

Biomarkers of Systemic Lupus Erythematosus and Systemic Sclerosis diseases activity in a sample of Egyptian patients :Soluble Intercellular Adhesion Molecule-1 and Soluble Interleukin-2 Receptor, Case Control Study

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Systemic Lupus Erythematosus(SLE) and systemic sclerosis(SSc) are systemic inflammatory autoimmune disorders characterized by a large spectrum of clinical and laboratory features. The aim of the present study was to investigate the possible use of serum level of soluble intercellular adhesion molecule-1(sICAM-1) and soluble interleukin-2 receptor (sIL-2Ra) as biomarkers for monitoring of SLE and SSc disease activity. Moreover, it aimed to compare the specificity and sensitivity as well as cut-off value of both biomarkers in a sample of Egyptian patients. 50 SLE patients, 30 SSc patients and 60 age and sex matched healthy controls were enrolled in our study. sICAM-1 and sIL-2Ra were measured in serum samples obtained from all participants. In addition to Erythro sedimentation rate(ESR), complete blood count (CBC), Antinuclear antibodies (ANA) estimation, disease activity of both diseases were also assessed. sICAM-1 and sIL-2Ra levels were higher in SLE and SSc patients versus control. Both parameters are correlated with each other as well as the activity parameters. A cut-off levels of 455.59 (ng/ml) & 2525935 (pg/ml) in both SLE & SScs respectively was observed with the highest specificity and sensitivity. It could be concluded that sICAM-1 and sIL-2Ra are noninvasive biomarkers for SLE and SSc that could play a pathophysiologic role in development and progression of both diseases. Moreover, sICAM-1 and sIL-2Ra are correlated with the disease activity at cut-off values of 455.59 (ng/ml) & 2525935 (pg/ml) respectively.

Keywords: Systemic Lupus Erythematosus, Systemic Sclerosis, Soluble Intracellular Adhesion Molecule-1, soluble Interleukin 2 Receptor.

Connective tissue diseases (CTDs) are systemic inflammatory autoimmune disorders characterized by a large spectrum of clinical and laboratory features. CTDs spectrum includes Systemic Lupus Erythromatosus (SLE) and Systemic Sclerosis (SSc)¹. SLE is a chronic, multi-organ, relapsing autoimmune disease mainly affecting young adults. It is commoner among female, with the female/male ratio being approximately 9/1².

SSc is an uncommon chronic systemic connective tissue autoimmune disease characterized by microvascular abnormalities and pathological thickening and tethering of the skin and involvement of internal organs (gastrointestinal tract, heart, lungs, and kidneys). SSc seems to result from a multifactorial process (alterations of the immune system, genetic and environmental factors) but its pathogenesis remains unclear³.

Autoantibodies/auto reactive T cells can attack any organ of the body, resulting in a wide array of signs and symptoms. Soluble molecules have been detected in a broad range of surface proteins, which include T cell antigens such as (CD8), adhesion molecules such as intercellular adhesion molecule-1 (sICAM-1) and cytokine receptors such as the alpha chain of the high affinity interleukin-2 receptor (sIL-2R). Soluble receptors are suggested to compete with the corresponding cellular receptors for ligands and thus inhibiting ligands action⁴.

Therefore, it was suggested that receptor shedding may be useful non-invasive markers for CTDs activity, especially in both SLE and SSc patients and also correlated with disease activity⁵. IL-2 deficiency affects multiple regulatory pathways in the host and in the case of SLE, this contributes to the multifaceted dysregulation of the immune response. The interleukin-2 receptor alpha (IL-2Ra) chain is a component of high-affinity IL-2 receptors and thus is a key regulator of lymphocyte proliferation⁵.

In SSc, it was found that the severity of the disease is correlated with sIL-2R and those with early onset had the highest sICAM-1 levels⁶. Although the role and functions of soluble ICAM-1 and IL-2Ra have not yet been completely elucidated, the evidence suggests its implication in disease progression, or at least its elevated levels may inform the clinician about pathological

processes associated with SLE and SSc.

Therefore, the aim of the present study was to investigate the possible use of serum level of sICAM-1 and sIL-2Ra as biomarkers for monitoring of SLE and SSc disease activity. Moreover, it aimed to compare the specificity and sensitivity as well as cut-off value of both biomarkers in a sample of Egyptian patients.

