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EARLY DETECTION AND ASSESSMENT OF LEFT VENTRICLE DYSFUNCTION IN SYSTEMIC LUPUS ERYTHROMATUS BY DIFFERENT PARAMETERS OF ECHOCARDIOGRAPHY IN BAGHDAD TEACHING HOSPITAL

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Abstract: Background: Systemic lupus erythematosus is a severe autoimmune disease which demonstrates variations in incidence, prevalence, disease activity, and prognosis and might affect all body systems. In the circulatory system, the SLE causes myocarditis, pericarditis, endocarditis, valvular lesions, and defects in the conduction system of the heart. Pericarditis is the most commonly recognized cardiac problem in SLE, which is reported in 60% of patients. The most frequent Echocardiographic lesions in SLE patients were valve regurgitations, and might be associated with disease severity and activity. Myocardial dysfunction in SLE is usually multifactorial and may result from immunological injury, ischemia, valvular diseases, or co-existent problems such as HTN.

Objectives: The study aimed to assess the echocardiographic changes in SLE patients, to study the relation of the echocardiographic changes to the disease activity, and to correlate subclinical echocardiographic features of LVD with the clinical, laboratory, and therapeutic profiles of the patients.

Methods: A cross-sectional study was conducted in the Echocardiography Department of Baghdad Teaching Hospital, Baghdad Medical City complex, Baghdad, Iraq. This study included 45 SLE female patients; they enrolled from April 2019 to April 2020. The following Echocardiography parameters of diastole function were studied: E/A ratio, tissue Doppler images (TDI), peak systole velocity (S”), E/e” ratio, and E’

septal, and E' lateral of early diastole velocity. LVEF was measured by the modified Simpson method. The disease duration and age at first diagnosis were recorded. Laboratory tests workup included complete blood picture (CBC), erythrocyte sedimentation rate (ESR), antinuclear antibody (ANA), and anti-ds DNA.

Results: The most distributed female age group studied was belonged to 31-40 years as (40% of the sample). The mean age was 32.58±10.14 years. The mean BSA= 1.75±0.18m2, overweight was reported in 44.4% of women. Arthritis was found in 82.2% of patients, whereas nephritis was found in 37.8% of patients. Most of the patients received anti-SLE drugs between 1-10 years duration (60%) of them. The hydroxychloroquine (Q) plus corticosteroid were the most drugs used in the treatment of SLE. The LVDD abnormal parameters were: E/A ratio presented in 24.4%, Abnormal S' was figured in 46.7%, abnormal E/e' was figured in 8.9%. The E' septal was abnormal in 31.1%. The E' lateral was abnormal in 40%. Regarding LA size, LAVI was abnormal in 20.9%. Elevated SPAP was found in 17.8%. The mean PAP was high in 51.1%. The Acceleration time (AT) was abnormal in 33.3%. The LVEF was abnormal in 11.1% of patients; the mean was 59.55±5.35. Left ventricular diastolic dysfunction (LVDD) was found in 18 patients (40%) of the sample studied. LVDD grade I was figured in 24.4%, while grade II was figured in 15.6%.

Conclusions: The SLE patients, increasing age, obese, and females, were more susceptible to the development of LVDD during their life. SLE-arthritis can affected TDI (S', and E/e') and LAVI, whereas SLE-nephritis affected more parameters than arthritis which E/A ratio, S', E/e' ratio, LAVI, and SPAP. The E' septal and E' lateral were mostly parameters affected. The hydroxychloroquine (Q) plus corticosteroid were the most drugs used in the treatment of SLE. Nearly most abnormalities of parameters have a crossing relationship with patients' demographic features and with SLE characteristics. Women with long or chronic history of SLE have more susceptible to echocardiographic abnormalities.

Key words: Systemic lupus erythematosus; Arthritis; Nephritis; Echocardiographic parameters; Left Ventricular Dysfunction.

Introduction

Systemic lupus erythematosus (SLE) is a multisystem autoimmune connective tissue disease involving various organ systems, including skin, joints, brain, lungs, heart, kidneys, gastrointestinal tract, serous membranes, and blood components.

Systemic lupus erythematosus (SLE) is a heterogeneous autoimmune disease characterized by an intermittent course of relapses and remission1. It mainly affects women of childbearing age and usually presents a more aggressive phenotype in the male population and in ethnic groups. It is a consequence of the interaction of genes and environmental factors that lead to the loss of immune tolerance of antibodies to self-antigens, mainly nucleic acids. Damage to multiple tissues such as skin, muscle, joints, kidney, heart, central nervous system, and lungs is due to the deposition of immune complexes or antibodies that lead to an increase in morbidity and mortality.

