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Musculoskeletal Ultrasound Assessment of Subclinical Arthritis in Systemic Lupus Erythematosus

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ABSTRACT

Background: Systemic lupus erythematosus (SLE) is a global chronic autoimmune disease (AID) that affects different body tissues. Radiological approaches in systemic lupus erythematosus (SLE) assist in confirming the diagnosis, monitoring disease progression, and improving the understanding of the pathological basis for its manifestations.

Aim: This study aimed to evaluate the role of musculoskeletal ultrasound (MSUS) in detecting subclinical arthritis in lupus and lupus nephritis (LN) patients.

Methods: This prospective cross-sectional study was conducted on 50 Lupus nephritis patients diagnosed based on International Society of Nephrology\Renal Pathology (ISN\RPS) and 50 lupus patients diagnosed based on systemic lupus international collaborating clinics (SLICC) classification criteria 2012. Renal biopsy detected classes, activity and chronicity of lupus nephritis. Evaluation of disease activity was done using the SLE Disease Activity Index (SLEDAI-2K) score. Assessment of arthritis of the joints was done using a grey-scale ultrasound.

Results: The results showed that 61% of studied cases had mild to moderate disease activity, 35% had severe activity according to SELDAI 2k score. There was no statistically significant difference between SLEDAI-2K score and radiocarpal and metacarpophalangeal joint findings including synovitis, synovial hypertrophy (SH), tenosynovitis and effusion. There was statistically significant association detected between presence of Achilles bursa and disease severity, where the more severity of the disease. There was a significant correlation between duration of disease and radiocarpal affection and ulnocarpal affection and intercarpal affection in LN patients with stage IV and V.

Conclusion: MSUS had a valuable role in detecting subclinical arthritis and it provided data on different pathophysiological aspects on joint affection. Interestingly MSUS showed a statistically significant correlation between affected joints and disease duration.

Keyword: Systemic lupus erythematosus, Musculoskeletal ultrasound, SLEDAI.

INTRODUCTION

Systemic lupus erythematosus (SLE) is a global chronic autoimmune disease (AID) that affects different body tissues. Genetic liability, environmental factors, and the hormonal changes play essential role in SLE development and activity [1], in which the immune system attacks its own tissues, causing extensive inflammation and tissue damage. It may affect several tissues, however the most common presentation is musculoskeletal, while the most dangerous is lupus nephritis (LN) [2]. Its pathogenesis is complicated, and is constantly evolving. A break in tolerance in genetically vulnerable subjects upon exposure to environmental factors activates autoimmunity. Cell damage from infections and environmental factors triggers the immune system to react to self-antigens, causing the chronic activation of T and B cells in a self-sustained immune response. Cytokine production, complement stimulation, and autoantibody production have been demonstrated to be associated with organ damage [3].

Musculoskeletal manifestations, which include arthralgia and arthritis have been recorded in about 85% of SLE cases. Although any joint could be affected most frequently, there is symmetrical affection of small joints which include hands, wrists, and knees. The name "ruphus" describes SLE arthritis, which shows a comparable presentation to rheumatoid arthritis (RA) and includes ulnar deviation and subluxation of the metacarpophalangeal joints [4].

The diagnosis of SLE is difficult, as no single clinical sign or lab abnormality could confirm the diagnosis. SLE diagnosis is mainly reliant on the group of manifestations and proper laboratory analysis. In addition, radiological techniques and histopathology might have an essential role. Multiple autoantibodies have been defined in SLE, with different sensitivity and specificity, which include antinuclear antibodies (ANA) and anti-double stranded DNA (anti-dsDNA) antibodies. While some autoantibodies could be accompanied by a particular clinical subset of SLE, others could act as a marker of disease activity [5]. Radiological approaches in RA and SLE could support diagnosis, follow-up of disease progression, and improving the identification of the pathologic basis for their manifestations. Radiographic imaging is reproducible, broadly available, and validated for erosive changes. Magnetic resonance imaging (MRI) and musculoskeletal ultrasound (MSUS) are well-approved approaches for detection of initial changes and follow-up disease activity in cases with RA [6]. The role of ultrasound (US) with power Doppler (PD) in inflammatory arthritis has been widely reported, with identical validity in the determination of synovitis compared to MRI, with the benefit of being available and cheap. Although US displays the morphology of the synovial membrane, PD detects the increase in vascularization within it, permitting the determination of active joint inflammation [7].