Subjects and methods

Sampling

Sample was calculated by EPI program with confidence 95%, power 85%, OR=5 and it was 77 participants in each group. So, cases were elevated to 80 (30 SSc and 50 SLE), and due to deficiency in the controls which were matched to the cases, and another who refused the sharing in the study, the controls were decreased to 60 participants.

The present case control study was performed on 140 subjects' enrolled equal from Rheumatology outpatient clinics and internal medicine departments of Cairo and Ain Shams University Hospitals during period from May 2016 to August 2018 according to the principles of the Helsinki Declaration. A Local ethics committee of the faculty of Medicine of Cairo and Ain Shams Universities approved the study.

An informed consent was obtained from all subjects participating in this study, after explaining its nature. The subjects were classified into 3 groups. Group I consist of 50 patients with SLE fulfilling the 'American College of Rheumatology (ACR)' criteria for diagnosis of SLE⁷. Group II consists of 30 patients with SSc fulfilling the ACR criteria for diagnosis of SSc⁸. Group III included age and sex matched 60 apparently healthy volunteers and served as control group.

All patients were not under immunosuppressive therapy at the time of enrolment. After taking their consent, all participants were subjected to full history taking, general, and local and skin examination.

Biochemical assessment

Ten milliliters venous blood samples were obtained from all participants via venipuncture. Five milliliters of them were placed into plain tubes and allowed to clot for 15 minutes. Sera were prepared by centrifugation at 1,500 g for 10 min, aliquoted and stored at - 80 °C for the

following investigation; CRP levels were measured by the turbidimetric method using a photometer (Biosystems S.A., Barcelona, Spain), and a level of <6 mg/L was accepted as normal and creatinine were measured by the ordinary commercial available kits.

Antinuclear antibody (ANA) was measured by indirect immune-fluorescence supplied by Immco Diagnostics (USA). Three milliliters were collected in K₂ EDTA tubes for complete blood count (Coulter STKS hematology flow cytometer, Block Scientific, Inc., Bohemia, New York, USA). The last two milliliters were collected in Sodium citrate tubes for measurement erythrocyte sedimentation rate (ESR). ESR was measured by using the Westergren method and expressed in mm/h⁹.

Moreover, all subjects were asked to collect 24 hours urine samples for quantitative measurement of 24 hours urinary proteins and complete urine analysis.

Quantikine Human sICAM-1 and sIL-2Ra (Cat. Number DY720-05; DR2A00 respectively-USA R&D Systems, Inc. 614 McKinley Place NE, Minneapolis, MN 55413) immunoassay kits were a solid phase ELISA designed to measure serum sICAM-1 and sIL-2Ra respectively. Results obtained using natural human sICAM-1 and sIL-2Ra showed linear curves that were parallel to the standard curves obtained using the Quantikine kit standards.

Statistical analysis

Statistical Science for Social Package (SPSS version 20, SPSS Inc., Chicago, IL, USA) was used for data analysis. Data were expressed as mean \pm SD for quantitative data, and frequency with its percentage with graphs of qualitative data. One-way ANOVA test was used for comparison parametric parameters and Chi square test for non-parametric parameters between different groups.

The Pearson's and Spearman correlation coefficient tests were used to evaluate associations between measured parameters and non-parametric parameters. The area under the receiver operating characteristic curve (AUC-ROC) analysis was performed to determine sensitivity and specificity of both sICAM-1 and sIL-2Ra as biomarker indicator test to SLE and SSc diseases activity. For all tests, $P < 0.05$ was considered significant.

RESULTS

All participants in this study were 140. The majority (75.0%) of them were female, while the males represent only 25%. Also, 50 (35.71%) from them had Systemic lupus erythromatosis, 30 (21.43%) had Systemic Sclerosis and; 60 (42.86%) were the controls (table 1).

The demographic characteristics and disease duration of all participants are presented in table (1). Females were more than males in SLE (84.0% versus 16.0%), in SSc (76.7% versus 23.3%) and in controls (66.7% versus 33.3%) with statistically insignificant difference between groups ($P=0.11$). In addition, there were also statistically insignificant differences between the studied groups in relation to age ($P=0.07$) but the duration of disease was significantly longer in SLE than SSc ($P=0.00$).