Prevalence rates of SLE vary widely in the literature. Reported prevalence frequencies worldwide range from 20–240 per 100,000 persons; Caucasian and African-American patients were most commonly affected, with a reported prevalence of 72.1–74.4 per 100,000 persons; African-American women had the highest rates [4]. In Iraqi patients, the reported prevalence was 53.6 per 100,000 persons, with higher rates for women (88.7

per 100,000 persons) [5,6]. Ninety percent of patients are women of reproductive age [7]. The female: male ratio is approximately 6–10:1, while in both children and elderly patients, the female: male ratio is approximately 2–3:1 [8].

The effect of the heart is written for the first time with the Libman and bags in 1920, including the inclusion of valvular lesions and autopsy murals3. According to historical descriptions, cardiac manifestations occur in more than half of patients with SLE. A difference in the global epidemiology, in Latin America, the prevalence of primary involvement and in the minor Heart (14%). If you want to affect a different anatomy system, the electronic device and the device, such as the valvular enlargement and the pericarditis in the halls, more frequently5. Within heart disease, patients with SLE present with a major cardiovascular disease (coronary artery disease, cerebrovascular accident, heart disease, and atrial fibrillation) that configure the main cause of the heart with a 4.1 heartbeat. 1,000/patients/year 6, as the dependent factor, comes with a salary of 1,987. The internal dysfunction is particularly effective for the heart, chronic inflammation, and the risk of traditional heart disease factors (hypertension, diabetes) and the effects of immune-suppliers including glucocorticoids8. Loss of factors that cause accelerated atherosclerosis at the site of the child, smoking, high levels of C-reactive protein

It is the most common cardiac manifestation of active SLE, which can occur at any time, and it may tend to be one of the earlier manifestations and can even be the first manifestation of lupus. Typically, present with positional precordial pain (aggravated by lying down) and sometimes with dyspnea. Coexistent pleurisy and/or effusions are common

[12]. Sometimes, pericardial effusions and tamponade may happen, however, even in treated patients [11]. The diagnosis of pericarditis can be confirmed besides symptoms by cardiac echocardiogram findings of pericardial effusion or thickened pericardium.

Effusions may be accompanied by a drop in voltage (low voltage). After severe attacks, T waves may not recover their original voltage. In the series of Godeau et al., of 28 total cases, 5 cases had low voltage, 10 had ST changes, and 20 had repolarization changes.

Patient and method

After approval by the College of Medicine / University of Baghdad, a cross- sectional study was conducted in a 12 months period in the Echocardiography Department of Baghdad Teaching Hospital, Baghdad Medical City complex, Baghdad, Iraq. Patients were subjected to clinical and investigational work-up including full history thorough clinical examination with special attention to the chest and cardiac examination.

This study included 45 SLE female patients with a mean age (32.58±10.14). All patients were enrolled at the Echocardiography Department of Baghdad Teaching Hospital from April 2019 to April 2020 and were diagnosed according to the Systemic Lupus International Collaborating Clinics (SLICC) classification criteria for SLE [23] and Data collection

The following variables were studied: age, female gender, BSA (m2), BMI (m2/Kg), symptoms associated with lupus, SLE duration (months), associated comorbidities with SLE, arthritis, and nephritis of lupus, exclusion criteria, anti- SLE drugs regimens, and drugs usage duration where They were selected consecutively from the patients attending the Echocardiography Department of Baghdad Teaching Hospital and about Inclusion were All patients met the diagnostic criteria of systemic lupus international collaborating

clinics (SLICC) [23]. All of the included patients had no clinical signs or symptoms of cardiac problems, histories of heart disease, or histories of conventional risk factors for atherosclerosis (e.g., hypertension, hyperlipidemia, diabetes mellitus, cigarette smoking, obesity, and postmenopausal state).

The clinical evaluation of patients with SLE involved recording disease duration, age, current drug administration, body mass index, and body surface area. Echocardiographic assessment was performed using GE Vivid E9 XDclear Echo and Philips echocardiography CX15, evaluating LV volume, pulmonary artery systolic pressure, resting wall motion abnormalities, valvular regurgitation, diastolic function, and pericardial effusion. Diastolic dysfunction was calculated according to a new guideline. All SLE cases were referred to the echocardiography department.

