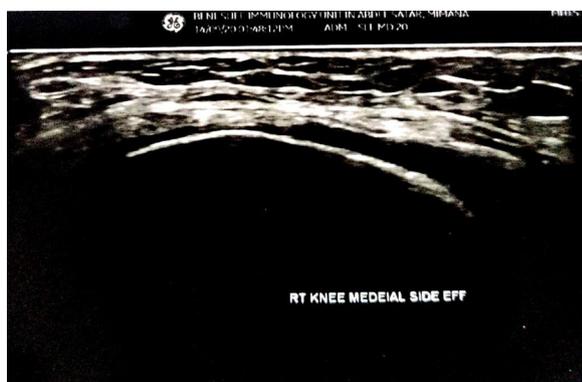


Fig. 3 Right knee effusion

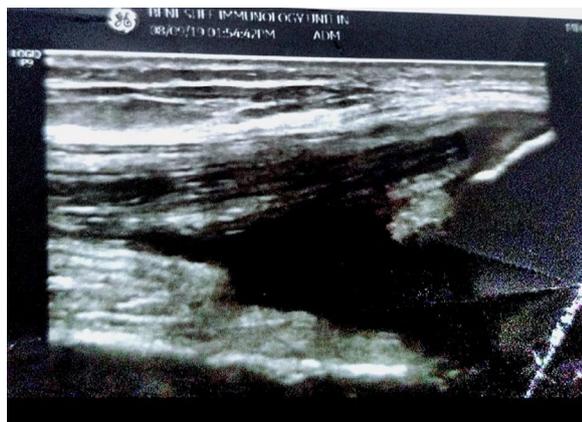


Fig. 4 Marked knee effusion and synovial hypertrophy

times than normal healthy individuals, also increase the age of the patient by 1 year increases the probability of getting abnormal findings in the knee joint with 1.156 times. Moreover, the only independent variable that can

Table 4 Binary logistic regression analysis for prediction of the presence of abnormal findings by the US in the knee and wrist joint from different risk factors (SLE, age, female sex, and SBP)

Independent variables	P value	OR	95% Confidence Interval for OR	
			Lower	Upper
<i>Knee joint</i>				
SLE patients	0.002	28.529	3.303	46.435
Age	0.009	1.156	1.036	1.289
Female sex	0.179	0.262	0.037	1.850
SBP	0.055	1.043	0.999	1.089
<i>Wrist joint</i>				
SLE patients	0.415	1.901	0.405	8.918
Age	0.477	1.029	0.951	1.114
Female sex	0.074	0.177	0.027	1.181
SBP	0.006	1.069	1.020	1.121

affect the acquisition of abnormal findings in the wrist joint detected by the US is the increase of SBP 1 mmHg with 1.06 times (Table 4).

4 Discussion

SLE is a chronic multi-systemic autoimmune disease with a wide spectrum of manifestations, ranging from mild musculoskeletal or mucocutaneous disease to a life-threatening renal, cardiac, or CNS affection. Musculoskeletal symptoms are very familiar and could be the first presenting symptom in 50% of patients and may affect more than 95% of patients during the clinical course [9].

The low prevalence of clinical synovitis makes recognition of musculoskeletal disease activity very challenging. These have significance for the selection of patients for immunosuppressive drugs and evaluating the responses to these therapies. As well as the assessment of musculoskeletal disease activity, MS ultrasonography may also be used to recognize the pathogenesis of associated arthritis. For example, SLE joint involvement has conventionally been sorted clinically into Rhupus (RA/SLE overlap syndrome), Jaccoud’s arthropathy (shows little or no evidence of synovitis or erosions on conventional radiographs but with apparent extensive deformities in hands and feet) and non-erosive non-deforming arthropathy [10]. However, the nature of hand, wrist, and feet US abnormalities are variable and the overall prevalence published findings range between 58 and 100% [11].