Table (2) illustrated the clinical and some laboratory characteristics in different studied groups. The arthritis, kidney diseases and heart diseases were more common in SLE than SSc patients were (72%, 36% and 16% versus 53%, 20% and 13%, respectively, $P > 0.05$). Antinuclear antibodies had a high percentage among SLE compared to SSc patients (92% versus 73%, $P < 0.05$). On the opposite side, lung diseases occur more in SSc patients compared to SLE (50% facing to 6%, respectively, $P < 0.05$). On the other hand, neurologic diseases and proteinuria occur only among the SLE patients (8% and 54% respectively, $P < 0.05$) while, myositis occurs only among SSc patients (13.3%, $P < 0.05$). Meanwhile, there was no statistically significant between the studied groups in relation to present of serosities or measurement of C-reactive protein ($P > 0.05$). In table (3), ESR was significantly higher in SLE and SSc versus control (76.88 \pm 45.40 and 65.73 \pm 72.61 versus 10.80 \pm 3.56, $P < 0.000$). Also, serum creatinine was significant higher in SLE than SSc and control (2.09 \pm 0.44 versus 0.85 \pm 0.24 and 0.76 \pm 0.19, $P < 0.0001$). While, Leucocytic Count showed insignificant difference in SLE, SSc and control groups (6.30 \pm 1.40, 6.55 \pm 1.77; and 6.23 \pm 1.83, respectively. $P = 0.696$).

Comparison of serum levels of sICAM-1 and sIL-2R in different studied groups is presented in table (4). sICAM-1 level was higher in SLE and

SSc patients versus control (498.80±205.90 and 437.62±172.52 versus 158.49±43.31, P <0.000). The same result was recorded in sIL-2R that was higher in SLE and SSc patients versus control (3.002.76 ± 749.12 and 2.167.24±509.43 versus 848.23±68.78, P <0.000) and these differences were statistically significant between SLE versus SSc (P<0.000).

Correlations of sICAM-1 and IL-2Ra with the measured parameters in SLE are illustrated in table (5). sICAM-1 shows strong, moderate or even weak correlation with the other main biochemical parameters (IL-2Ra) [positive correlation]. Moreover, sICAM-1 shows a correlation with cutaneous limitation, subcutaneous activity, photosensitivity, oral ulcer, discoid rash [positive correlation], molar rash and proteinuria [negative correlation]. While, it shows no correlation with the other measured parameters.

The correlation of sICAM-1 and IL-2Ra with the measured parameters in SSc is presented in table (6). sICAM-1 and IL-2Ra are strongly correlated with each other and with Raynaud's phenomenon, gastrointestinal affection, myositis

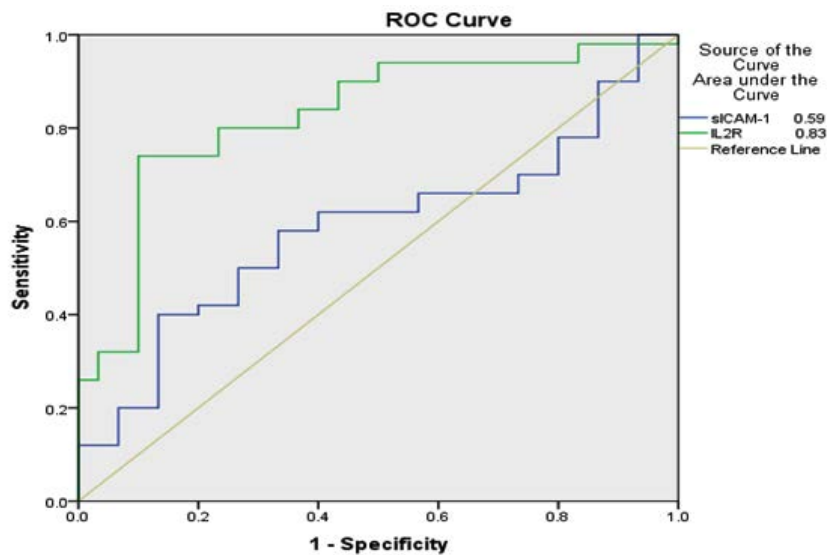
and skin scars [positive correlation]. While, they are negatively correlated with Antinuclear antibodies as well as each other. No correlation is detected with the other measured parameters.

