The frequency and structure of heart damage in systemic lupus erythematous

Abstract:

This study focused on the immunological aspect of the effect of immunosuppressive therapy in systemic lupus erythematous (SLE), specifically choriokinin, corticosteroids, and glucocorticoids (GCs), on the exposure of cardiovascular disease. The study period extended from 2022 to early 2024 and relied on the results of screening of 88 SLE patients and a control group of 85 patients. The causes of heart damage in SLE patients were identified to assess the relationship with disease activity, duration, and rheumatic treatment. Previously, we first determined NT_proBNP levels in SLE patients not receiving specific rheumatic treatment and identified a relationship between biomarker and immunological marker concentrations of SLE activity (increased serum levels of anti cardiolipin IgG, anti_dsDNA, antinuclear antibodies, and decreased complement C4) and markers reflecting impaired kidney function [1, 2]. Corticosteroids are effective in preventing the progression of SLE and increasing patient survival, while reducing the exposure of atherosclerosis and thrombosis [1, 3, 4] and hypercholesterolemia [2, 5], ultimately reducing a exposure of cardiovascular disease at SLE patients, despite isolated reports of cardiac toxicity [4].

Keywords : immunosuppressant , systemic lupus erythematous (SLE) , choroquine , corticosteroids , cardiac and circulatory complications , BNP , ACA , dsDNA

Introduction:

Systemic lupus erythematous (SLE) is a chronic, multisystem immunological disorder of unknown causality and genetic predisposition it presents with diverse clinical features and follows an unpredictable progression [1]. Heart disease affects more than 55% of SLE patients and is a leading cause of fatal condition. All cardiac anatomical structures can be affected by SLE, such as the pericardium,

endocardium, coronary vessels, and myocardium, with heart failure (HF) being the final stage of cardiac and circulatory disease [2].

The pathogenesis of cardiac damage in SLE is thought to depend on the combined or independent effects of chronic immunological disorder inflammation, accelerated progression of atherosclerosis, and the use of certain ant rheumatic drugs [3]. According to an epidemiological study (n = 500 people), in patients with systemic lupus erythematous M cardiac damage was more frequently recorded [6]: arrhythmia and electrical disturbances in 22% and 6%, coronary heart disease - in 13% and 4%, major valve insufficiency in 11% and 2%, myocardial infarction (MI) - in 6% and 2%, cor pulmonale in 2.2% and 0.2%, heart failure (HF) in 1.0% .

Materials and Methods:

study embraced 88 patients, 80 (92%) females and 8 (9.5%) males, with a mean age of 35 years, making it an ideal sample for the study [5,9]. Patients were monitored at Al-Mawadah Private Hospital and private laboratories specializing in immunodiagnostics from 2022 to 2024. Systemic lupus erythematous (SLE), in its most severe form, leads to impaired carbohydrate metabolism and cardiac and circulatory complications in rheumatoid arthritis and SLE.

Table 1 : Explains immunological laboratory procedures, their procedures and the aims of performing them.

Immunological test	Examination (Manufacturer)	Aim
SLLICC_DI	N/N	The aim of the examination is to assess the amount of accumulated damage to the organs resulting from lupus
Anti_dsDNA	ELISA test (thermo fisher scientific)	It aims to detect autoantibodies, which are responsible for attacking the body's tissues.
NT_proBNP	Cobas (Beckman Coulter)	The purpose of screening is to diagnose a heart condition by

		detecting the level of peripheral brain peptide
ACA	ELISA test (Euroimmun)	The aim is to detect anti-centromere antibodies responsible for attacking healthy tissues in an immunological disorder disease.
Anti_ENA	ELISA test (Inova)	It aims to detect antibodies to nuclear antigens and is used to detect Sjögren's syndrome and polymyositis.
SLEDAI_2K	N/N	The index is used to evaluate lupus disease and helps doctors assess the patient's response to treatment.
Anti_JO_1 Antibody	ELISA test (Inova)	Type of Anti _ENA test
Anti_RNP Antibody	ELISA test (Inova)	Type of Anti _ENA test
Anti_SCI70 Antibody	Topoisomerase test	The aim of detecting SCI70 antibodies in the blood is to diagnose systemic scleroderma.
Anti_Sm _ Antibody	ELISA test (Inova)	Type of Anti _ENA test
Anti_SSA Antibody	ELISA test (Inova)	Type of Anti _ENA test
Anti_SSB Antibody	ELISA test (Inova)	Type of Anti _ENA test
B2_GPI Autoantibodies	ELISA test (Euroimmun)	The aim of detecting antiphospholipid syndrome is to detect antibodies to beta-2 protein.

