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ORIGINAL ARTICLE

Circulating IL 6 and IL 23 Levels in Systemic Lupus Erythematosus Patients and Association with Disease Activity

[1]Fatma el zahraa Y. Fathy, [2]Rasha N. Thabet, [3]Aya Elgendy, [1]Nagwa M Abo El Magd*

[1]Medical Microbiology and Immunology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt
[2]Internal Medicine and Rheumatology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt
[3]Internal Medicine and Allergy and Clinical Immunology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt

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Corresponding Author:
Nagwa M Abo El Magd
Medical Microbiology and Immunology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt
Tel. 01064888068
dr.nagwamahmoud@med.asu.edu.eg

ABSTRACT

Background: *SLE is a systemic autoimmune disease that is characterized by immune mediated tissue damage.* ***Objectives:*** *to determine the serum levels of IL- 6 and IL-23 in SLE patients and to evaluate their association with disease parameters and activity.* ***Methodology:*** *The study included sixty participants that were divided into (30) SLE patients and (30) healthy controls (HCs).* *Lupus Erythematosus Disease Activity Index (SLEDAI-2K) was assessed. Serum IL-6 and IL-23 level were measured by ELISA in all participants.* ***Results:*** *The SLE patients were 28 females and 2 males with a mean age of 34±11 years. Thirty healthy controls were 27 females and 3 males with a mean age of 40±7 years. The mean disease duration was 6.31± 5.36 with the mean SLEDI-2K 9±7.24 patients had active disease, 73.3% had mucocutaneous manifestations as malar rash, alopecia and oral ulcers, 70% had arthritis, 10% had neuropsychiatric lupus and 17 cases had lupus nephritis confirmed by renal biopsy. IL-6 and IL-23 serum levels were significantly increased in SLE patients than the control group ($p < 0.001$). Serum IL-6 and IL-23 significantly discriminated SLE patients from healthy controls at a cut-off value of 112.5ng/L and 121.82 ng/L respectively with 83.3% and 96.7% sensitivity and 80% and 90% specificity respectively .****Conclusion:*** *Serum levels of IL-6 and IL-23 were elevated in SLE patients in comparison to control group and might be potential biomarkers for disease activity monitoring in SLE patients.*

INTRODUCTION

SLE is a long-lasting, heterogeneous autoimmune disorder characterized by intricate and variable immunological dysfunction. Multiorgan systems like the musculoskeletal, mucocutaneous, cardiac, renal, and hematological systems, are significantly implicated in SLE. Clinical consequences are preceded by activation of the immune system signaling pathway and a buildup of pathogenic autoantibody particularities that indicates immunological tolerance breaches and a feed-forward pathway of disease pathophysiology [1].

Major components of innate and adaptive immune system are seen to be activated in SLE patients. During the disease course, elevated levels of a broad range of interleukins are seen. These cytokines can be detected in the saliva, urine and serum and target organ tissues such as skin, kidney, and synovia. Although some of these cytokines may have immunomodulatory or anti-inflammatory activities, most of them have pro-inflammatory characteristics[2].

Despite 20–30% of SLE patients have quiescent or chronically active disease, many of them undergo a waxing and waning disease pattern, with episodes of active clinical disease and flares alternating with periods of poor clinical disease activity[3].

SLE manifests in Egypt in a wide range of clinical and immunological characteristics, with several similarities to that seen in various countries and some distinctions seen among the same nation[4].

Several cytokines have been linked to disease activity in SLE patients and proposed as therapeutic targets for SLE patients with active disease. Cytokine blockage targeting Interleukin-6 (IL-6) and tumor necrosis factor alpha (TNF-α) had been successfully developed for treatment of rheumatoid arthritis, although no anti-cytokine therapies have been successfully introduced as therapy SLE patients[5].

A biomarker could help in decision making regarding diagnosis and treatment and be a handy tool to the clinicians. Many investigators defined the ideal biomarker for SLE that it should be specific, easy to detect, monitor the disease activity, useful in follow-up and with reasonable price[6].