Regrading ROC analysis, cut off levels of both sICAM-1 and IL2Ra are 455.59 (ng/ml) & 2525935 (pg/ml) in both SLE & SSc respectively. with the highest sensitivity and specificity. The cut-off levels as well as area under curve for both are presented in graphs (1 & 2).

DISCUSSION

In the current study, there were significant increase level of sICAM- in SLE patients was higher than that in healthy control as reported by Egerer *et al.*¹⁰; Sabry *et al.*¹¹; Kluzet *et al.*¹². In addition, the mean level of sICAM-1 in SSc was higher compared to healthy controls. A finding previously reported by Hasegawa *et al.*¹³.

Circulating sICAM-1 has been considered as the result of proteolytic cleavage of cell-bound ICAM-1 close to the cell membrane. ICAM-1 cleavage is regulated by tumor necrosis factor-a-



Graph 1. Comparison of Soluble Intracellular Adhesion Molecules-1 (sICAM-1) and Soluble Interleukin 2 Receptor (sIL-2R) as an indicator test to SLE disease, ROC Curve

ROC Curve analysis	AUC (95 % CI)	Cut off point	Significant
sICAM-1	0.587(.461-.712)	455.59	0.196
IL2Ra	0.828(.733-.923)	2.528.935	0.000

converting enzyme and multiple kinases, including mitogen-activated protein kinase, S locus receptor kinase, and phosphoinositide 3-kinase pathways¹³.

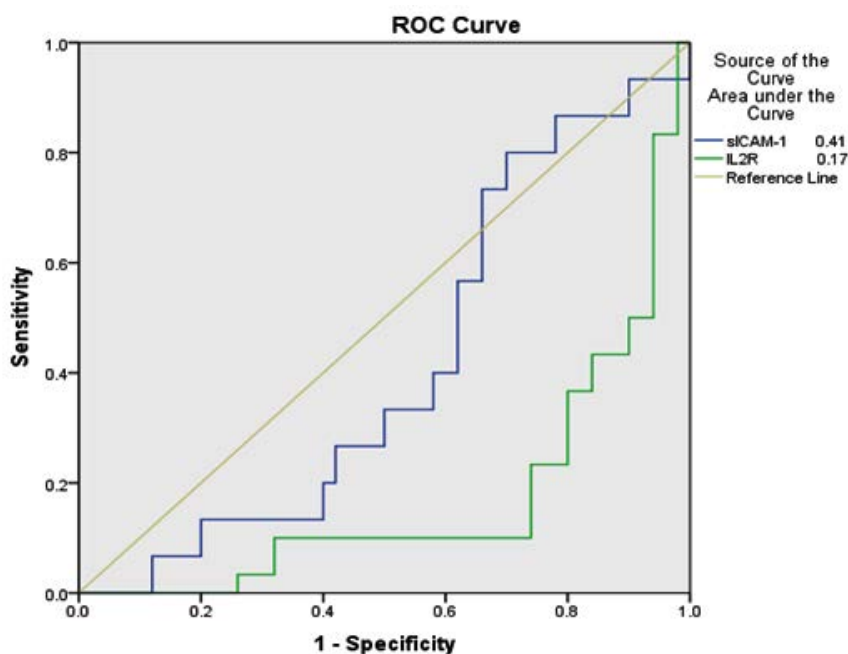
SLE pathophysiologic events are mediated by formation of immune complexes and complement cascade activation with progressive tissue destruction and major organ damage complication like lupus nephritis and cardiovascular morbidity. On basis of evidences ,inflammation plays a major role in SLE induced vascular dysfunction and consequently associated morbidity and mortality¹¹.

Cytokines are known to be produced by inflammatory cells. Endothelial cell adhesion molecules could play a pathophysiologic role in the initiation and progression of autoimmune diseases as well as atherosclerosis. ICAM-1, VCAM-1, and E-selectin are the major adhesion molecules that are mostly induced by the increased proinflammatory cytokines. They are detected by

tissue immunohistochemistry in atherosclerotic lesions in animal as well as human studies reported by Sabry *et al.*¹¹.