Exclusion Criteria:

Patients aged 16 years and older, aged 63 years and older, and those with comorbidities such as tumors, malignancies, or infectious diseases were excluded from the clinical study. Clinical and lab analyses were carried out with standard methods. SLE disease activity was determined utilizing the SLEDAI_2K index (Systemic Lupus Erythematous Disease Activity Index 2000) [6]. The SLICC_DI (Systemic Lupus Erythematous International Collaborating Clinics Damage index) was used to assess changes [7].

The medical reports provided by cardiologists were reviewed for all patients, and they had conventional hazard factors for cardiac and circulatory disease . Transthoracic echocardiography was performed. Patients were evaluated for left ventricular diastolic and systolic function, ejection fraction (EF), left ventricular myocardial thickness, chamber sizes, systolic pulmonary artery and diastolic pressure , pericardial status, and valves.

Laboratory and Statistical Diagnosis:

Concentration of the N-amino terminal fragment of (probrain- natriuretic – peptide) (NT_proBNP) in serum was determined by electrochemical analysis (ECL) on a Cobas analyzer utilizing the Elecsys proBNP II test system.

Typically, NT_proBNP levels are ≤125 pg/ml, according to procedural guidelines [8]. Statistical analysis was performed utilizing parametric and nonparametric statistical methods of Applied Statistics NT_proBNP in the two groups is equal to 12. Variables were presented as medians (ME), with the upper and lower quartiles indicated in parentheses (25th percentile; 75th percentile). The reliability of variations between the two groups was assessed utilizing the (SPSS software) criterion,. Qualitative indicators were compared in two unrelated groups in association table utilizing the $\chi 2$ test. The significance level was $p < 0.05$ [9].

Procedures:

median duration of SLE was two years [, with moderate disease activity (SLEDAI_2K) 9 coordinates [4] , and the SLICC_DI damage index was 2 coordinates [2]. The main clinical manifestations of the disease embraced hematological disorders (49%), nephritis (45%), arthritis (37%), skin lesions (34%), and synovitis (33%). Eighty-six patients (98%) had immune disorders: elevated levels of antinuclear factor (ANF) were recognition in 95%, and anti_dsDNA antibodies were recognition at 78% of SLE patients. Associated antiphospholipid syndrome (allergic fungal sinusitis (AFS) and Sjögren's syndrome were identified in 9 (9%) and 10 (11%) patients, respectively. [10]

Valvular regurgitation with varying degrees of regurgitation (not requiring surgical treatment) was the most frequently observed cardiac abnormality in systemic lupus erythematous (SLE), identified in 79 patients (90%): 78 patients (89%) with tricuspid regurgitation, 72 patients (82%) with mitral regurgitation, 57 patients (7%) with pulmonary artery regurgitation, and 15 patients (14%) with aortic regurgitation. Endocarditis was identified in 26 patients (30%), and mitral or tricuspid valve prolapse in 30 patients (34%). The rarest was mitral, tricuspid, and aortic stenosis, identified in one patient (1%). The median concentration of NT_proBNP was 92 (27–332) pictograms per milliliter, an elevated level of NT_proBNP (> 125 pictograms per milliliter) was identified in 29 patients (32%).

The possible association of cardiac disorders with therapy used in SLE, patients had divided into two groups.

- **Group 1** : embraced 43 patients (40 women - 3 men) with a median age of 30 ± 15 years who, at time of examination, had not received glucocorticoids (GC), immunosuppressant

- **Group 2** : embraced 45 patients (40 women - 5 men), the median age was 30 ± 15 years patients took a variety of combinations of these drugs . choroquine, corticosteroids at a dose of 150 mg/day. Among them were both newly ill and long-term patients with SLE, but who canceled previously prescribed therapy. HA was received by 44 (98%) of them, the median dose was 20 mg /day when calculated for prednisone. During the entire period of the disease, cyclophosphamide was used in 23 (48%) patients, azathioprine in 17 (38%),

mycophenolate mofetil in 16 (36%), methotrexate in 9 (19%), choroquine , corticosteroids in 43 (96%).