IL-6 is a cytokine that enhances inflammation; it is secreted by fibroblasts, macrophages, lymphocytes, dendritic cells, and endothelial cells. By upregulating IL-2 and IL-2R, IL-6 can promote cytotoxic T cell differentiation and directly trigger naive B cell maturation into plasma cells. IL-6 enhances systemic autoimmune and pathological inflammatory processes because of these actions. According to several studies, IL-6 level was increased in the serum of SLE patients in comparison to healthy controls, suggesting that IL-6 might be involved in the pathogenic mechanism of SLE. Additionally, data reported that the SLE disease activity was highly correlated with elevated serum IL-6 release[7].

Interleukin-23 (IL-23) a heterodimeric cytokine that belongs to the IL-12 family, has a special p19 subunit and p40 subunit[8].IL-23 enhances amplification of the proliferation of a subtype of CD4+ T cells (Th17) that yield IL-17, a pro-inflammatory cytokine that promotes the release of molecules as IL-1, IL-6, TNF-α, nitric oxide synthase-2 and several chemokines. Such pathologic agents promote the rapid activation and recruitment of granulocytes and macrophages, arming them with a wide array of tools to inflict tissue damage that results in chronic inflammation and eventually the development of clinical manifestations[9].

A fundamental regulatory mechanism that links the innate and adaptive immune systems is the IL-23/IL-17 axis. It is also very important for the evolution of inflammatory autoimmune disorders [10].

Several studies including SLE patients reported that serum level of IL-23 was elevated in SLE patients compared with healthy controls [11].

Currently, the importance of many cytokines as IL-6 and IL-23 in disease pathogenesis and correlation with disease activity in SLE patients are poorly understood, Therefore, we conducted this study to ascertain the association between IL-6, IL-23 and SLE disease activity.

The current study aims to determine the serum levels of IL- 6 and IL-23 in SLE patients and to evaluate their association with disease parameters and activity.

METHODOLOGY

The present study is a case control study performed in the Medical Microbiology and Immunology Department in cooperation with Internal Medicine and Rheumatology and Allergy and Clinical Immunology Department, Faculty of medicine, Ain Shams University, Egypt. The study was conducted on 60 participants divided into the SLE patients' group (n = 30) and healthy controls (n=30). The study was approved by the ethical committee of the Faculty of Medicine, Ain-Shams University (FMASU R 184 /2022). Prior to recruitment, written informed consent was obtained from each participant. On processing the data base, confidentiality was assured.

Study subjects:

SLE patients' group:

30 SLE patients were recruited from the Allergy, Immunology and Rheumatology Units, Ain Shams University Hospitals during the period from September to November 2022. A comprehensive clinical examination and laboratory tests were performed for each patient. Laboratory and immunology profiles included the complete blood count (CBC), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), 24-hours urine protein, antinuclear antibodies (ANA), anti-double stranded deoxyribonucleic acid (anti-dsDNA) and serum levels of complement components [C3, C4]. Renal biopsy was performed to confirm the diagnosis of lupus nephritis (LN). The disease activity was evaluated by the Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K). Each patient was evaluated according to the SLEDAI-2K score calculator (https://qxmd.com/calculate/calculator_335/sledai-2k) and active disease was defined as SLEDAI-2K > 4[12].

Inclusion and exclusion criteria:

Inclusion criteria:

SLE patients, who met the Systemic Lupus International Collaborating Clinics (SLICC) criteria for diagnosis of SLE [13].

Exclusion criteria:

SLE patients younger than 18 years old; Patients having other autoimmune disease; patients with malignancy; Patients with cognitive or communication disorders; Patients with liver or kidney dysfunction, Pregnant patients.

Control group:

30 apparently healthy individuals matching in age and sex were included as healthy controls.

Serum collection, IL-6 and IL-23 measurement:

From all study subjects, 5 ml blood samples were collected then centrifuged, and serum samples were stored at -80°C until analysis. Serum levels of IL-6 and IL-23 were measured by enzyme linked immunosorbent assay (ELISA) using specific cytokines kits (Bioassay technology laboratory, Cat.No: E0090Hu; Cat.No : E0074Hu, Shanghai, China). According to the manufacturer's instructions, the optical density (OD) was measured within the 10 minutes after having added the stop solution at 450 nm wavelength by a micro-plate reader (CLARIOstar®, BMG Labtech, Germany). Finally, according to standards' concentration and the corresponding OD values, the standard curve linear regression equation was calculated out, and then the OD value of the sample was applied on the regression equation to calculate the corresponding sample's concentration.