Inflammation, endothelial dysfunction, and atherosclerosis are interlinked pathological events. All share a common pathogenesis process. Elevated serum sICAM-1 is an evident biomarker and considered as indirect indicator for SLE induced tissue damage¹⁴. They reported sICAM-1 tissue up-regulation. Recently in 2017, Gensouset *al.*¹⁵ concluded that s ICAM-1 is an evident biomarker for both SLE pathogenesis and disease progression.

At the level of genetic study, *ICAM* polymorphisms have been studied and linked to their serum levels as well association with SLE risk and disease activity. rs3093030 and G in rs5498 alleles of sICAM-1 gene were found to be linked to SLE susceptibility. The genotype–phenotype relationships are evident and could explain the



Graph 2. Comparison of Soluble Intracellular Adhesion Molecules-1 (sICAM-1) and Soluble Interleukin 2 Receptor (sIL-2R) as an indicator test to SSc disease, ROC Curve

ROC Curve analysis	AUC (95 % CI)	Cut off point	Significant
sICAM-1	0.413 (.288-.539)	455.59	0.196
IL2Ra	0.172 (.077-.267)	2.528.935	0.000

raised plasma levels of soluble ICAM-1 in patients with SLE and its underlying etiological role¹⁶.

Previous studies described sICAM-1 as a potential biomarkers. sICAM-1 may provide information about the endothelial cells integrity and dysfunction in SSc¹⁷ but it lacks specificity to SSc¹⁸ and it is contradictory up to date¹⁹.

There are some reports demonstrating the critical roles of these biomarkers in SSc patients or animal model of SSc²⁰. sICAM-1 is functionally active and retains the ability to inhibit leukocyte endothelial cell interaction. On the other hand, sICAM-1 has also been reported to promote angiogenesis and induce the production of TNF- α ,

IFN- α , IL-6, and macrophage inflammatory protein-2. Thus, sICAM-1 may also have proinflammatory potential²¹. In 2010 Yoshizaki *et al.*²² suggested that L-selection and ICAM-1 regulate Th2 and Th17 cell accumulation into the skin and lung, leading to the development of fibrosis, and ICAM-1 deficiency inhibited the development of dermal sclerosis and pulmonary fibrosis with decreased inflammatory cell infiltration in the bleomycin-induced SSc model^{23,22}.

In accordance with the results of the present study, IL-2R was also seen on lymphocytes (CD30) of SLE and SSc diseases²⁴. Their expression indicates a regulatory role for these

Table 1. Demographic Characteristics and Disease Durations of all Studied Groups

Studied Sample Demographic Characteristics:	Systemic lupus erythromatosis (SLE)		Systemic Sclerosis (SSc)		Controls		Significant Tests P-value
	No.	%	No.	%	No.	%	
Number	50	35.71%	30	21.43%	60	42.86%	
Sex:							
• Female	42	84.00%	23	76.70%	40	66.70%	
• Male	8	16.00%	7	23.30%	20	33.30%	0.11
Age(years):	44.68 \pm 10.47		47.31 \pm 12.04		41.58 \pm 11.89		0.07
Disease duration (years):	7.97 \pm 3.44		5.93 \pm 2.55		-		0.00*

Data are expressed as mean \pm standard deviation or number (%) as appropriate.

P: significance versus control; *P: significance versus SSc used One-way ANOVA test (Post Hoc test)

Table 2. Clinical and Some Laboratory Characteristics in Different Studied Groups

Studied Sample Clinical Characteristics:	Systemic lupus erythromatosis (SLE) (n=50)		Systemic Sclerosis (SSc) (n=30)		Significant Tests χ^2 -test
	No.	%	No.	%	
Systemic involvement Arthritis	36	72%	16	53.3%	0.09
Serositis (pleurisy only)	4	8%	6	20%	0.11
Kidney	18	36%	6	20%	0.13
Heart	8	16%	4	13%	0.75
Lung	3	6%	15	50%	0.00*
Neurological	4	8%	0	0%	0.00*
Myositis	0	0%	4	13.3%	0.00*
Proteinuria positive	27	54%	0	0%	0.00*
Antinuclear antibodies +ve	46	92%	22	73.3%	0.02*
C-reactive protein +ve	19	38%	11	36.7%	0.91

Data are expressed as number (%) as appropriate.

