Serum Sirtuin-1 Level in Systemic Lupus Erythematosus and its Relation to Disease Activity and Metabolic Syndrome

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Abstract

Background: Background: Systemic lupus erythematosus is a chronic autoimmune disease characterized by immune dysregulation, multisystem involvement, and increased cardiovascular risk. Sirtuin-1 is a regulatory protein involved in immune response, inflammation, and metabolic pathways, and its role in disease activity and vascular involvement in systemic lupus erythematosus remains incompletely defined.

Objectives: To assess serum Sirtuin-1 levels in patients with systemic lupus erythematosus and to evaluate their relationship with disease activity, metabolic parameters, and carotid intima-media thickness.

Methods: This case-control study included 25 patients with systemic lupus erythematosus and 25 age- and sex-matched healthy controls. Disease activity was assessed using the Systemic Lupus Erythematosus Disease Activity Score. Laboratory investigations included inflammatory markers, immunological profile, lipid parameters, and serum Sirtuin-1 levels measured by enzyme-linked immunosorbent assay. Carotid intima-media thickness was evaluated using Doppler ultrasonography.

Results: Serum Sirtuin-1 levels were significantly higher in systemic lupus erythematosus patients compared to controls ($P < 0.001$). Serum Sirtuin-1 showed a significant positive correlation with disease activity score ($P < 0.001$) and anti-double stranded DNA antibody levels ($P = 0.018$), and a significant negative correlation with complement C3 levels ($P = 0.011$). Receiver operating characteristic analysis demonstrated good diagnostic performance of serum Sirtuin-1 in discriminating patients from controls, with an area under the curve of 0.89, sensitivity of 96.97%, and specificity of 84.85% at a cut-off value of 8.20 ng/mL. Carotid intima-media thickness was significantly higher in patients compared to controls ($P < 0.001$) and correlated positively with body mass index ($P = 0.042$) and low-density lipoprotein levels (right side $P = 0.023$, left side $P = 0.026$).

Conclusion: Serum Sirtuin-1 is significantly elevated in systemic lupus erythematosus and is closely associated with disease activity and immune activation. Increased carotid intima-media thickness reflects early subclinical atherosclerosis in these patients. Serum Sirtuin-1 may serve as a useful biomarker for disease activity assessment and cardiovascular risk evaluation in systemic lupus erythematosus.

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Keywords: *Sirtuin-1, Systemic Lupus Erythematosus , Disease Activity, Metabolic Syndrome*

Introduction

Systemic lupus erythematosus is a chronic autoimmune disease with an unpredictable relapsing course and variable clinical expression. The disease may affect several organs simultaneously or sequentially, including joints, kidneys, serosal membranes, blood vessels, and the nervous system. Laboratory abnormalities are a consistent feature and commonly include reduced complement levels and the presence of multiple autoantibodies, particularly antinuclear antibodies, anti-double stranded deoxyribonucleic acid antibodies, and anti-Smith antibodies, reflecting underlying immune dysregulation [1].

Altered immune tolerance is central to lupus pathogenesis. Abnormal B-cell development and survival lead to sustained autoantibody production and immune complex formation, which subsequently contribute to tissue inflammation and organ damage. Genetic and immunologic studies have highlighted disturbed interactions between innate and adaptive immune cells, with loss of regulatory mechanisms that normally suppress autoreactive responses [2].

Sirtuin-1 is a nicotinamide adenine dinucleotide dependent deacetylase belonging to the class III histone deacetylase family. Structurally, it is composed of a conserved catalytic core flanked by disordered N-terminal and C-terminal regions, allowing interaction with multiple intracellular targets. Through these interactions, Sirtuin-1 participates in the regulation of transcription, cellular metabolism, apoptosis, aging, and immune responses [3].

At the immune level, Sirtuin-1 modulates dendritic cell activity and cytokine production through hypoxia inducible factor-1α signaling. This regulation affects the balance between helper T-cell subsets and regulatory T cells, influencing immune tolerance and inflammatory responses. Such mechanisms suggest a potential role for Sirtuin-1 in autoimmune diseases characterized by dysregulated T-cell function [4].

Experimental and translational studies have linked Sirtuin-1 to lupus pathogenesis. Altered Sirtuin-1 activity has been associated with changes in histone acetylation in CD4 positive T cells, leading to modulation of autoantibody production and renal involvement in lupus models. These observations support the concept that Sirtuin-1 contributes to immune imbalance and organ injury in systemic lupus erythematosus [5].

Animal studies further support this association. Sirtuin-1 deficient mice demonstrate immunoglobulin deposition within renal tissues and elevated serum antinuclear antibodies, resembling features of lupus nephritis. Conversely, activation of Sirtuin-1 using resveratrol has shown protective effects in pristane-induced lupus models, with reduction in proteinuria and immune complex deposition in renal tissue [6].