Results immunological:

Immunology and laboratory characteristics of patients of both groups are presented in Table2. The groups were comparable in age and gender, women predominated (93% - 90%).

Patients of the 2nd group had a longer duration of illness than participants of the 1st group $p < 0.00001$), less activity (SLEDAI_2K and 12 coordinates, $p < 0.001$), a higher damage index (SLICC_DI 1 - 0 coordinates, $p < 0.001$), they exhibited a lower incidence of skin lesions (11% and 57%, $p < 0.0001$), joints (22% - 52%, $p < 0.05$) and hematological disorders (24% and 73.8%, $p < 0.0001$) .

The main immunology examination manifestations of SLE in group 1 patients have hematological disorders (74%), skin lesions (57%), kidneys (55%) and joints (52%), all also revealed immunological disorders an increase the level of antinuclear factor (ANF) in 100%, anti dsDNA in 80% patients.

• **Group 1 :** Nephritis (36%), sororities (29%), hematological disorders (24%) and arthritis (22.2%) .

• **Group 2:** Immunological disorders have identified in 96% of patients. no relevant variations were identified in the concomitant Sjogren's syndrome and Allergic Fungal Sinusitis (AFS).

This, division of patients with SLE into groups upon taking ant rheumatic therapy (immunosuppressant, GIBP) allowed us to assess its relationship with the activity and duration of SLE, since the groups differed relevantly in these indicators.

value level of NT_proBNP in untreated patients was elevated than in group 2nt (151 - 33 pictograms per milliliter, respectively, $p < 0.01$), while exceeding normal values

Note: that the mean value of and the mean value of the control group is equal to 4, noting that P. value NT_proBNP equal 0.05 mean value lupus value is equal 19.37

Table 2 : Comparison immunological and laboratory characteristics of patients of both groups are presented

Characters	SLE (n = 88)	Control (n=85)	P. value	Notes
NT_proBNP (mean)	19.37	4	0.05	Based on the assumption that the overall mean for both groups is equal to 12, the probability value indicates the difference in statistical significance
Age (mean ± SD)	30 ± 15	30 ± 14	<0.001	There is a difference in the statistical results regarding the distribution of ages
Gender (male)	3 (10%)	5 (4%)	<0.0001	The statistical difference in results is very high between the two genders
Gender (female)	40 (90%)	40 (96%)	<0.0001	The statistical difference in results is very high between the two genders
Total sample size	88	85		
N. of individuals with determined gender	43	45		

Table 3: key immune related manifestation of condition

main immunological manifestations of diseases	
SLEDAI_2K	4- 15 coordinates
SLICC_DI (damage index)	0- 1 coordinates
hematological disorders	22%
nephritis	31%
arthritis	25%
skin lesions	22%
sororities	22%
antinuclear factor (ANF)	94%, antibodies to double-stranded DNA (anti_dsDNA)
ant phospholipid syndrome	76% of patients (positive)

Sjogren's syndrome	7%(positive)

Figure 1: Volumetric Effect Of Immunological disorder Manifestations Of The Disease