P: significance versus control; *P: significance versus SSc used One-way ANOVA test (Post Hoc test)

molecules in SLE and SSc. Shedding of soluble IL-2R molecules into the circulation is the result of proteolytic cleavage of the membrane bound molecules. Other previous studies have reported that IL-2R levels were higher in patients with SLE than that in controls^{25,26}. Serum sIL-2R is a reliable marker of disease activity in patients with SLE and could be used as an indicator of early renal involvement with the possibility of using it for follow-up²⁷. Swadzba *et al.*²⁸ reported that increased level of sIL-2R is connected with definite SLE where inflammatory processes prevail²⁸.

Klonowska-Szymczyk *et al.*²⁹ revealed higher concentrations of sIL-2R in the cell culture in the active phase of SLE in their study. They explained this by that cells from patients with active SLE have marked response to stimulation by TLR3 and TLR9 ligands. The higher response and increased sIL-2R may be related to greater cell reactivity and involvement of the receptors of lymphocyte activation. They also, confirmed presence of significant correlation sIL-2R concentration and the activity of lupus

nephritis²⁹. Moreover, Dejica²⁶ reported that sIL-2R concentration (marker of lymphocyte activation) positively correlates with SLE induced renal inflammation.

At the level of genetic study, Carret *al.*³⁰ proved association of *IL2RA* locus with SLE. They explain this by that soluble IL-2RA concentrations correlate with rs11594656 genotype in SLE^{30, 31}.

Regarding the positive correlation that is detected between sICAM and sIL-2Ra in both SLE and SSc as autoimmune diseases, This correlation was previously reported in multiple sclerosis as another example of autoimmune diseases by Witkowska *et al.*³². The significant correlation of sICAM-1 and most of SLE disease activity that are observed in the current study confirm a nearly similar results of Sari *et al.*³³. They reported a significant positive correlation between sICAM-1 serum levels and SLE disease activity index (SLEDAI) score in SLE patients in their study. They also concluded that sICAM-1 serum level measurement and follow up may be considered as

Table 3. Some Laboratory Investigations in Different Studied Groups

Studied Sample Laboratory Characteristics	Systemic lupus erythromatosis (SLE) (n=50) mean ± SD	Systemic Sclerosis (SSc) (n=30) mean ± SD	Controls (n=60) mean ± SD	Significant Tests P-value
Erythrocytic Sedimentation rate (mm/hour)	76.88±45.40	65.73±72.61	10.80±3.56	0.00
Leucocytic Count (x 10 ³ /mm ³)	6.30 ± 1.40	6.55±1.77	6.23±1.83	0.69
Serum Creatinine (mg/dl)	2.09±0.44	0.85±0.24	0.76±0.19	0.00*

Data are expressed as mean ± standard deviation (mean ± SD).

P: significance versus control; *P: significance versus SSc used One-way ANOVA test (Post Hoc test).

Table 4. Comparison of Serum Levels of Soluble Intracellular Adhesion Molecules-1 (sICAM-1) and Soluble Interleukin 2 Receptor (sIL-2R) in Different Studied Groups

Studied Sample Variables	Systemic lupus erythromatosis (SLE) (n=50) mean ± SD	Systemic Sclerosis (SSc) (n=30) mean ± SD	Controls (n=60) mean ± SD	Significance Tests P-value
sICAM-1 (ng/ml)	498.80±205.90	437.62±172.52	158.49±43.31	0.000
sIL-2R (pg/ml)	3.002.76 ± 749.12	2.167.24±509.43	848.23±68.78	0.000*

Data are expressed as mean ± standard deviation (mean ± SD).

P: significance versus control; *P: significance versus SSc used One-Way ANOVA test (Post Hoc test)

Table 5. Correlations between sICAM-1/ sIL-2R and Measured Parameters in Systemic Lupus Erythromatosis Patients