Statistical Analysis:

Statistical package for social science (SPSS) software version 25 was used. Quantitative data were expressed as mean, and standard deviation, while qualitative data were expressed as frequency and percentages. Different types of graphs were used to illustrate the distribution and the associations between data. t-test was used to assess the differences between the two groups, and the association between the qualitative data by chi-squared test. The Correlation coefficient (r): Pearson's' correlation test was done to measure the interdependency between different quantitative data Receiver operating characteristic (ROC) curve analysis was performed to discover the predictive and cutoff value for the disease. P value < 0.05 was considered significant.

RESULTS

Our study included 60 participants divided into two groups. The SLE patient's group were 28 females and 2 males with a mean age of 34±11 years. The control group included 27 females and 3 males with a mean age of 40±7 years. No statistically significant difference regarding the age and gender of SLE patients and healthy controls was detected (p=0.07, 0.06, respectively). Regarding the clinical characteristics of SLE patients, the mean disease duration was 6.31± 5.36 years with the mean SLEDI-2K 9±7 and 24 patients had active disease. Regarding the clinical presentations, 73.3% had mucocutaneous manifestations as malar rash, alopecia and oral ulcers, 70% had arthritis, 10% had neuropsychiatric lupus and 17 cases had lupus nephritis confirmed by renal biopsy that revealed; 3 class II, 7 class III, 5 class IV and 2 class V. All patients received antimalarial and prednisolone (5-30 mg/day), Azathioprine was received by 15 (50%), mycophenolate mofetil was received by 8 (26.7%) and cyclophosphamide was prescribed for 3 (10%). Laboratory parameters of the SLE patients is also presented in (Table 1).

Table 1: Demographics, clinical characteristics and laboratory parameters of SLE patients

Parameter	SLE patients (N=30) Mean ± SD or N(%)
Age	33.87±11
Gender	Female = 28 (93.3%)
	Male = 2 (6.7%)
Disease duration	6.31± 5.36
SLEDAI-2K	9± 7
Disease activity	Active disease = 24 (80%)
	Inactive disease = 6 (20%)
Mucocutaneous manifestations (Malar rash, alopecia, oral ulcers)	22 (73.3%)
Arthritis	21 (70%)
Neuropsychiatric lupus	3 (10%)
Lupus nephritis	17 (56.7%)
Serositis	0 (0%)
WBC	6.09±2.40
HB	10.60±1.84
PLT	235±90
ESR	46±32
Protein/creatinine ratio	0.33±0.51
C3 consumption	8 (26.7%)
C4 consumption	6 (20%)
Granular casts	4 (13.3%)
Pyuria	3(10%)
ANA	30 (100%)
Anti-ds DNA	17 (56.7%)

WBCs: White Blood Cells, HB: Hemoglobin, PLT: Platelets, ESR: Erythrocyte Sedimentation Rate, C: Complement, ANA: Antinuclear Antibody, Anti-ds DNA: Anti Double Stranded DNA

Serum levels of IL-6 and IL-23 in SLE patients in comparison to the control group:

IL-6 and IL-23 were significantly elevated in the serum of SLE patients (163±40.371 ng/L, 200±31.110 ng/L respectively) compared to the healthy controls (90.60±54.427 ng/L, 76.50±45.072 ng/L respectively) (p < 0.001) (Table 2, figure 1).

Table 2: Comparison of serum levels of IL-6 and IL-23 in SLE patients and control group

	SLE patients		Control group		"t" test	P value	Sig
	Mean	SD	Mean	SD			
IL-6	163.00	40.371	90.60	54.427	7.22	<0.001	S
IL-23	200.00	31.110	76.50	45.072	12.76	<0.001	S