The presence of joint effusion, synovial hypertrophy (SH), bony erosions, and tenosynovitis was assessed

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using Outcome Measures in Rheumatology Clinical Trials definitions**,** and described Joint synovitis as the presence of joint effusion and/or SH [8].

Bony erosions were described as a cortical defect in the bone surface, noticed in the transverse and longitudinal scans. Tenosynovitis is characterized by hypoechoic or anechoic thickened tissue, with or without fluid, observed in two perpendicular planes within the tendon sheath. PD was conducted to assess the vascularity of joints and tendons [9]**.** Thus, this study aimed to evaluate the role of musculoskeletal ultrasound (MSUS) in detecting subclinical arthritis in lupus and lupus nephritis patients and to correlate these findings with lupus disease activity using standard disease activity score index (SLEDAI-2K).

PATIENTS AND METHODS

This prospective cross-sectional study was conducted on 50 Lupus nephritis patients diagnosed based on ISN\RPS and 50 lupus patients diagnosed according to SLICC classification criteria 2012 (as control group) attending Rheumatology & Immunology Unit of Internal Medicine Department, Mansoura University Hospital over a period of one year. SH and intra-articular PD signal were scored using semiquantitative grading scales (zero–III). Individual scores were graded as normal (SH≤I and PD=zero) or abnormal (SH≥II or PD≥I). In addition, Global indexes for SH and PD were calculated too.

Exclusion criteria: Patients who did not fulfill the SLICC criteria for diagnosis of SLE or for diagnosis of Lupus nephritis, lupus patients who presented or develop arthritis during their disease course, lupus patients with other associated autoimmune disease (Rhupus or Overlap syndrome) and lupus patients with known osteoarthritis, traumas or surgeries of examined joints.

Methods: A full lupus history was taken, including the onset, course, and duration of the disease and manifestations of various system affections. A complete clinical examination was performed with a special focus on lupus manifestation and on renal involvement. Laboratory investigations comprised complete blood count (CBC), kidney and liver function tests, urine analysis, total 24 h urinary proteins, erythrocyte sedimentation (ESR), C-reactive protein (CRP), ANA, anti-dsDNA antibodies and serum complement levels (C3, C4). Renal biopsy detected classes, activity and chronicity of lupus nephritis. Assessment of disease activity was conducted using the SLEDAI-2K score. Assessment of arthritis of the joints was done using a Logiq E9 machine (General Electric Medical Systems Milwaukee, USA) conventional grey-scale ultrasound machine with a 6-12 MHz linear array probe operating at 12 MHz. PD assessments was conducted with a PD frequency of 10 MHz, gain fifty percent and low wall filter.

All patients were examined in the sitting position with examined joint in resting position, using a multiplanar scanning approach based on European Alliance of Association for Rheumatology (EULAR) guidelines for musculoskeletal US in rheumatology. During ultrasound examination, a proper amount of warm gel was used and compression with the probe was avoided, to precisely assess synovial vascularization. All joints were scanned bilaterally. Ultrasound evolution of SH and synovial vascularity with PD was done based on definitions provided by the Outcome Measures in RA Clinical Trials [10].

Ethical considerations: Throughout its implementation, the study complied with the Helsinki Declaration. Approval was taken from Mansoura University Institutional Ethics Committee (Code number MS.23.05.2415). An informed written consent was taken from each patient. All patients were informed about the study design. Data were collected by the researcher himself.

Statistical analysis

Data were fed to the computer and analyzed using IBM SPSS 20.0. Qualitative data were defined using number and percent. Quantitative data were defined using median for non-parametric variables and mean, SD for parametric variables following testing normality using Kolmogorov-Smirnov test. All tests were 2-tailed. The student t-test was used to compare continuous data, and the Chi-square test was used for categorical data. U test was used for quantitative non-parametric variable, to compare between 2 groups, whereas Kruskal Wallis Test post Hoc was used to detect any significance among three or more groups. Relation between variables was done by Spearman correlation coefficient. P-values ≤ 0.05 were considered statistically significant.