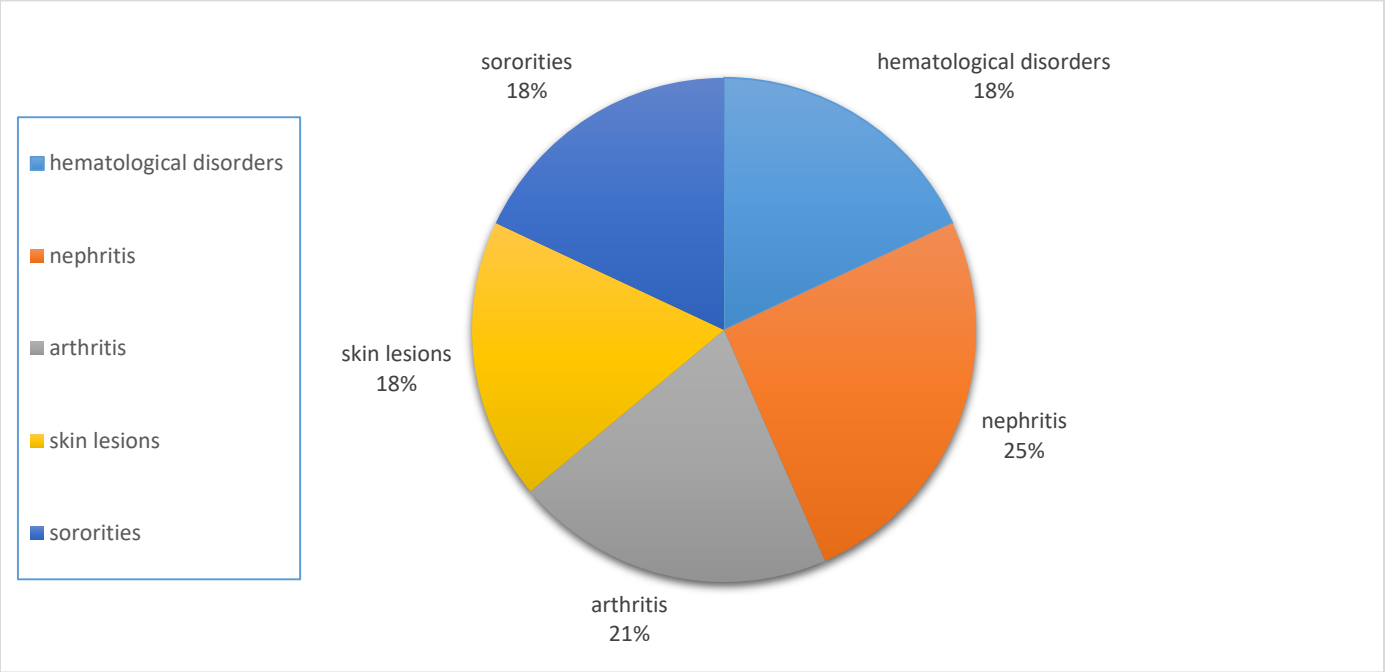
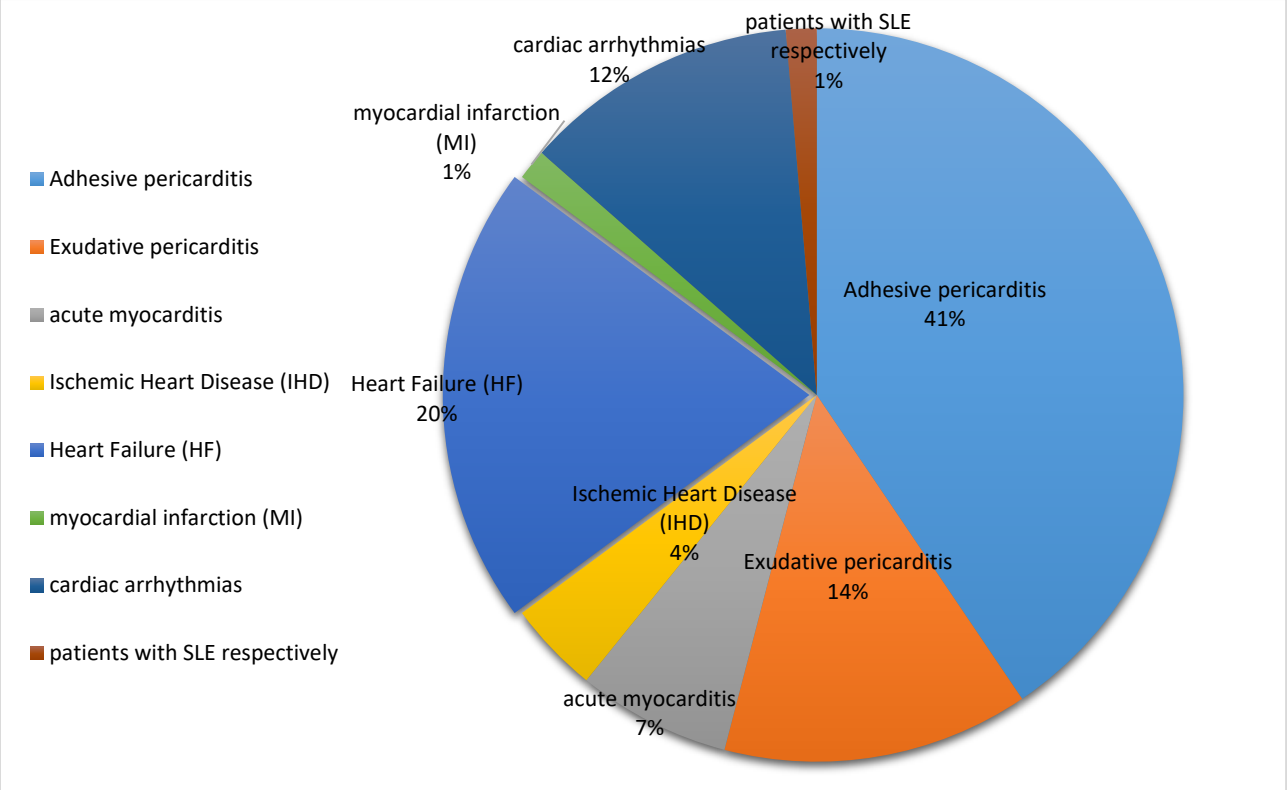