Beyond immune regulation, Sirtuin-1 has an important role in metabolic homeostasis. It interacts with adipose tissue–derived mediators such as adiponectin and influences lipid metabolism and insulin sensitivity. Through these pathways, Sirtuin-1 contributes to adipose tissue remodeling and energy balance, suggesting a link between immune activation, metabolic disturbance, and cardiovascular risk [7].

Sirtuin-1 is also involved in vascular function. Activation of Sirtuin-1 enhances endothelial nitric oxide synthase activity, leading to increased nitric oxide production and improved endothelial performance. While excessive overexpression may adversely affect cardiac function, physiological or moderately increased Sirtuin-1 activity appears to exert protective cardiovascular effects [8,9].

Patients with systemic lupus erythematosus are at increased risk of metabolic syndrome and premature atherosclerosis, driven by chronic inflammation, immune dysfunction, and metabolic abnormalities. Identifying biomarkers that reflect both disease activity and metabolic risk remains a clinical priority. Despite accumulating experimental evidence, data regarding serum Sirtuin-1 levels in systemic lupus erythematosus and their relationship with disease activity and metabolic syndrome are still limited.

Up to our knowledge, such evaluation has not been previously conducted at Zagazig University

Hospitals. That's why, the present study aimed to assess serum Sirtuin-1 levels in patients with systemic lupus erythematosus and to explore their association with disease activity and metabolic syndrome.

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This case control study was conducted at the Rheumatology and Rehabilitation Department, Faculty of Medicine, Zagazig University Hospitals. The study was carried out after approval of the Institutional Review Board of the Faculty of Medicine, Zagazig University (IRB No. 101024-27-8-2023).

A total of 50 participants were included in the study. They comprised 25 patients diagnosed with systemic lupus erythematosus and 25 apparently healthy individuals matched for age and sex with the patient group. Patients were recruited from both inpatient wards and outpatient clinics during the study period.

Sample size estimation was based on previously reported differences in serum Sirtuin-1 levels between patients and controls, assuming a study power of 80% and a confidence level of 95%. Accordingly, 25 participants were included in each group.

Inclusion criteria

Patients were eligible for inclusion if they were aged 16 years or older and fulfilled the revised American College of Rheumatology / Systemic Lupus International Collaborating Clinics classification criteria for systemic lupus erythematosus. According to these criteria, patients were classified as having SLE if they had biopsy-proven lupus nephritis in the presence of antinuclear antibodies or anti-double stranded DNA antibodies, or if they fulfilled at least four criteria including at least one clinical and one immunologic criterion [10].

Exclusion criteria

Exclusion criteria included age below 16 years, presence of liver disease, renal diseases not related to systemic lupus erythematosus or advanced renal failure, smoking, and the presence of any other inflammatory arthritis or autoimmune disease that could interfere with study results.

Ethical considerations and consent

A written informed consent was obtained from all participants prior to enrollment. All subjects were informed about the nature and objectives of the study.

Clinical assessment

All participants underwent detailed history taking including age, sex, disease duration, comorbid conditions, current medications, and special habits of medical importance. Present history focused on musculoskeletal complaints such as joint pain, swelling, limitation of movement, and morning stiffness, as well as other lupus-related manifestations including oral or nasal ulcers, hair loss, skin rash, photosensitivity, sicca symptoms, and color changes of extremities.

Systemic review included central nervous system symptoms, cardiovascular complaints, respiratory symptoms, gastrointestinal manifestations, genitourinary symptoms, and ocular complaints such as redness, dryness, photophobia, or decreased vision. Past medical history included chronic illnesses, previous surgeries, and medication intake. Menstrual and obstetric history were obtained for female patients, including history of abortion or stillbirth. Family history of autoimmune diseases was also recorded.

General and systemic examination

All subjects underwent thorough general examination including assessment of blood pressure, pulse, temperature, and general appearance. Body mass index was calculated and classified according to the World Health Organization classification of adult weight [11]. Examination also included assessment of lymph nodes and lower limb edema.

Mucocutaneous examination focused on malar rash, discoid rash, photosensitivity, oral ulcers, and alopecia. Cardiac examination included inspection, palpation, and auscultation for abnormal heart sounds or pericardial rubs. Chest examination was performed to detect crepitations or pleural rubs. Abdominal examination assessed for hepatosplenomegaly and renal angle tenderness. Neurological examination included cranial nerve assessment and motor and sensory evaluation. Ophthalmological

examination was performed when indicated.

Locomotor system examination

Local examination of the locomotor system included inspection for redness, swelling, deformity, and muscle wasting. Palpation assessed joint warmth, tenderness, synovial thickening, effusion, and crepitus. Joint tenderness was graded using a standardized tenderness scoring system ranging from no tenderness to tenderness with withdrawal response [12]. Active and passive range of motion were assessed for examined joints.