Sig. = significance, S = significant

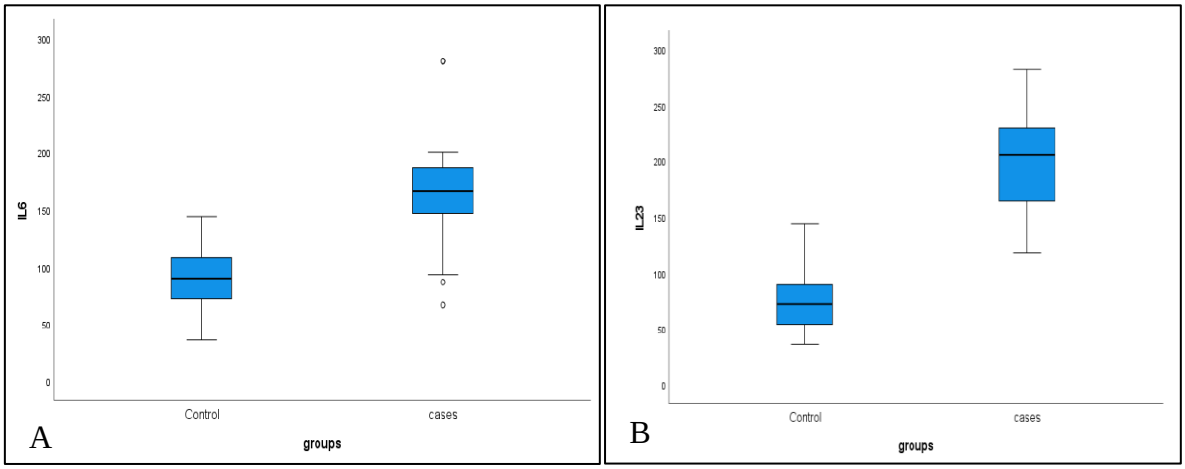

Fig 1: Comparison of serum levels of IL-6 and IL-23 in SLE patients and healthy controls.

Serum levels of IL-6 and IL-23, different clinical, serological parameters and disease duration of SLE patients with active disease compared to SLE patients with inactive disease

According to the SLEDAI-2K score, 24 SLE patients had active disease and 6 patients had inactive disease. By comparing the levels of IL-6 and IL-23 in the sera of SLE patients, it was revealed that the serum levels of IL-6 and IL-23 were elevated in active SLE patients (166.53±49.397ng/L, 203.68±44.590ng/L respectively) compared to inactive SLE patients (148.89±36.918ng/L, 185.29±51.785ng/L respectively) but not statistically significant. Regarding ESR and HB, they were significantly positively correlated with SLEDAI-2K score (p=0.027 and 0.028 respectively). Nonetheless, it wasn't correlated neither with disease duration nor WBC and protein/creatinine ratio. Also, on comparing active and inactive SLE patients, it was found that mucocutaneous manifestations and anti-ds DNA autoantibodies were significantly positive in relation to disease activity (p=0.013 and 0.007 respectively). Surprisingly, arthritis, neurological manifestations, nephritis, complement components (C3 and C4) didn't exhibit any statistical significance (Table 3, figure 2).

Table 3: Comparison between active and inactive SLE patients regarding serum levels of IL-6 and IL-23, different clinical, serological parameters and disease duration

Parameter	SLE patients (Active disease) N=24		SLE patients (Inactive disease) N=6		"t" test	P value	Sig
	Mean	SD	Mean	SD			
IL-6	166.53	49.397	148.89	36.918	0.815	0.422	NS
IL-23	203.68	44.590	185.29	51.785	0.799	0.451	NS
Mucocutaneous manifestations	4(16.7%)	20(83.3%)	4(66.7%)	2(33.3%)	6.136	0.013	S
Arthritis	20 (83.3%)	24(100.0%)	5 (83.3%)	1 (16.7%)	10.15	0.001	NS
Neurological manifestations	21 (87.5%)	3 (12.5%)	6 100.0%	0 0.0%	0.833	0.361	NS
Nephritis	9 (37.5%)	15(62.5%)	4 (66.7%)	2(33.3%)	1.66	0.197	NS
anti-ds DNA	7 (29.2%)	17(70.83%)	6 (100.0%)	0 (0.0%)	9.808	0.007	S
C3	normal 16 (66.7%)	consumed 8 (33.3%)	normal 6 (100.0%)	consumed 0(0.0%)	2.72	0.099	NS
C4	normal 18 (75.0%)	consumed 6 (25.0%)	normal 6 (100.0%)	consumed 0(0.0%)	1.875	0.171	NS
WBCs	6.1167	2.45316	5.9833	2.37690	-0.120	0.906	NS
HB	10.3208	1.91402	11.7000	1.01193	2.426	0.028	S
ESR	50.54	32.840	25.33	18.864	-2.469	0.027	S
Protein/creatinine ratio	0.3908	0.6585	0.1083	0.06585	1.27	0.084	NS
Disease duration	6.1729	5.55171	6.8333	4.95648	0.265	0.793	NS