RESULTS

Table (1) demonstrated that among 100 cases with systemic lupus, mean age was 33.80 ± 11.42 years ranging from 17 to 70 years, 86% were females, 50% rural residence, 26% are working, 93% were non-smokers, 28% had previous history of abortion with median number of abortions was 0 (0 to 5). As regards systemic lupus history, 36% were chronic onset, 41% insidious and 23% acute onset. 56% had progressive course and 44% were regressive. Median disease duration was 3 years (1 to 19) years. The Presenting lupus symptoms showed that 46% combined, 19% renal, 17% dermatology, 12% hematology, 4% serositis and 2% neurological symptoms and 43 % of our cases classified as lupus nephritis by renal biopsy. Median hemoglobin level was 9.9 gm/dl, median WBCS count was 6.5^3 µL, median platelet count was 234, median creatinine level was 0.9 mg/dl, median serum albumin was 3.2 gm/dL, median AST was 20 (9 to 94) U/L, median ALT was 21, median ESR was 80 mm/h, median CRP was 12 mg/L, median ANA was 87.5, median Antids-DNA was 67.5, median C3 was 60 mg/dl, median 24 h urinary protein was 306.5 mg/24 hour, 35% of cases had pus in urine, 29% RBCS in urine and 44% protein in urine.

Table (1): Socio-demographic data, lupus history and laboratory findings of studied lupus patients (n=100)

Personal history		n %
Age /year mean (±SD)*		33.80±11.42 (17-70)
Gender		
Male		14 (14%)
Female		86 (86%)
Residence	Rural	50 (50%)
	Urban	50 (50%)
Occupation	Not worker	74 (74%)
	Worker	26 (26%)
Special habits	Smoker	93 (93%)
	Non smoker	7 (7%)
Abortions	No abortions	76 (76%)
	Abortion	24 (24%)
No. of abortions. Median (min-max)#		0(0-5)
Lupus history		
Onset	Acute	23 (23%)
	Insidious	41(41%)
	Chronic	36 (36%)
Course	Progressive	56 (56%)
	Regressive	44 (44%)
Duration (years) Median (min-max)		3(1-19)
Presenting symptom		
Hematology		12 (12%)
Renal		19 (19%)
Serositis		4 (4%)
Neurology		2 (2%)
Dermatology		17 (17%)
Combined*		46 (46%)
Complications		
-ve		58 (58%)
+ve		42 (42%)
Lupus nephritis (biopsy proved)		
Yes		43 (43%)
No		57 (57%)
Laboratory Findings		
HB (g/dl)		9.9(3.2-16.2)
WBCs (10^3/µL)		6.5(1.6-17)
Platelets (10^3/µL)		234(29-851)
Creatinine(mg/dL)		0.9(0.3-6.2)
s. Albumin (g/dL)		3.2(1.4-4.8)
AST(U/L)		20(9-94)
ALT (U/L)		21(3-53)
ESR (mm/h)		80(8-150)
CRP (mg/L)		12(0-263)
ANA		87.5(2.4-500)
Anti dsDNA (IU/mL)		67.5(3-1687)
C3 (mg/dl)		60(20-161)
C4 (mg/dl)		8(2-39)
24 h urinary protein (mg/24h)		306.5(32-45000)
Urine analysis*		
Pus		35.0%
RBCs		29.0%
ptns		44.0%

*mean (±SD), #median (min-max).

Table (2) illustrated MSUS of different enthesopathy, where only 1 patient had thickened proximal part of patellar tendon with irregular appearance, Doppler activity and enthesitis. While, at distal part of patellar tendon, only 3 patients had hyperechoic appearance and 25 of them showed enthesitis, with no other findings such as bursa or tear, 30 patients had mild grade of prepatellar effusion, meanwhile 24 patients had moderate grades of effusion. About 44 of our patients suffered from bursa at Achilles tendon, while 30 patients had enthesitis. There was no significant finding detected at the planter fascia except one patient had enthesitis.