The present study agreed with Abdel-Magied et al. [12] who studied thirty SLE patients and 20 controls. The mean age of lupus patients was 28.9±8.7 years. They were 28 females and 2 males with a disease duration of 8.9±1.7 years. Arthritis was identified clinically in 18 patients, MSUS detected synovitis in 20 patients;

tenosynovitis was clinically presented in 50% and 56.7% by MSUS. Ten patients with arthritis had PD signals, and erosions were detected in 7 of them. SLEDAI-2 k significantly correlated with GSUS, PDUS, erosions, and tenosynovitis. HAQ-DI significantly correlated with the GSUS, erosions, and tenosynovitis.

According to Zayat et al. [11] erosive arthritis had been detected in lupus patients with arthritis and influenced disease activity and functional status. Together with Torrente-Segarra et al. [6] they concluded that articular affection in SLE may contribute to deteriorated functional ability and the quality of life and PDUS is a reliable tool for its assessment.

On the other hand, Iagnocco et al. [13] and Delle Sedie et al. [14] reported that there was no significant correlation between systemic disease activity and US findings.

In the present study, six SLE patients having clinical deforming arthropathy (JA) were detected to have US abnormalities in the wrist and hand examination in form of synovial hypertrophy and or tenosynovitis with PD signal, erosions, and effusion. Gabba et al. [15] studied 108 cases of SLE using US examination and found that 6 patients had JA and four had US abnormalities; tendon involvement was detected in 3 patients, effusion was detected in 2 patients (wrist, second and third MCP joints), and erosion was detected in one patient. Wright et al. [16] studied 17 patients with SLE, and “some of them” were also diagnosed as having JA. As they had not specified the number of patients with JA, it was not possible to conclude from the US findings in those patients. Similarly, Dreyer et al. and Mosca et al. [17] also studied 2 and 10 patients diagnosed as having JA, respectively, and did not describe the US findings’ details.

Buosi et al. [18] studied 62 patients with SLE, among which 7 patients had JA, and 10 erosions were identified by the US examination, but they did not mention how many participants had these findings.

According to Ruano et al. [19] SH (Synovial Hypertrophy) index was higher in the asymptomatic SLE group than in the control group. On contrary, it was lower than in the symptomatic SLE group. No significant correlation was demonstrated between US PD findings and clinical or laboratory variables and disease activity indices. Contrary to our study, there was a significant correlation between US findings and clinical or laboratory variables and disease activity indices.

The current study showed that there was no relation between the incidence of LN and the presence of abnormal findings in the US in the knee and wrist joints (P value > 0.05). So LN and arthritis are considered two separate entities of SLE activity manifestations.

Moreover, the current study revealed that SLE could be considered a risk factor for getting true joint affection

whether detected clinically or by MSUS than normal individuals. Some studies have suggested an association between US abnormalities and SLE disease activity measures; nevertheless, one study found the opposite [20].

The presence of SLE increases the risk of US abnormalities in knee joints 28 times than controls, while the only independent variable that can affect US abnormal findings in the wrist joint is the increase of SBP 1 mmHg with 1.06 times.

(SLE) is associated with a high burden of cardiovascular disease (CVD), such as hypertension. Hypertension is frequent among patients with SLE and studies show it is more prevalent in SLE patients than in people without SLE. There is no obvious cause can explain the high incidence of hypertension in SLE patients, but many theories may give explanation as treatment with corticosteroids, immune-suppressants, and non-steroidal anti-inflammatory drugs, widely used for the control of inflammatory symptoms, may cause, among other complications, BP elevation or the worsening of existing essential hypertension, which may have deleterious health effects. Renal disease, which occurs in the natural evolution of some systemic autoimmune diseases, may also result in secondary arterial hypertension. Chronic vascular inflammation, a hallmark of SLE, may contribute to the development of vascular stiffness. Immune complexes may act as a source of arterial injury and can upregulate specific adhesion molecules involved in the atherogenic step of binding and recruiting monocytes/macrophages and T-lymphocytes. Immune complex deposition into the glomeruli can also result in nephritis and hypertension. The acute-phase response might increase the risk of vascular disease. This inflammatory mediators can contribute also in developed arthritis of both wrist and knees joints in SLE patients as one of activity manifestations. So, there is positive correlation between cardiovascular complications such as hypertension and developing arthritis in SLE patients as a part of chronic inflammatory disease activity.