Assessment of disease activity in SLE patients

Disease activity in systemic lupus erythematosus patients was assessed using the Systemic Lupus Erythematosus Disease Activity Score over the last ten days prior to the visit. The score included clinical domains such as arthritis, localized and generalized cutaneous lupus rash, alopecia, mucosal ulcers, mucocutaneous and systemic vasculitis, neuropsychiatric involvement, cardiac or pulmonary involvement, serositis, and myositis. Laboratory domains included proteinuria, hypocomplementemia, increased anti-double stranded DNA antibodies, thrombocytopenia, leukopenia, and hemolytic anemia [13].

The SLE-DAS score was calculated using the published weighted formula. Low lupus disease activity state was defined using a cut-off value of 6.62. Patients were classified as having low disease activity when the score was below 6.62 and high disease activity when the score exceeded this value [14].

Imaging assessment

Doppler ultrasonography of the common carotid arteries was performed for patients and controls to measure carotid intima-media thickness as an indicator of subclinical atherosclerosis [15]. Measurements were obtained using a standardized ultrasound technique with assessment of near and far walls at predefined segments of the common carotid artery [16]. Carotid intima-media thickness was considered normal if it did not exceed 0.9 mm [17].

Laboratory investigations

Venous blood samples were obtained after overnight fasting. Complete blood count including differential leukocyte count was performed using an automated hematology analyzer, with peripheral blood film review when needed [18]. Erythrocyte sedimentation rate was measured using an automated ESR analyzer [19]. C-reactive protein was assessed using an automated chemistry analyzer [20].

Antinuclear antibodies were detected by indirect immunofluorescence on HEp-2 cells [21]. Anti-double stranded DNA antibody titers were measured by indirect immunofluorescence using *Crithidia luciliae* [22]. Serum complement C3 and C4 levels were measured using automated analyzers and interpreted according to established reference distributions [23].

Liver enzymes and kidney function tests were measured using automated chemistry systems [24]. Lipid profile parameters were assessed according to established reference intervals [25]. Fasting and postprandial blood glucose levels were measured using automated analyzers [26]. Serum uric acid was measured and interpreted according to published reference ranges [27]. Twenty-four-hour urine collection was performed for evaluation of proteinuria and creatinine clearance when indicated [24]. Antiphospholipid antibodies including anticardiolipin antibodies, lupus anticoagulant, and anti-β2 glycoprotein I were assessed according to standardized recommendations [28].

Measurement of serum Sirtuin-1

Serum Sirtuin-1 levels were measured using a commercially available human Sirtuin-1 enzyme-linked immunosorbent assay kit according to the manufacturer instructions. The assay is based on a double-antibody sandwich ELISA principle. Serum samples were obtained after coagulation at room temperature, followed by centrifugation at 2000–3000 revolutions per minute. The separated serum was stored at −20 °C until analysis, avoiding repeated freeze–thaw cycles.

Standard solutions were prepared by serial dilution to generate a calibration curve. Serum samples were added to pre-coated wells followed by addition of biotin-labeled antibody and streptavidin-HRP conjugate. After incubation and washing steps, chromogenic substrates were added and the reaction was

stopped. Optical density was measured at 450 nm, and serum Sirtuin-1 concentrations were calculated from the standard curve. The assay sensitivity was 0.306 ng/mL, with a detection range of 0.5–40 ng/mL.

Statistical analysis

Statistical analysis was performed using IBM SPSS software version 23.0 for Windows (SPSS Inc., Chicago, IL, USA). Qualitative data were presented as numbers and percentages, while quantitative data were expressed as mean and standard deviation. Chi-square or Fisher's exact test was used for qualitative variables, independent t-test or one-way analysis of variance for quantitative comparisons, and Pearson's correlation for assessing relationships between continuous variables. Receiver operating characteristic curve analysis was applied to evaluate diagnostic accuracy. A P value ≤ 0.05 was considered statistically significant.

Results

Table 1: Demographic data among the studied groups

Variables	SLE group (n=25)	Control group (n=25)	Test	P value
Age *(years)* *Mean ± SD*	39.8 ± 6.93	42.68 ± 9.81	0.34	0.321[1]
Sex *(N. %)*				
– Female	23 (92%)	18 (72%)		
– Male	2 (8%)	7 (28%)	3.54	0.171[2]

[1]: One way ANOVA test, [2]: Chi square test, P-value > 0.05: Non-significant, P-value ≤ 0.05: Significant

Table (1) shows no significant difference between the studied groups as regard age or sex (P>0.05).