Sig. = significance, S = significant, NS=non-significant

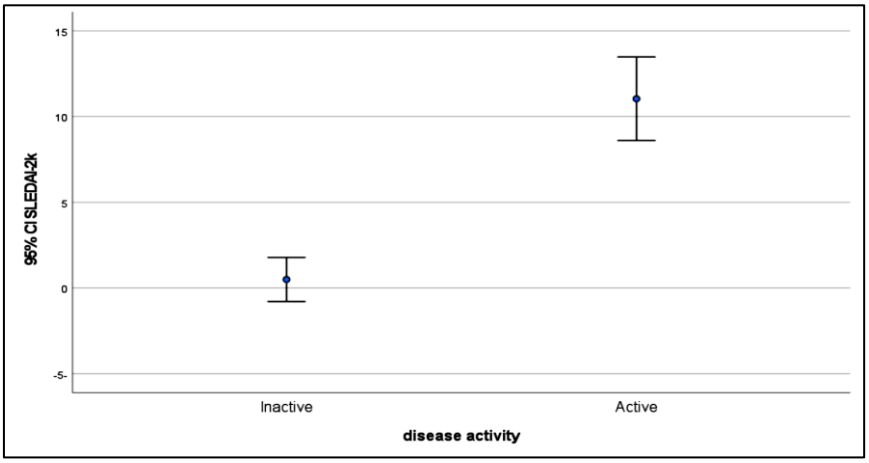

Fig 2: Classification of SLE patients by SLE disease activity index SLEDAI-2K score

Correlation between IL-6, IL-23 and SELDI-2K in the patients' group:

IL6 and IL-23 serum levels showed positive correlation with SELDI-2K score of the patients and there was moderate significant correlation between IL-6 and IL-23. Also, there was mild correlation between IL-6 and SELDI-2K but statistically non-significant (Table 4, figure 3).

Table 4: Correlation between IL6, IL23 and SELDI-2K in SLE patients:

	r / P value	SLEDAI-2K	IL6	IL23
SLEDAI-2K	r	1	0.394	0.065
	P value	---	0.059	0.732
IL 6	r	0.394	1	0.690**
	P value	0.059	-----	<0.001*
IL 23	r	0.065	0.690**	1
	P value	0.732	<0.001*	----

*Significant.

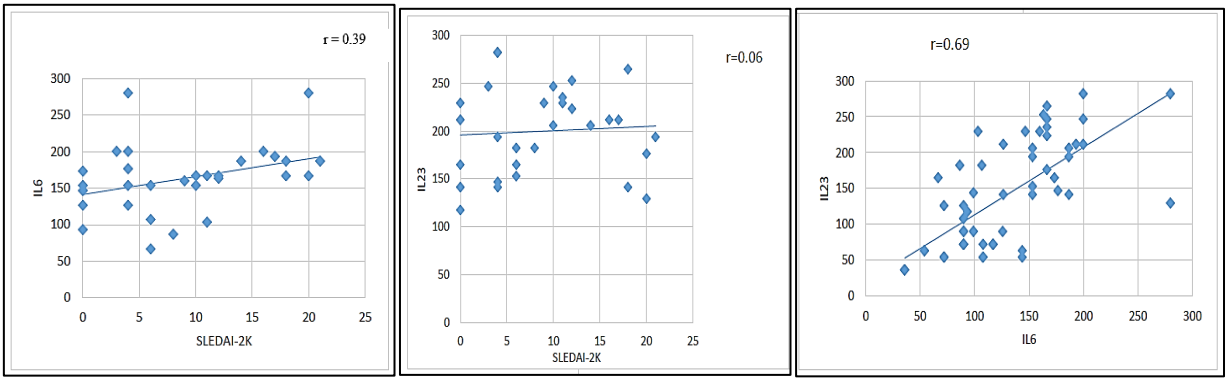

Fig. 3: Correlation between IL6, IL23 and SELDI-2K in SLE patients

Correlation between IL-6 and IL-23 with different laboratory parameters and disease duration in SLE patients:

On correlating the serum levels of IL-6 and IL-23 with different laboratory parameters and disease duration, it was found that IL-6 level was positively correlated with ESR (r= 0.35, p value = 0.05). On the contrary, IL-6 and IL-23 were not correlated with WBC, PLT, HB or disease duration (Table 5).