Table 4 : Immunodiagnostic with systemic lupus erythematous cautilizing myocardial infection

N. SLE	Immunological disorder cardiomyopathy by systemic lupus erythematous	Rate values
16	pericardium	26%
18	Adhesive pericarditis	30%
15	Exudative pericarditis	10%
4	acute myocarditis	5%
5	Ischemic Heart Disease (IHD)	3%
10	Heart Failure (HF)	15%
2	myocardial infarction (MI)	1%
16	cardiac arrhythmias	9%
2	patients with SLE respectively	1%

Figure 2: values cardiomyopathy by systemic lupus erythematous



Anti_ENA (Extractable Nuclear Antibodies):

antibody ranges intermediate to SLE sufferers and manipulate organization is supplied in table 5. The evaluation outcomes reveal there haven't extensive variations ($P > 0.015$) within the detection results of Anti_JO1 and anti_Scl70 antibody <0.001 intermediate to SLE patients and manage institution. but, the SLE patient institution exhibited relevantly raised of antiRNP levels <0.001 , anti_Sm <0.001 , anti SSA, and anti SSB compared with group of control, with all variations being statistically relevant ($P < 0.01$). These results in the bottom

Table 5 : Comparison Levels Anti_ENA

Antibody	SLE (n = 88)	Control (n = 85)	P. values
Anti_JO1			
Negative	6(7%)	78(92%)	<0.001

Positive	82(93%)	7(8%)	
Anti-RNP			<0.001
Negative	13(15%)	72(85%)	
Positive	75(85%)	13(15%)	
Anti_Scl70			0.15
Negative	77(88%)	81(95%)	
Positive	11(12%)	4(5%)	
Anti_Sm			<0.001
Negative	66(75%)	83(98%)	
Positive	22(25%)	2(2%)	
Anti_SSA			<0.001
Negative	35(40%)	68(80%)	
Positive	53(60%)	17(20%)	
Anti_SSB			0.005
Negative	72(82%)	77(90%)	
Positive	16(18%)	8(10%)	

Analysis of Associate Chartered Accountant (ACA) levels:

Results comparing ACA levels in patients with SLE to those in the control group are outlined in Table 6. The analysis revealed that positive rate of ACA antibodies had increased over time , ACA (IgA, IgG, IgM), are elevated in SLE group compared to the control group, with these variations achieving statistically relevant ($P < 0.05$) as shown in Table 6.

- P25 represents the first quartile of the 25% percentile.
- P75 represents the middle quartile of the 75% percentile.

- Interquartile range (IQR) measure of spread and dispersion shows the least effect of infection and the result is the first quartile - the middle quartile.

Table 6 : Comparison of ACA detection results between SLE group and the control group.