Table (2): Musculoskeletal ultrasound finding of Enthesopathy (patellar, Achilles tendon and patellar fascia) among studied patients (n=100)

	Patellar tendon		**Achilles tendon (n)**	**Planter fascia(n)**
	Proximal (n)	Distal(n)		
Thickness 0=normal 1=thick	 99 1	 100 0	 100 0	 100 0
Regularity 0=regular 1=irregular	 99 1	 100 0	 100 0	 100 0
Echogenicity **0=normal** 1=hypoechoic **2=**hyperechoic	 96 0 4	 97 0 3	 95 2 3	 100 0 0
Bursa	0	0	44	0
Tear	0	0	0	0
Doppler activity	1	0	0	0
Enthesitis 0=no 1=yes	 99 1	 75 25	 70 30	 99 1
Prepatellar effusion No Mild Moderate	 46 30 24			

Figure **(1)** showed that 61% of studied cases had mild to moderate disease activity, 35% had severe activity and 4% of them had no flare according to SELDAI 2k score.

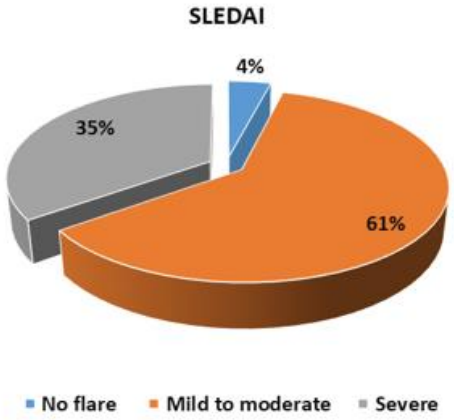

Figure (1): Disease activity score of studied patients according to (SLEDAI-2K 2k) score.

Table (3) demonstrated no statistically significant difference between SLEDAI-2K score assessing disease activity and radiocarpal findings including degree of synovitis (p=0.400), degree of synovial hypertrophy (p=0.630), degree of tenosynovitis (p=0.194) and degree of effusion (p=0.145).

There was no statistically significant difference between SLEDAI-2K score assessing disease activity and metacarpophalangeal joint findings including degree of synovitis (p=0.831), degree of synovial hypertrophy (p=0.726), degree of tenosynovitis (p=0.729) and degree of effusion (p=0.763).

Table (3): Relation between SLEDAI-2K score and Radio-carpal and MCP joints findings among studied patients (n=100)

Radiocarpal	**No flare N=4**	**Mild to moderate N=61**	**Sever N=35**	**Test of significance**	**P value**
Synovitis					
0=no	3(75)	28(45.9)	18(51.4)	6.22	0.400
1=mild	1(25)	26(42.6)	9(25.7)		
2= moderate	0	7(11.5)	7(20)		
3=sever	0	0	1(2.9)		
Synovial hypertrophy					
0=no	3(75)	31(50.8)	16(45.7)		
1=mild	1(25)	26(42.6)	14(40)	4.35	0.630
2= moderate	0	3(4.9)	5(14.3)		
3=sever	0	1(1.6)	0		
Tenosynovitis					
0=no	3(75)	26(42.6)	14(40)	8.65	0.194
1=mild	0	20(32.8)	6(17.1)		
2= moderate	1(25)	12(19.7)	9(25.7)		
3=sever	0	3(4.9)	6(17.1)		
Effusion					
0=no	3(75)	35(57.4)	17(48.6)	9.54	0.145
1=mild	0	22(36.1)	9(25.7)		
2= moderate	1(25)	4(6.6)	8(22.9)		
3=sever	0	0	1(2.9)		
MCP					
Synovitis					
0=no	3(75)	36(59)	19(54.3)	2.82	0.831
1=mild	1(25)	17(27.9)	11(31.4)		
2= moderate	0	8(13.1)	4(11.4)		
3=sever	0	0	1(2.9)		
Synovial hypertrophy					
0=no	3(75)	36(59)	22(62.9)	2.05	0.726
1=mild	1(25)	18(29.5)	7(20)		
2= moderate	0	7(11.5)	6(17.1)		
Tenosynovitis					
0=no	3(75)	34(55.7)	18(51.4)	3.61	0.729
1=mild	0	13(21.3)	5(14.3)		
2= moderate	1(25)	8(13.1)	8(22.9)		
3=sever	0	6(9.8)	4(11.4)		
Effusion					
0=no	3(75)	38(62.3)	19(54.3)	3.35	0.763
1=mild	0	15(24.6)	9(25.7)		
2= moderate	1(25)	7(11.5)	5(14.3)		
3=sever	0	1(1.6)	2(5.7)		