Table 5: Correlation of serum IL-6 and serum IL-23 with different laboratory parameters and disease duration in SLE patients

	IL6		IL23	
	r	P-value	r	P-value
WBC	0.04	0.82	-0.01	0.944
HB	-0.34	0.06	0.01	0.92
PLT	0.03	0.854	0.105	0.58
ESR	0.35	0.05*	-0.162	0.39
Disease duration	0.107	0.08	0.08	0.66

*Significant.

Serum levels of IL-6 and IL- 23 in different SLE-related clinical manifestations and laboratory parameters:

Patients with mucocutaneous manifestations had higher mean serum IL-23 in comparison to patients without, patients with arthritis had higher mean serum IL-6 and IL-23 in comparison to patients lacking it. Serum IL-23 was significantly elevated in SLE patients with lupus nephritis compared to patients without lupus nephritis, but serum IL-6 was increased in lupus nephritis positive patients compared to lupus nephritis negative patients although not statistically significant (Table 6).

Table 6: Serum IL-6 and IL-23 in different SLE-related clinical manifestations and laboratory parameters

		IL6		t test	p value	IL23		t test	p value
		Mean	SD			Mean	SD		
Mucocutaneous manifestations	Negative	174	54	0.77	0.44	198	64	0.12	0.9
	Positive	159	45			201	39		
Arthritis	Negative	150	38	0.98	0.33	186	48	1.13	0.26
	Positive	169	50			206	45		
Lupus nephritis	Negative	150.81	54.427	1.115	0.274	155.96	45.072	5.229	< 0.001*
	Positive	169.80	40.371			227.68	31.110		
anti-ds DNA	Negative	157	37	0.172	0.86#	206	45	0.425	0.58#
	Positive	160	47			200	45		
C3	Normal	155	45	1.48	0.14	202	47	0.41	0.67
	Consumed	184	48			194	45		
C4	Normal	158	44	1.08	0.28	203	45	0.63	0.52
	Consumed	182	57			198	64		

*Significant # krusal wallis test

Diagnostic accuracy of serum IL-6 and IL-23 in discriminating SLE patients from healthy controls:

ROC curve analysis revealed that both IL-6 and IL-23 had excellent diagnostic accuracy in discriminating SLE patients from healthy controls with an AUC of 0.910 at a cut-off >112.5 ng/L and 0.992 at a cut-off >121.82 ng/L with 83.3% and 96.7% sensitivity and 80% and 90%specificity respectively (Table 7, Figure 4).

Table 7: Diagnostic accuracy of serum IL-6 & IL-23 levels in discriminating SLE patients from healthy controls

Interleukins	Cut-off level	AUC	95% CI	Sensitivity	Specificity	P value
IL-6 (ng/L)	112.5	0.910	0.830- 0.990	83.3%	80%	<0.001*
IL-23 (ng/L)	121.82	0.992	0.978-1.0	96.7%	90%	<0.001*

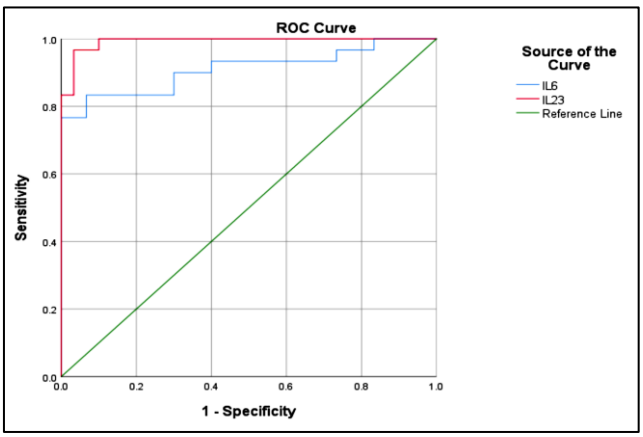

Fig 4: ROC curve for serum IL-6 and IL-23 levels in SLE patients

DISCUSSION

Systemic lupus erythematosus is an autoimmune disease that causes widespread inflammation and tissue damage affecting multiple body organs. The disease has diverse clinical presentations with unpredictable course. it is characterized by stimulation and dysregulation of both innate and adaptive immune responses. The pathogenic mechanism of SLE is complex, and the directed therapies are still a challenge for the physicians. Also, it is unknown if elevated levels of certain cytokines are causing the disease, or it is an epiphenomenon to the malfunctioning immune responses and regulation[2].