ACA (n (%)	SLE (n = 88)	Control (n = 85)	P. values
Negative	59(67%)	53(62%)	<0.001
Positive	29 (33%)	32(38%)	
Antibody	Median	IQR = P75- P25	P. values
ACA IgA (P75-P25)	5 (7.67-2.32)	5.35	0.017
ACA IgG (P75-P25)	6 (8.75-2.63)	6.12	0.001
ACA IgM (P75-P25)	9 (13.51-4.82)	8.69	0.004

B2_GPI Autoantibodies levels:

When detecting antibodies B2_GPI Autoantibodies and comparing the results with the lupus disease and control group, it was identified that positive results for antibodies B2_GPI Autoantibodies were higher in lupus patients compared to the control group as shown in Table 7

Table 7 : Comparison of B2_GPI Autoantibodies detection results between SLE group and control group .

antibody	**SLE (n = 88)**	**Control (n = 85)**	**P. value**
B2_GPI Autoantibodies	25(28%)	14(17%)	<0.001
IgA (median)	8(12.94-4.08)	6(8.36-2.77)	<0.001
IgG (median)	6(8.36-2.8)	5(7.84-2.53)	<0.001
IgM (median)	6(8.35-3)	5(7.84-2.53)	<0.001

Discussion:

The influence of immunological disorder inflammation in the endocardium, valves, aortic dissection and hypertension and HA therapy are discussed as possible causes of these changes. The use of HA can lead to rapid "healing" of inflammation of a valve especially of the heart (valvulitis). [6]

Despite the fact that bacterial or nonbacterial thrombotic endocarditis is a characteristic classic valve lesion in SLE[13], most researchers agree that the most common change in heart valves is insufficiency with varying degrees of regurgitation[14]. Some indicate a high incidence of aortic valve insufficiency, others indicate mitral valve insufficiency [2].

In my study, tricuspid and mitral valve insufficiency was more common, and aortic valve insufficiency was less common; the changes were not clinically relevant and did not require surgical correction.

An increase in the level of natriuretic peptide (BNP) is not specific for myocarditis, Based on the dynamics of the NT_proBNP level, the effectiveness of treatment is evaluated and a prognosis is made. While maintaining its high concentration, it can be assumed that there is active inflammation, its carbonization. Therefore, according to the recommendations immunologic and cardiologists, all patients with clinical suspicion of myocarditis should conduct a study of the initial level of NT_proBNP and its dynamics [4].

They do not have any special features, and associations with SLE-specific autoantibodies and therapy have also not been identified. In the present study, rhythm disturbances were recognition in 18% of patients

The number of atherosclerotic plaques in the coronary and femoral arteries is twice as high in patients with disease as in people suffering from rheumatoid arthritis and DM diseases with high cardiovascular hazard [5].

In my study, I did not observe a statistical difference in the incidence of various heart diseases and heart failure between those who received immunosuppressant and high blood pressure treatments and those who did not receive them, but the difference was clear in those who developed lupus.

98% of cases, HA was used, hypertension, an increase in total cholesterol and BMI values were more often observed, which confirms the opinion about the effect of HA on the frequency of TFR.

Currently, the determination of the concentration of NT_proBNP is used for the screening of HEART FAILURE (HF), assessment of its severity and prognosis, as well as monitoring the effectiveness of therapy. In addition, a high level of NT_proBNP is an independent hazard factor not only for Heart Failure (HF),

There are isolated studies on the concentration of BNP NT_proBNP in immunological disorder inflammatory diseases. In SLE, the level of this biomarker was determined only in patients receiving pathogenesis therapy [3,6]. The concentration of BNP NT_proBNP in patients with SLE was higher than in the control group, this increase was primarily associated with myocardial dysfunction, but was not associated with vascular damage, including atherosclerotic, inflammatory markers, and SLE activity.

Conclusion:

Despite the young age of patients, therapy (primarily with glucocorticoids, HA) and a long duration of certain SLE are linked to a higher prevalence hazard factors (hypertension, hypercholesterolemia, overweight), and myocarditis A practicing rheumatologist should pay attention to the need for joint management of patients with SLE with a cardiologist and immunological , assessment of markers of Heart Failure (HF) as a potentially fatal complication, especially in patients with high disease activity under medical control of TFR utilizing a minimum dose of HA during remission and low activity.

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