Table 2. Comprehensive Clinical, Disease Activity, Laboratory, Immunological, Renal, Therapeutic, and Cardiovascular Characteristics of the SLE Group (n = 25)

Category	Variable	Result
Demographic / Disease Characteristics	Disease duration (years), Mean ± SD	6.20 ± 2.01
	Arthritis, n (%)	7 (28%)
	Arthralgia, n (%)	18 (72%)
	Malar rash, n (%)	24 (96%)
	Skin rash, n (%)	8 (32%)
	Photosensitivity, n (%)	23 (92%)
	Alopecia, n (%)	18 (72%)
	Oral ulcers, n (%)	12 (48%)
	Lower limb edema, n (%)	5 (20%)
	Fever, n (%)	14 (56%)
	Raynaud's phenomenon, n (%)	3 (12%)
	Cardiovascular disease, n (%)	6 (24%)
	Pulmonary affection, n (%)	18 (72%)
	Abdominal manifestations, n (%)	12 (48%)
	Neurological disease (CTs, PN), n (%)	6 (24%)
	Lupus nephritis, n (%)	5 (20%)
	Ocular affection, n (%)	2 (8%)
Disease Activity (SLE-DAS)	SLE-DAS score, Mean ± SD	7.11 ± 2.07
	Remission, n (%)	0 (0%)
	Low activity, n (%)	16 (64%)
	Moderate activity, n (%)	0 (0%)
	High activity, n (%)	9 (36%)
Hematological Parameters	WBCs (×10³/µL), Mean ± SD	6.75 ± 3.34
	Leucopenia, n (%)	3 (12%)
	Hemoglobin (g/dL), Mean ± SD	11.58 ± 1.57
	Hemolytic anemia, n (%)	5 (20%)
	Reticulocyte count (%), Mean ± SD	2.25 ± 0.87
	Reticulocytosis, n (%)	5 (20%)
	Platelets (×10³/µL), Mean ± SD	283.8 ± 48.97

Category	Variable	Result
	Thrombocytopenia, n (%)	0 (0%)
Acute Phase Reactants	ESR (mm/hr, 1st hour), Mean ± SD	37.56 ± 13.54
	CRP (mg/dL), Mean ± SD	8.85 ± 2.14
Liver Function Tests	Albumin (g/dL), Mean ± SD	3.87 ± 0.53
	ALT (U/L), Mean ± SD	17.03 ± 5.59
	AST (U/L), Mean ± SD	18.02 ± 6.78
Renal Function Tests	BUN (mg/dL), Mean ± SD	1.98 ± 0.73
	Creatinine (mg/dL), Mean ± SD	0.62 ± 0.14
Urinary / Renal Parameters	Hematuria (>5 RBCs/HPF), n (%)	6 (24%)
	Pyuria (>5 WBCs/HPF), n (%)	3 (12%)
	Cellular casts, n (%)	0 (0%)
	Proteinuria (>500 mg/24h), n (%)	10 (40%)
Immunological Profile	ANA positivity, n (%)	25 (100%)
	Anti-dsDNA positivity, n (%)	21 (84%)
	Anti-dsDNA level (IU/mL), Mean ± SD	19.7 ± 6.2
	C3 level (mg/dL), Mean ± SD	23.65 ± 17.6
	C3 hypocomplementemia, n (%)	2 (8%)
	C4 level (mg/dL), Mean ± SD	3.93 ± 0.43
	C4 hypocomplementemia, n (%)	0 (0%)
	Anticardiolipin IgM positivity, n (%)	7 (28%)
	Anticardiolipin IgG positivity, n (%)	7 (28%)
	Lupus anticoagulant positivity, n (%)	6 (24%)
Medications Used	NSAIDs, n (%)	5 (20%)
	Corticosteroids, n (%)	25 (100%)
	Hydroxychloroquine, n (%)	25 (100%)
	Azathioprine, n (%)	14 (56%)
	Cyclophosphamide, n (%)	1 (4%)
	Mycophenolate mofetil, n (%)	5 (20%)
	Biological therapy, n (%)	2 (8%)
Cardiovascular Risk Factors	Diabetes mellitus, n (%)	3 (12%)
	Hypertension, n (%)	4 (16%)
	BMI (kg/m²), Mean ± SD	29.3 ± 4.45
	Serum uric acid (mg/dL), Mean ± SD	5.61 ± 1.53
	Total cholesterol (mg/dL), Mean ± SD	165.4 ± 42.7
	Triglycerides (mg/dL), Mean ± SD	114.7 ± 60.8
	HDL-C (mg/dL), Mean ± SD	53.9 ± 16.8
	LDL-C (mg/dL), Mean ± SD	101.3 ± 37.4
	Right cIMT (mm), Mean ± SD	0.66 ± 0.17
	Left cIMT (mm), Mean ± SD	0.67 ± 0.16

SLE: Systemic lupus erythematosus; SLE-DAS: Systemic Lupus Erythematosus Disease Activity Score; WBCs: White blood cells; ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; BUN: Blood urea nitrogen; ANA: Antinuclear antibodies; Anti-dsDNA: Anti-double stranded DNA antibodies; BMI: Body mass index; HDL-C: High-density lipoprotein cholesterol; LDL-C: Low-density lipoprotein cholesterol; cIMT: Carotid intima media thickness; DM: Diabetes mellitus; HTN: Hypertension; HPF: High-power field. Data are presented as mean ± standard deviation or number (percentage) as appropriate.