Parameter	sICAM-1		sIL-2R	
	r	P-value	r	P-value
1. Sex	0.049	0.515	0.139	0.334
2. Age	0.098	0.497	0.214	0.136
3. Duration	-0.049	0.733	0.174	0.226
4. Arthritis	0.284	0.046	-0.030	0.837
5. Serositis (pleurisy only)	-0.016	0.912	0.161	0.912
6. Kidney	0.076	0.600	-0.264	0.064
7. Heart	0.126	0.382	0.106	0.464
8. Lung	0.228	0.111	-0.019	0.897
9. Neurological	0.057	0.696	-0.157	0.277
10. Cutaneous limitation	0.248	0.083	0.150	0.298
11. Subcutaneous activity	0.341	0.015	0.341	0.515
12. Photosensitivity	0.151	0.296	0.316	0.025
13. Malar rash	-0.244	0.088	-0.078	0.588
14. Oral ulcers	0.141	0.328	-0.021	0.885
15. Discoid rash	0.190	0.185	-0.120	0.407
16. ESR	0.199	0.166	-0.203	0.157
17. C Reactive protein	-0.079	0.588	0.383	0.037
18. Leucocytic count	0.187	0.194	-0.115	0.428
19. Serum creatinine	-0.095	0.511	0.492*	0.000
20. Antinuclear antibody	0.174	0.226	0.004	0.977
21. Proteinuria	-0.104	0.472	-0.277	0.052
22. sIL-2R	0.132	0.360	1	1

The correlation between parametric parameters was made using Person correlations

Table 6. Correlations between sICAM-1/ sIL-2R and measured parameters in Systemic Sclerosis patients

Parameter	sICAM-1		sIL-2R	
	r	P-value	r	P-value
1. Sex	0.363	0.045	-0.136	0.474
2. Age	0.045	0.812	-0.153	0.418
3. Duration	0.191	0.31	-0.305	0.101
4. Raynaud s phenomenon	0.019	0.922	0.204	0.279
5. Gastrointestinal	0.067	0.723	-0.103	0.590
6. Arthritis	-0.659*	0.000	0.338	0.068
7. Kidney	0.021	0.912	0.021	0.912
8. Heart	0.019	0.920	-0.067	0.726
9. Lung	-0.070	0.714	-0.344	0.062
10. Myositis	0.285	0.127	-0.280	0.134
11. Skin score	0.162	0.39	0.379	0.392
12. ESR	0.088	0.642	-0.303	0.104
13. C Reactive protein	-0.060	0.755	0.383	0.037
14. Leucocytic count	0.092	0.627	-0.112	0.555
15. Serum creatinine	-0.003	0.986	-0.158	0.404
16. Antinuclear antibody	-0.409*	0.025	0.451*	0.012
17. sIL-2R	0.511*	0.00	1	1

The correlation between parametric parameters was made using Person correlations.

an important serologic marker of disease activity for assessment a patient with SLE.

Many previous studies demonstrated a positive correlation of sIL-2R with SLE disease activity as it flares with active course of the disease and decreases with therapy and clinical improvement. These studies are mentioned in a review written by Illei *et al.*³⁴. So, sIL-2R levels paralleled lupus disease activity as observed in our study. Findings that confirm our observation related to the correlation of both parameters with systemic sclerosis disease activity were found as Mittag *et al.*³⁵ regarding sICAM-1 and Witkowska *et al.*³² regarding sIL-2Ra.

To the best of our knowledge, it is the first study that investigate the cut off value with the highest specificity and sensitivity of both sICAM-1 and sIL-2Ra that can be used as abiomarker for mentoring the disease activity in both SLE and SSc in Egypt. The levels of 455.59 (ng/ml) & 2525935 (pg/ml) for sICAM-1 and IL-2Ra respectively could be considered as remarkable value of both diseases which need further multicentric investigation over larger samples to confirm the results of the current study. From the results of the current study, it could be concluded that sICAM-1 and sIL-2Ra are noninvasive biomarkers for SLE and SSc that could play a pathophysiologic role in development and progression of both diseases. Moreover, sICAM-1 and sIL-2Ra are correlated with the disease activity at cut-off values of 455.59 (ng/ml) & 2525935 (pg/ml) respectively.

Limitation of the current study could that the patients were recruited from the inpatient wards and outpatient clinics of Cairo and Ain-Shams Universities Hospitals. That is considered unicenter study. Moreover, the small number of selected patients that are enrolled in our study especially SSc patients.

In conclusion, the authors recommended that further multicentric studies should be done on a large number of SLE and SSc patients to evaluate and confirm our hypothesis in the role of ICAM-1 and sIL-2Ra as markers in Systemic Lupus Erythematosus and Systemic Sclerosis. Then clinician may ask for both ICAM-1 and Soluble Interleukin-2 receptor levels to monitor the disease activity and the response of their patients to the treatment.

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