Used test: Chi-Square test and Fisher exact test, data expressed as number (%)

Table (4) demonstrates that there was no statistically significant relation between disease severity assessed using SLEDAI-2K score and Patellar tendon (Proximal) findings including thickness (p=0.391), regularity (p=0.724), echogenicity (p=0.724) and enthesitis (p=0.391). Also, there was no statistically significant relation between disease severity and Patellar tendon (distal) findings including echogenicity (p=0.497) and enthesitis (p=326). For Achilles tendon, the only statistically significant association detected between presence of bursa and disease severity (p=0.047), where the more severity of the disease, the more likely to find Achilles bursa. For planter fascia and Tennis elbow, there was no statistically significant association with disease severity.

Table (4): Relation between SLEDAI-2K score and enthesopathy (patellar, Achilles tendon and patellar fascia) among studied patients (n=100)

	No flare N=4	**Mild to moderate N=61**	**Sever N=35**	**Test of significance**	**P value**
Patellar tendon (Proximal)					
Thickness 0=normal 1=thick	 4(100) 0	 61(100) 0	 34(97.1) 1(2.9)	1.88	0.391
Regularity 0=regular 1=irregular	 4(100) 0	 60(98.4) 1(1.6)	 35(100) 0	0.646	0.724
Echogenicity 0=normal 2=hyperechoic	 4(100) 0	 60(98.4) 1(1.6)	 35(100) 0	0.646	0.724
Enthesitis 0=no 1=yes	 4(100) 0	 61(100) 0	 34(97.1) 1(2.9)	1.88	0.391
Patellar tendon (Distal)					
Echogenicity 0=normal 2=hyperechoic	 4(100) 0	 60(98.4) 1(1.6)	 3(94.3) 2(5.7)	1.39	0.497
Enthesitis 0=no 1=yes	 4(100) 0	 47(77) 14(23)	 24(68.6) 11(31.4)	2.24	0.326
Achilles tendon					
Echogenicity 0=normal 1=hypoechoic 2=hyperechoic	 4(100) 0 0	 59(96.7) 2(3.3) 0	 32(91.4) 0 3(8.6)	6.93	0.140
Bursa 0=no 1=yes	 4(100) 0	 37(60.7) 24(39.3)	 15(42.9) 20(57.1)	6.13	0.047*
Enthesitis 0=no 1=yes	 3(75) 1(25)	 41(67.2) 20(32.8)	 26(74.3) 9(25.7)	0.579	0.749
Planter fascia					
Enthesitis 0=no 1=yes	 4(100) 0	 61(100) 0	 34(97.1) 1(2.9)	1.88	0.391
Tennis elbow					
Echogenicity normal Hyperechoic	 4(100) 0	 60(98.4) 1(1.6)	 35(100) 0	0.646	0.724
Bursa	0	1(1.6)	2(5.7)	1.39	0.497

Concerning musculoskeletal ultrasound findings of wrist joints and disease characteristics, table (5) showed that there was a significant correlation between duration of disease and radiocarpal affection (synovitis, synovial hypertrophy, tenosynovitis and joint effusion) in LN patients with stage IV and V. There was a significant correlation between duration of disease and ulnocarpal affection (synovial hypertrophy and joint effusion) in LN patients with stage IV and V and there was also a significant correlation between duration of disease and intercarpal affection (tenosynovitis and joint effusion) among LN patients with stage IV and V.