Table 2 summarizes the baseline characteristics of the SLE cohort (n = 25), with a mean disease duration of 6.20 ± 2.01 years. Musculoskeletal and mucocutaneous manifestations were frequent, including arthralgia (72%), arthritis (28%), malar rash (96%), photosensitivity (92%), alopecia (72%), and oral ulcers (48%). Cardiovascular involvement was reported in 24%, pulmonary affection in 72%, and lupus nephritis in 20% of patients. The mean SLE-DAS score was 7.11 ± 2.07, with 64% of patients having low disease activity and 36% high activity, and no patients in remission or moderate activity categories. Hematological parameters showed mean hemoglobin 11.58 ± 1.57 g/dL, leukopenia in 12%, hemolytic anemia in 20%, and reticulocytosis in 20%, while thrombocytopenia was absent. Inflammatory markers were elevated with mean ESR 37.56 ± 13.54 mm/hr and CRP 8.85 ± 2.14 mg/dL. Immunologically, 100% were ANA positive, 84% anti-dsDNA positive with a mean level of 19.7 ± 6.2 IU/mL, mean C3 23.65 ± 17.6 mg/dL (hypocomplementemia 8%), and mean C4 3.93 ± 0.43 mg/dL. All patients received

corticosteroids and hydroxychloroquine, with azathioprine used in 56%. Regarding metabolic and cardiovascular parameters, mean BMI was 29.3 ± 4.45 kg/m², diabetes mellitus was present in 12%, hypertension in 16%, mean total cholesterol 165.4 ± 42.7 mg/dL, triglycerides 114.7 ± 60.8 mg/dL, HDL-C 53.9 ± 16.8 mg/dL, LDL-C 101.3 ± 37.4 mg/dL, and mean right and left cIMT values were 0.66 ± 0.17 mm and 0.67 ± 0.16 mm, respectively.

Table 3: Correlation between Carotid intima media thickness (cIMT) , BMI and cardiovascular risk factors among SLE group

Variable	Right cIMT		Left cIMT	
	r	*P-value**	*r*	*P-value**
BMI	0.456	**0.031**	0.412	**0.042**
Serum uric acid levels	0.079	0.707	0.231	0.267
Cholesterol *(<200 mg/dL)*	-0.247	0.233	0.299	0.147
Triglycerides *(<150 mg/dL)*	0.256	0.216	0.179	0.391
HDL *(>60 mg/dL)*	0.083	0.692	0.209	0.316
LDL *(<100 mg/dL)*	0.512	**0.023**	0.499	**0.026**

**Person correlation coefficient, Non-significant: P >0.05, Significant: P ≤0.05. BMI: Body Mass Index, HDL: High Density Lipoprotein, LDL: Low Density Lipoprotein*

Table (3) shows significant positive correlation between BMI with right cIMT (r=0.456, P=0.031) and left cIMT (r=0.412, P=0.042).). Also, there was significant positive correlation between serum LDL levels with right cIMT (r=0.512, P=0.023) and left cIMT (r=0.499, P=0.026), while there was no significant correlation between cIMT and HDL,total cholesterol, triglycerides levels among SLE patients (P >0.05).

Table 4: Comparison of cIMT between SLE and control groups

Variables	SLE group (n=25)	Control group (n=25)	T	P value
Left cIMT *Mean ± SD*	0.67 ± 0.16	0.56 ± 0.12	2.75	**0.008**
Right cIMT *Mean ± SD*	0.66 ± 0.17	0.53 ± 0.13	3.04	**0.004**

** Independent sample t-test, Non-significant: P >0.05, Significant: P ≤0.05*

Table (4) shows a statistically significant increase in carotid intima-media thickness (cIMT) among SLE patients compared to the control group (P <0.05).