The current study had many limitations. The first of them was the small sample size which may reduce the general inability. The second one was the highly prevalent steroid used among SLE patients which reduces the global inflammatory burden and the prevalence and grading of the US PD findings. Furthermore, the intake of non-steroidal anti-inflammatory drugs at the time of US imaging is considered a potential confounder in US PD evaluation. Even though the subclinical joint abnormalities detected by the US have been previously associated with the development of musculoskeletal symptoms, the prognostic benefit of these findings continues to be determined. So, we recommend larger longitudinal studies to confirm the significance of subclinical US PD

findings, specifically the predictive value for the development of long-term joint damage.

5 Conclusion

The present study demonstrated that MSUS with applied PD is a good tool for the detection of early affection of joints either in symptomatic or asymptomatic SLE patients. There was a statistically significant prevalence of US abnormality of knee joints in both asymptomatic and symptomatic cases versus controls contrary to the wrist and hand US abnormality. The presence of SLE increases the risk of US abnormalities in knee joints 28 times more than controls, while the only independent variable that can affect US abnormal findings in the wrist joint is the increase of SBP 1 mmHg with 1.06 times.

Abbreviations

ACR	An American Colleague in Rheumatology
AIHA	Autoimmune hemolytic anemia
ANA	Anti-nuclear antibody
Anti-ds DNA	Anti-double stranded
AZA	Azathioprine
BMI	Body mass index
C3	Complement 3
C4	Complement 4
CNI	Calcineurin inhibitor
CRP	C-reactive protein
CsA	Cyclosporin A
CTS	Carpal tunnel syndrome
CYC	Cyclophosphamide
DBP	Diastolic blood pressure
DIPs	Distal interphalangeal
DMARD	Disease-modifying anti-rheumatic drugs
ECLAM	European Consensus Lupus Activity Measurement
Emps	Enteric-coated tablets of mycophenolate sodium
ESR	Erythrocyte sedimentation rate
GCs	Glucocorticoids
GSUS	Gray-scale ultrasound
HAQ	Health assessment questionnaire
HCQ	Hydroxychloroquine
IV	Intravenous
IVIG	Intravenous immunoglobulin
JA	Jaccoud's arthropathy
LN	Lupus nephritis
MMF	Mycophenolate mofetil
MS	Musculoskeletal
MSUS	Musculoskeletal ultrasound
MTX	Methotrexate
NDNE	Non-deforming non-erosive
OMERACT	Outcomes Measures in Rheumatology Clinical Trials
PD	Power Doppler
PDUS	Power Doppler ultrasound
PIPs	Proximal interphalangeal
PLT	Platelet
PSA	Psoriatic arthritis
RA	Rheumatoid arthritis
RBCs	Red blood cells
SBP	Systolic blood pressure
SH	Synovial hypertrophy
SJ	Swollen joint
SLE	Systemic lupus erythematosus
SLEDAI	SLE Disease Activity Index
SLICC	Systemic Lupus International Collaborating Clinics
TJ	Tender joint

TLC	Total leucocytic count
U.ALB/CREAT	Urinary albumin creatinine ratio
WBCs	White blood cells

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Author contributions

SHE and HAT conceived and designed the study. SHE analyzed and interpreted data. SHE wrote the first and final draft of the manuscript under the supervision of MF, MNS, and TMA. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

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Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Declarations

Ethics approval consent to participate

The study protocol was following the Helsinki Declaration of human rights and is approved by the Faculty of Medicine Beni-Suef University Research Ethics Committee (FM-BSU REC) dated the seventh of March 2018, approval no: FWA 00015574. Written informed consent was obtained from each patient and control.

Consent for publication

Consent for publication was obtained from all participants.

Competing interests

We declare that this manuscript is original, has not been published before, and is not currently being considered for publication elsewhere. We know of no conflicts of interest associated with this publication, and there has been no significant financial support for this work that could have influenced its outcome.

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