Table (5): Correlation between disease characteristics and musculoskeletal ultrasound finding of wrist joints among severe LN cases (n=35)

		Onset	Course	Duration	Activity Index	Chronicity Index
Rad_car_synovitis	**r**	**.123**	**-.020-**	**.345**	**-.164-**	**-.083-**
	P value	**.483**	**.907**	**.043**	**.347**	**.636**
RC_syn_hypertrophy	**r**	**.032**	**-.098-**	**.336**	**-.093-**	**-.002-**
	P value	**.857**	**.574**	**.048**	**.595**	**.992**
RC_tenosynovitis	**r**	**.051**	**-.024-**	**.378**	**-.026-**	**.041**
	P value	**.770**	**.893**	**.025**	**.882**	**.814**
RC_effusion	**r**	**.114**	**.016**	**.447**	**-.125-**	**-.044-**
	P value	**.516**	**.926**	**.007**	**.475**	**.804**
Ulna-carpal synovitis	**r**	**.055**	**.105**	**.320**	**-.119-**	**-.033-**
	P value	**.753**	**.547**	**.061**	**.496**	**.851**
UC_syn_hypertrophy	**r**	**.066**	**-.028-**	**.408**	**-.009-**	**.056**
	P value	**.706**	**.871**	**.015**	**.957**	**.751**
UC_tenosynovitis	**r**	**.004**	**-.012-**	**.290**	**.037**	**.104**
	P value	**.983**	**.946**	**.092**	**.832**	**.550**
UC_effusion	**r**	**.091**	**.033**	**.431**	**-.046-**	**.027**
	P value	**.604**	**.853**	**.010**	**.793**	**.878**
inter-carpal synovitis	**r**	**.046**	**-.016-**	**.263**	**-.160-**	**-.079-**
	P value	**.791**	**.926**	**.127**	**.358**	**.653**
IC_syn_hypertrophy	**r**	**.030**	**-.033-**	**.296**	**-.054-**	**.014**
	P value	**.864**	**.853**	**.084**	**.756**	**.937**
IC_tenosynovitis	**r**	**.032**	**-.012-**	**.374**	**-.005-**	**.063**
	P value	**.855**	**.946**	**.027**	**.976**	**.721**
IC_effusion	**r**	**.141**	**.073**	**.457**	**-.196-**	**-.120-**
	P value	**.420**	**.678**	**.006**	**.260**	**.491**

DISCUSSION

Systemic lupus erythematosus is a global chronic AID, which may affect every organ and tissue. Genetic liability, environmental factors, and the hormonal changes, interplay in disease development and activity [1]. LN is an inflammatory state of the kidneys that includes different patterns of renal disease comprising glomerular and tubulointerstitial pathology. It is a main predictor of poor prognosis in patients with SLE [11].

Musculoskeletal manifestations in SLE cases can include arthritis, tenosynovitis, transient or migratory arthralgia and non-specific musculoskeletal symptoms without conclusive objective clinical signs. Despite the absence of clinical synovitis in many patients, musculoskeletal manifestations cause significant disability, loss of function and socio-economic impact [12]. Ultrasound is a non-invasive diagnostic technique with good accuracy in the determination of joint effusion, assessment of integrity of tendons and muscles, and visualization of cartilage/bone surface. The main benefit of the US is its ability to identify findings even at the subclinical stage [13].

So, our study aimed to evaluate the role of musculoskeletal ultrasound (MSUS) in detecting subclinical arthritis in lupus and lupus nephritis patients and to correlate these findings with lupus disease activity using standard disease activity score index (SLEDAI-2K score). It was noticed that the majority of studied patients were middle-aged females, which is in agreement with **Siegel and Sammaritano** [14] who displayed that women are more likely than males to have SLE.

By evaluation of the patients' risk of having an a bortion, there were about 28% of studied patient were aborted, which is lower than that in the study conducted by **Sieiro Santos *et al.*** [15] who said that 42% of studied patients were linked to adverse outcomes. The difference can result from orientation and improvement of knowledge of both patients and medical personnel about SLE patients' obstetric health and adherence to medical services.

In our study, we observed that near half of studied patients had an insidious onset of SLE which is consistent with **Frankovich *et al.*** [16] who found that 75% of his studied group had an insidious onset while 40% had an acute one.