In Egyptian patients, SLE patients have a wide diverse clinical presentations and immunological abnormalities that could be identical to those in other countries or distinct within the same within the same nation [9].

IL-6 plays an important role in systemic autoimmunity and pathologic inflammation. Several researches have investigated IL-6 levels in the sera of SLE patients and their correlation with disease activity[7].

IL-23, which is the second target in our study, is secreted by macrophages, keratinocytes, dendritic cells,, and other antigen-presenting cells, has a crucial role in inflammation, including the activation of Th17 cells [10].

The IL-23/IL-17 axis is developing into a fundamental regulator that unites the innate and adaptive immune systems and is essential for the emergence of autoimmune inflammatory disorders[14].

Our study was performed on Egyptian SLE patients to assess these cytokines level and correlating them with different parameters of disease activity, using SLEDAI-2K score >4 defining activity**.** Our study concluded that ESR, anti-dsDNA ab level and mucocutaneous manifestations were positively correlated with the SLE disease activity that agreed with the study done by Thanadetsuntorn et al. [15] who found that ESR and anti-dsDNA revealed a significant positive correlation with the SLEDAI-2K, while no correlation found between active patients with disease duration, WBCs or protein/creatinine ratio which might be attributed to different patient selections.

In addition to the ESR level, we observed a significant correlation between the hemoglobin level and SLE disease activity that agreed with the Egyptian study done by El Shafey et al.[16].

As regard cytokines study, we detected the serum IL6 higher in SLE patient than the control group; in addition to that it was increased in SLE patients with active disease than those with inactive SLE disease (although not significant) that all agreed with many studies done by Ding et al.[7] and Thanadetsuntorn et.al.[15].

In *2021* Idborg and Oke [2] found higher IL6 level in active lupus than inactive patients which agree with our study. Also, in 2010**,** according to Ball et al**.**[18], Tocilizumab is a humanized monoclonal that suppresses IL-6 signaling and is effective in treating SLE patients.

By studying different SLE parameters we reported significant correlation with IL6 with ESR level but there was non-significant correlation with complement level, anti-dsDNA ab or mucocutaneous manifestations which agreed also with ELShafey et al. [16] and Thanadetsuntorn et al.[15] who correlated ESR with IL6 but not with complement or anti ds DNA ab levels.

Previous studies by Eilertsen et al.[17] and Ball et al.[18] who investigated IL-6 plasma concentration in relation to SLE arthritis have reported that elevated IL-6 was correlated with active ongoing arthritis which was consistent with our findings.

An Egyptian study done by Sabry et al.[19]**,** concluded that there wasn't any significant correlation between IL-6 and platelets or white blood cell levels and that also agreed with our work, while the same study concluded finding a negative correlation between these elevated levels and mean blood hemoglobin level that disagreed with us, we didn't detect any correlation regarding the hemoglobin level, this may be attributed to the smaller sample size included in this study.

As regard lupus nephritis patients, a higher level of IL6 was detected in comparison to SLE patients without nephritis (not strongly significant) that agreed with Idborg and Oke[2] study in addition to study by Kamabayana et al.[20].

It was discovered in experimental and clinical research that IL-6 facilitated renal damage in glomerulonephritis and other renal illnesses. In research on mice with lupus nephritis, IL-6 was discovered to promote fibrosis, tissue destruction, and several lupus nephritis-related illnesses. [21].

Regarding IL-23**,** its serum level was observed to be significantly higher in SLE patients than healthy controls that agreed with different studies[22-23].

IL-23 level was increased in active SLE patients than inactive but not statistically significant which is agreement with studies *by* Hegab et al. [23] and Vukelic et al.[24] who reported that serum IL-23 was positively correlated with disease activity assessed with the SLEDAI. On the contrary study by Katarzyna et al. [25] who did not observe any correlation between serum IL-23 and SLE disease activity restrained with SLEDAI.