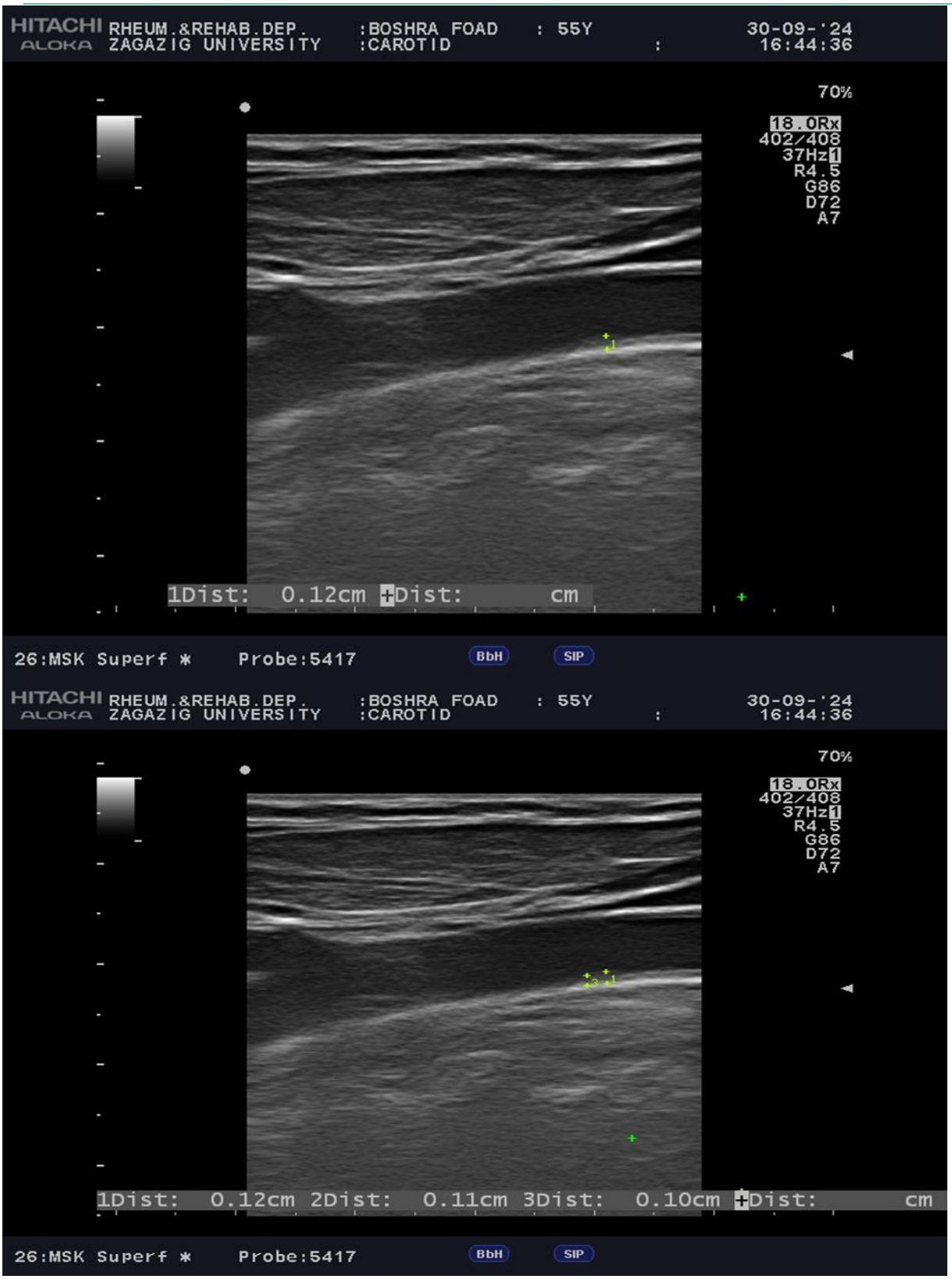

Figure 1: SLE Female patient 55 years old , ultrasonography showed CIMT of right and left common carotid artery (1.1mm and 1.2 mm).

Table 5: Serum Sirtuin-1 Levels among the SLE group and control group

Variables	SLE group (n=25)	Control group (n=25)	T	P value
Serum SIrt1 level *(ng/ml)* *Mean ± SD*	11.64 ± 3.37	7.44±2.23	5.19	**<0.001**

**Independent sample t-test, Non-significant: P >0.05, Significant: P ≤0.05*

Table (5) shows a statistically significant differences between SLE patients and control group as SLE patients had higher levels of SIrt1 levels in comparison to control group (P <0.001).

Table 6. Correlation Between Serum Sirt1 Levels and Clinical, Laboratory, Disease Activity, and Cardiovascular Risk Factors Among the SLE Group (n = 25)

Category	Variable	Correlation coefficient (r)	P value
Demographic / Disease Characteristics	Age	0.158	0.451
	Disease duration	-0.101	0.630
Disease Activity	SLE-DAS score	**0.418**	**0.038**
Hematological Parameters	WBCs	0.211	0.311
	Hemoglobin	-0.029	0.892
	Platelets	-0.365	0.073
Inflammatory Markers	ESR	**0.407**	**0.043**
	CRP	0.156	0.490
Liver Function Tests	Albumin	0.138	0.510
	ALT	0.216	0.299
	AST	0.098	0.641
Renal Function Tests	BUN	0.138	0.509
	Serum creatinine	0.253	0.223
Renal / Urinary Parameters	Urine protein / 24 h	**0.410**	**0.042**
	Pyuria	0.158	0.450
	Hematuria	0.067	0.749
Immunological Profile	Anti-dsDNA	**0.497**	**0.011**
	C3	**-0.418**	**0.037**
	C4	-0.220	0.290
Cardiovascular Risk Factors	BMI	0.251	0.227
	Serum uric acid	0.174	0.406
	Total cholesterol	0.221	0.289
	Triglycerides	0.028	0.895
	HDL-C	0.295	0.152
	LDL-C	0.158	0.450
	Right cIMT	0.124	0.554
	Left cIMT	0.034	0.872

SLE: Systemic lupus erythematosus; SLE-DAS: Systemic Lupus Erythematosus Disease Activity Score; WBCs: White blood cells; ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; BUN: Blood urea nitrogen; BMI: Body mass index; HDL-C: High-density lipoprotein cholesterol; LDL-C: Low-density lipoprotein cholesterol; cIMT: Carotid intima media thickness. Correlations were assessed using Spearman's rank correlation test. Significant correlations were defined as P ≤ 0.05 (highlighted in bold), while non-significant correlations were defined as P > 0.05.