In the current study, disease duration (from the start of SLE symptoms to diagnosis) was about 3 years that is in disagreement with **Tarr *et al.*** [17] who said that mean disease duration was 17 years and this may be due to availability of health care centre, early diagnosis, early treatment and increase awareness among general population.

We demonstrated that half of the studied SLE patients had lupus nephritis proved by renal biopsy, which is in the same line with **Mahmood *et al.*** [18] who displayed that kidney is the most frequently comprised visceral organ to be affected in SLE and the importance of doing renal biopsy for histopathological findings.

Antinuclear antibodies (ANA) is an antibody which was commonly positive in most of studied patients. This is consistent with **Andrade *et al.*** [19] who concluded that ANA was a major entity in diagnosis of SLE that reflect the importance of ANA as screening tool among SLE patients.

We noticed that Anti-dsDNA antibodies was positive in most of studied SLE patients which is in accordance with **Qu *et al.*** [20] who found that Anti-dsDNA antibodies were highly positive in sensitivity and specificity in diagnosis of SLE. Most of studied lupus patients had microproteinuria that reflects efficient management of our studied patients that was matched with **Kharouf *et al.*** [21] who stated that around 60% of his studied patients had low level proteinuria and added that treatment efficiently reduced range of proteinuria in SLE patients.

It was noticed that ESR was elevated in most of studied patients and this is in accordance with **Schäfer *et al.*** [22] who revealed that ESR was elevated in patients with SLE flare that reflect the impact of ESR to predict the disease activity.

It was observed that most of studied patients had mild to moderate disease activity according to SLEDAI-2K score and this is similar to **Pedro *et al.*** [23] who demonstrated that half of his examined patients had mild to moderate disease activity that reflect remission of disease after effective treatment.

By assessment of the SLEDA, it was noticed that there was insignificant difference between SLEDAI-2K score and examined joints by MSUS, which is in agreement with **Zayat *et al.*** [12] who showed that there was poor to moderate relationship between US abnormalities and disease activity indices and immunologic findings**.** On the other hand, the study conducted by **Shedid *et al.*** [24] concluded that there was a significant correlation between US-detected synovitis and higher SLEDAI-2K score and anti-dsDNA titer. These wide variations may be due to different sample sizes, number of joints assessed per patient.

MSUS examination of wrist and hand revealed that less than half of our studied patients had synovitis and synovial effusion and there was neither bone erosion, osteophyte nor PD activity that was matched with the study conducted by **Hua-Li *et al.*** [25] who concluded that Musculoskeletal US is highly sensitive in assessing subclinical synovitis in cases with SLE.

It was observed that half of our studied patients had mild grade of synovitis in MCP, PIP and DIP and that was in agreement with **Salliot *et al.*** [26] who found 61 of his examined patients had synovitis mainly located at metacarpophalangeal joint and wrist which reflect the importance of MSUS in detecting synovitis among lupus patients.

It was noticed that most of examined patients had mild grade SH in flexor and extensor tendons by MSUS, which is consistent with the study conducted by **Dörner *et al.*** [6] who reported an increased presence of SH in the wrists of SLE patients, that reflect the importance of MSUS examination of wrist to detect abnormal pathology in SLE patients.

We noticed that minority of examined cases had abnormal size in median nerve with compression manifestation, which is in contrast with **Mahran *et al.*** [27] who mentioned that 56% of patients developed abnormal ultrasound finding in median nerve by MSUS. This discrepancy may be attributed to MSUS, which is a physician dependent and the well-known high sensitivity, reliability and detective power of combination of electrodiagnosis and ultrasound.

During demonstration of knee, we found significant prepatellar effusion with different grades (mild, moderate and severe) that is in agreement with **El genedi *et al.*** [28] who displayed knee effusion in 40% of his examined patients, which supports that small and large joints may be affected in SLE.

About half of our studied patients had retrocalcaneal bursa by MSUS, which is against the study conducted by **Emerah *et al.*** [29] who found that around 11% of SLE patients had retrocalcaneal bursa. This difference was due to effective management of his patients with high doses of corticosteroid that helped in regression of bursa.