Regarding IL23 there was no statistically significant correlation with ESR, complement level, anti-dsDNA antibody, mucocutaneous manifestations but higher in patients manifested with arthritis, Vukelic et al.[24] reported that serum IL-23 was correlated with skin manifestations and arthritis, but no correlation was detected with cytopenias or serositis. IL-23 was similarly correlated with anti-dsDNA antibody positivity and contrarywise correlated with C3 levels. A study by Rafat et al.[9] reported that patients with oral

ulcers, arthritis, alopecia, and positive anti-dsDNA antibody had considerably increased levels of IL-23.

IL-23 was significantly elevated in SLE patients with lupus nephritis than in patients not having nephritis that agreed with many different studies [9- 26-28].

Reiterating that IL-23 levels were significantly increased in the urine and serum of lupus patients with lupus nephritis (LN) and those without LN in comparison to controls, Xia et al.[29] concluded that IL-23 might have a role in the etiology of LN.

The pathogenic mechanism of systemic lupus erythematosus is complex and characterized by heterogeneity, this is a crucial factor that impacts the different clinical phenotypes that subsequently impact the biomarkers used for monitoring the activity of disease and the choice of specific therapies that suit each patient. Numerous mechanisms could explain the positive relation between the levels of IL-6 in serum and SLE. Excessive formation of autoantibodies leads to several immune complex depositions which aids in SLE pathogenesis by enhancing autoreactive B lymphocyte proliferation and differentiation of naive B cells into plasma cells [7].

Also, IL-6 could upregulate the recombination-activating genes and enhances their expression that leads to autoantibody over formation in SLE [30]. Additionally, an imbalance in the T helper 17 (Th17)/ regulatory T cell (Treg) ratio leads to the development of numerous autoimmune disorders. Because IL-6 may hinder Treg differentiation, it may contribute to the occurrence of systemic lupus erythematosus by creating an imbalance between Th17 and Treg ratio [26].

Another study reported that IL-6 might increase vascular permeability by enhancing the secretion of vascular endothelial growth factor from fibroblast-like synoviocytes[31], increased immune complex accumulation and infiltration of inflammatory cells. Thus, IL-6 might be involved in SLE development by compromising vascular endothelial efficiency. All of this backs up our findings that increased serum IL-6 levels are related positively to SLE disease[7].

IL-23 is generated and has both pro-inflammatory and inhibitory roles. It is also essential for the development of naive CD4 T cells [32]. IL-23 is crucial for Th17 development because it maintains the Th17 phenotype and increases IL-17 expression [33].

It has been demonstrated that T helper 17 cells and regulatory T cells both contribute to the pathophysiology of SLE[34]. Anti-IL-23 therapy aims to block various inflammatory processes that are crucial for triggering autoimmune diseases[35].

CONCLUSION

In conclusion, this study detected that the levels of IL-6 and IL-23 were elevated in the sera of SLE patients than control group. Furthermore, serum IL-6 and IL23 levels were correlated positively with disease activity. Therefore, IL-6 and IL23 might be potential biomarkers for disease activity monitoring in patients with SLE. Interestingly, IL-6-targeted therapy could serve as an effective strategy for treating SLE patients. However, further studies with larger sample size are needed to validate our results.

This manuscript has not been previously published and is not under consideration in the same or substantially similar form in any other reviewed media. I have contributed sufficiently to the project to be included as author. To the best of my knowledge, no conflict of interest, financial or others exist. All authors have participated in the concept and design, analysis, and interpretation of data, drafting and revising of the manuscript, and that they have approved the manuscript as submitted.

Declaration of interest and funding information:

The authors have no conflicts of interest. No funds have been received for this research.

Contributors

All authors have made substantial contributions to the design of the study. Sample collection, clinical examination and clinical diagnosis were performed by **Dr. Rasha Nabil, Dr. Aya Elgendy**. The Serological tests were performed by **Dr/Nagwa Mahmoud** and **Dr. Fatma El zahraa Youssef**. Data analysis and interpretation were contributed to all the authors. Drafting the article was performed by **Dr. Nagwa Mahmoud, Dr. Fatma El zahraa Youssef, Dr. Rasha Nabil and Dr. Aya Elgendy**. Revising the draft critically for important intellectual and scientific content was carried out by all the authors. All the authors provided final approval of the version to be published.

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