Table 6 demonstrates the correlations between serum Sirt1 levels and clinical, laboratory, disease activity, and cardiovascular parameters in the SLE group (n = 25). Serum Sirt1 showed a significant positive correlation with SLE-DAS score (r = 0.418, p = 0.038), ESR (r = 0.407, p = 0.043), 24-hour urine protein (r = 0.410, p = 0.042), and anti-dsDNA levels (r = 0.497, p = 0.011). In contrast, a significant negative correlation was observed with C3 levels (r = −0.418, p = 0.037). No significant correlations were detected between serum Sirt1 levels and age, disease duration, hematological indices

(WBCs, hemoglobin, platelets), CRP, liver or renal function tests, C4 levels, BMI, lipid profile parameters, serum uric acid, or carotid intima-media thickness measurements (all $p > 0.05$).

Table 7: ROC curve analysis of serum SIrt1 levels to discriminate between SLE patients and healthy controls

Cut-point	Sensitivity (%)	Specificity (%)	PPV (%)	NPP (%)	AUC (%)
8.20	96.97%	84.85%	86.5%	96.5%	89%

On conducting ROC analysis (Receiver operation Curve) to determine the optimal cutoff value to discriminate SLE patients from control group, analysis showed that serum SIrt1 had highest sensitivity (96.97%) and specificity (84.85%) at cut-off point 8.20 ng/ml with area under the curve (89%). So, serum SIrt1 can be considered as good biomarker to discriminate healthy subjects from SLE patients.

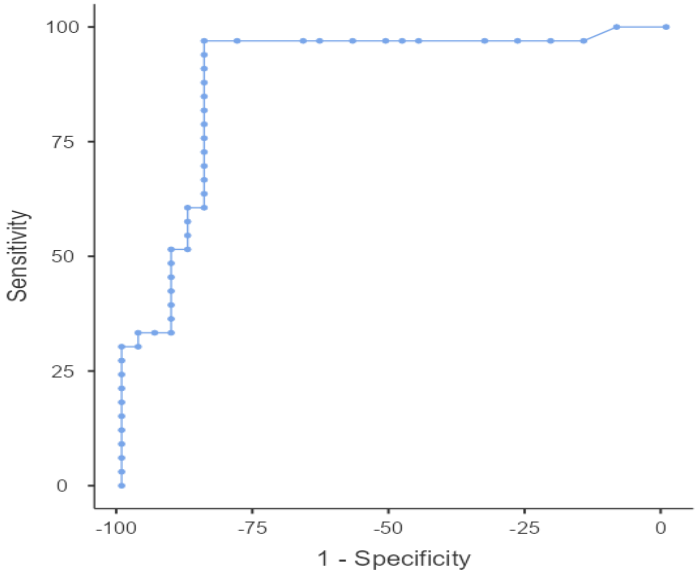

Figure 3: ROC curve analysis of serum SIrt1 to discriminate between SLE patients and healthy controls

Discussion

Regarding the demographic characteristics of the studied systemic lupus erythematosus cohort, the present study demonstrated a marked female predominance, with females representing 92% of cases, and a mean age of 39.8 ± 6.93 years. No statistically significant differences were observed between patients and controls concerning age or sex distribution. This demographic pattern reflects the well-recognized epidemiology of SLE. Pons-Estel et al. [29] reported a female-to-male ratio approaching 9:1, with most patients diagnosed between the third and fourth decades of life. Similarly, Barber et al. [30] confirmed that nearly 90% of SLE cases occur in females, with peak disease onset in the late thirties, which closely matches the characteristics of our study population.

Concerning clinical manifestations, the present study revealed a predominance of mucocutaneous involvement, with malar rash, photosensitivity, and alopecia being the most frequently observed features. Chest manifestations were also common, followed by arthritis, cardiac and central nervous system involvement, while renal affection in the form of proteinuria was detected in one-fifth of patients. In a study by Abozeid et al. [31], photosensitivity, alopecia, and malar rash were reported in 60%, 56%, and 32% of patients, respectively. The higher prevalence of mucocutaneous manifestations in our cohort may be related to differences in disease activity, genetic background, or environmental exposure.

Hematological and inflammatory findings in the current study showed mild anemia with relatively preserved white blood cell and platelet counts, alongside elevated ESR and CRP values, reflecting active

systemic inflammation. Immunologically, all patients demonstrated positive antinuclear antibodies, while anti-double stranded DNA antibodies were detected in 84% of cases. These findings are consistent with those reported by Abdallah et al. [32], who observed anti-dsDNA positivity in approximately 85.7% of SLE patients. Similarly, Abozeid et al. [31] reported ANA positivity in 90% and anti-dsDNA positivity in 70% of their cohort, supporting the immunological profile observed in the present study.