We observed that most of our lupus nephritis patients had positive Anti-ds-DNA and had a significant positive correlation with disease activity that is matched with **Mavragani *et al.*** [30] who found Anti-ds-DNA positive in 76% of his examined patients and added the impact of using Anti-ds-DNA as a risk factor for proliferation of nephritis.

We noticed that in our examined LN patients who staged class (IV and V), they had a positive significant correlation between activity index and 24 h urinary protein, which is matched with **Yuan *et al.*** [31] who said that 24-hour proteinuria was significantly increased in cases with active LN compared to inactive LN.

It was observed that there was positive correlation between joint affection of radiocarpal joint (synovitis, SH and effusion) with duration of disease and that is matched with **Guillén-Astete *et al.*** [32] who concluded that the finding of subclinical synovitis in patients with SLE is accompanied by the development of joint disease progression clinically and ultrasonographically.

The current study displayed that there was significant relationship between SH of ulna-carpal joint and disease duration, which is in agreement with **Marsico *et al.*** [33] who concluded that the radiocarpal and ulnocarpal joints are particularly affected in form of

synovitis and synovial hypertrophy and should be prioritized in imaging protocols, but he didn't correlate this finding with disease duration. However, the study conducted by **Iagnocco *et al.*** [34] concluded that there was synovial hypertrophy in ulnocarpal joint in 7% of his examined patients without correlation to disease duration.

It was noticed that there was positive correlation between consumed complement (C3) and synovial hypertrophy of ulna-carpal joint and that is matched with **Shedid *et al.*** [24] who found that patients with sonographic evidence of synovitis were associated significantly with lower C3 ($P<0.01$) that reflects role of complement in disease pathogenesis and presentation.

ESR was negatively correlated with joint affection (synovitis, SH, bone erosion and effusion) that is in contrast to **Han and Tian** [35] who stated that only ESR had correlation with gray-scale/PD US examinations in the detection of subclinical SH. This difference may be related to different sample size, disease activity and racial reasons.

To the best of our knowledge, this is the first study to demonstrate a significant correlation between SLEDAI-2K score and retrocalcaneal bursitis in SLE patients, suggesting that as disease activity increases, there may be a greater risk of enthesitis-like changes detectable by MSUS, which reflect that retrocalcaneal bursitis is indicator of SLE disease activity. Interestingly, our study revealed a significant positive correlation between disease duration and radiocarpal affection (SH, tenosynovitis & synovial effusion). To our knowledge, few studies have explicitly reported this association, making this finding particularly noteworthy.

Notably, we observed a significant correlation between disease duration and intercarpal joint affection (SH). This finding has not been highlighted in the literature to date and this may shed light to the role of MSUS as noninvasive method to predict SLE disease duration. It was peculiar that our study showed a robust and statistically significant correlation between disease duration and metacarpophalangeal joint affection (synovitis and synovial effusion), while several prior studies failed to establish this correlation.

Our study was the first to demonstrate a significant correlation between disease duration and joint affection among lupus nephritis patients as other literatures separate between them and demonstrate them as a closed entity with no relation to each other. As we demonstrated a positive correlation between disease duration and radiocarpal synovitis among all examined lupus nephritis patients. Notably, we observed a statistically significant correlation between disease duration and radiocarpal joint affection (synovitis, SH, tenosynovitis and effusion) in proliferative lupus nephritis who staged class IV and V, which in turn provides an impact of examining lupus nephritis patients. Interestingly, our study revealed a significant positive relationship between disease duration and ulnocarpal affection (SH and synovial effusion) among lupus nephritis patients who were stage IV and V, given that no prior study has addressed this association. We observed that there was a significant positive relationship between disease duration and intercarpal affection (tenosynovitis and synovial effusion) among lupus nephritis patients who were stage IV and V, given how this finding may provide new insights into disease progression in lupus nephritis.

CONCLUSION

MSUS had a valuable role in detecting subclinical arthritis and it provided data on different pathophysiological aspects on joint affection. Interestingly MSUS showed a statistically significant correlation between affected joints and disease duration. MSUS is a noninvasive tool that can detect SLE disease activity and correlation to standard scores.

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