Regarding treatment patterns, most patients in this study were receiving hydroxychloroquine, with more than half treated with azathioprine, while smaller proportions had been exposed to mycophenolate mofetil, cyclophosphamide, or biologic therapy. This reflects real-world therapeutic strategies tailored to disease severity and organ involvement.

In relation to cardiovascular risk, the present study demonstrated a statistically significant positive correlation between body mass index and carotid intima-media thickness. In contrast, Shaaban et al. [33] reported no significant association between BMI and cIMT in SLE patients. This discrepancy may be explained by differences in sample size, disease duration, cumulative inflammatory burden, or treatment exposure between study populations.

Additionally, a significant positive correlation was identified between serum low-density lipoprotein levels and carotid intima-media thickness on both sides, while no significant associations were observed with other lipid parameters. Conversely, El-Hady et al. [34] reported significant correlations between cIMT and total cholesterol and triglycerides, with negative correlations with high-density lipoprotein. Such variations may reflect differences in metabolic profiles, disease activity, and population characteristics.

The present study also demonstrated significantly increased carotid intima-media thickness in SLE patients compared with healthy controls, indicating the presence of subclinical atherosclerosis and heightened cardiovascular risk. These findings support the clinical value of carotid ultrasonography as a non-invasive tool for early detection of vascular involvement in SLE. Similar results were reported by Abozeid et al. [31], who found significantly higher bilateral cIMT values in SLE patients. Likewise, Nasser et al. [35] confirmed increased cIMT among SLE patients compared with controls, reinforcing the concept of accelerated atherosclerosis in this population.

A key finding of the current study was the significant elevation of serum Sirtuin-1 levels in SLE patients compared to healthy controls. Receiver operating characteristic analysis demonstrated strong diagnostic performance, suggesting that serum SIRT1 may serve as a reliable biomarker for identifying SLE patients. These findings are in agreement with Abdallah et al. [32], who reported markedly elevated SIRT1 levels in SLE patients with excellent diagnostic accuracy, further supporting its potential clinical utility.

Moreover, serum SIRT1 levels in the present study were significantly associated with disease activity grades, with higher levels observed in patients with more active disease. A significant positive correlation was also identified between serum SIRT1 levels and the SLE Disease Activity Score, alongside a significant negative correlation with complement component C3 levels. These observations suggest a link between SIRT1 expression and immune activation in SLE. Abdallah et al. [32] similarly reported that SIRT1 levels correlated positively with disease activity indices and negatively with C3 levels, supporting our findings.

In addition, serum SIRT1 levels showed a significant positive correlation with anti-double stranded DNA antibody levels. This finding is consistent with Yang et al. [36], who reported elevated SIRT1 levels in SLE patients and suggested a potential role for SIRT1 in organ damage, particularly lupus nephritis.

In contrast, no significant associations were observed between SIRT1 levels and specific clinical manifestations such as arthritis, mucocutaneous involvement, or fever. This differs from the findings of Yang et al. [36], who reported positive associations between SIRT1 levels and several clinical features, including arthritis and headache. Such differences may be attributed to variability in disease phenotype, sample size, and disease activity across studies.

The present study has some limitations that should be acknowledged. The relatively small sample size may limit the generalizability of the findings to the wider systemic lupus erythematosus population. The cross-sectional design also precludes establishing causal relationships between serum Sirtuin-1 levels, disease activity, and subclinical atherosclerosis. In addition, variations in treatment regimens and disease duration among patients may have influenced inflammatory and metabolic parameters. Finally, the single-center nature of the study may limit extrapolation of the results to other populations with different genetic or environmental backgrounds.

Conclusion

In patients with systemic lupus erythematosus, serum Sirtuin-1 levels were significantly higher compared to healthy controls and showed a clear positive correlation with disease activity. These findings suggest that serum Sirtuin-1 may serve as a useful biomarker for assessing disease activity in SLE. In addition, carotid intima-media thickness was significantly increased in SLE patients, particularly among those with higher body mass index, indicating the presence of early subclinical atherosclerosis and increased cardiovascular risk. A significant positive correlation was also observed between low-density lipoprotein levels and carotid intima-media thickness, while other lipid parameters showed no such association.

Further longitudinal studies involving larger numbers of systemic lupus erythematosus patients are recommended to confirm these findings and to evaluate the role of serum Sirtuin-1 in monitoring disease activity over time. Additional research is needed to assess the impact of different therapeutic regimens on serum Sirtuin-1 levels and their relation to disease control. Future studies should also explore the utility of serum Sirtuin-1 as an early diagnostic and prognostic biomarker in SLE, as well as its potential role in cardiovascular risk stratification in this patient population.

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