Statistical analysis

Statistical package for social science (SPSS Statistics for Windows, version 11.0, Chicago: SPSS, Inc.) software version 20 was used. Results were described in the form of percentage distribution for qualitative data and (mean and standard deviation) calculation for quantitative data. Cross tabulation test was used for comparison between numerical values. Pearson's correlation test was used to detect the relationship between continuous variables to determine the relationship between each echocardiographic parameter and disease characters. A one-sided P value of 0.05 or less was considered statistically significant.

Results

Table 1: Patient demographic distribution of this study (n=45).

Characteristics		**No (%)**	**Mean±SD (Median)**
Age (years)	10-20	6 (13.3)	32.58±10.14 (33)
	21-30	12 (26.7)	
	31-40	18 (40)	
	41-50	8 (17.8)	
	51-60	1 (2.2)	
	Total	45	
BSA (m^2)	<1.77	20 (44.4)	1.75±0.18 (1.77)
	>1.77	25 (55.5)	
	Total	45	
BMI (m^2/Kg)	Underweight (<18.5)	2 (4.4)	24.66±10.23 (28.25)
	Normal (18.6-24.9)	13 (28.9)	
	Overweight (25-29.9)	20 (44.4)	

	Moderate obesity (30-34.9)	5 (11.1)	
	Severe obesity (35-39.9)	5 (11.1)	
	Morbid obesity (>40)	0	
	Total	45	

Table 2: SLE characteristics distribution of this study (n=45).

Characteristics			**No (%)**
Symptoms of SLE	Fever	Present	23 (51.1)
		Absent	22 (48.9)
	Joints pain	Present	40 (88.9)
		Absent	5 (11.1
	Chest pain	Present	7 (15.6)
		Absent	38 (84.4)
	Dyspnea	Present	18 (40)
		Absent	27 (60)
SLE duration (months) [mean=51.3±58, median=36]	0-36		28 (62.2)
	>36		17 (37.8)
Associated diseases	HTN		8 (17.8)
	VHD		3 (6.7)
	CKD		12 (26.7)
	IHD		2 (4.4)
	CMP		0
SLE activity	Arthritis	Present	37 (82.2)
		Absent	8 (17.8)
	Nephritis	Present	17 (37.8)
		Absent	28 (62.2)

Table 3: SLE therapies details of this study (n=45).

Variables		**No (%)**
Duration of drugs	1-3 weeks	5 (11.1)
	1-12 months	13 (28.9)
	1-10 years	27 (60)
Drug types	*p-Q	22 (48.9)
	*p-Q plus others	15 (33.3)
	NSAD	1 (2.2)
	R-CHOP	2 (4.4)
	Other regimens	5 (11.1)

Table 4: Laboratory tests used (n=45).

Tests		**No (%)**
ESR	Positive	32 (71.1)
	Negative	13 (28.9)
CBC	Positive	29 (64.4)
	Negative	16 (35.5)
ANA	Positive	25 (55.6)
	Negative	20 (44.4)
AdsA	Positive	26 (57.8)
	Negative	19 (42.2)

Table 5: Echocardiography findings regarding Pulse Doppler Imaging (n=45).

Findings (Normal value) [24]		**No (%)**	**Mean±SD (Median)**
E/A ratio (0.8-1.8)	<0.8	11 (24.4)	1.11±0.42 (1.2)
	0.8-1.8	34 (75.6)	
	Total	45	

Table 6: Echocardiography findings regarding LVD function (n=45).

Findings (Normal value) [24]		**No (%)**	**Mean±SD (Median)**
S" (10.5 cm/s)	<10.5	21 (46.7)	10.82±1.46 (11)
	≥10.5	24 (53.3)	
E/e" ratio (<10)	<10	21 (46.7)	10.6±3.3 (10)
	10-14	20 (44.4)	
	>14	4 (8.9)	
E' septal (7 cm/s)	<7	14 (31.1)	8.93±2.94 (9)
	≥7	31 (68.9)	
E' lateral (10 cm/s)	<10	18 (40)	11.41±3.37 (11)
	≥10	27 (60)	

Regarding LA size, we evaluated LAVI (<34 ml/m^2); LAVI was abnormal in 9 (20.9%) of women, as shown in (Table 7).

Table 7: Echocardiography findings regarding LA size (n=45).

Findings (Normal value) [24]		**No (%)**	**Mean±SD (Median)**
LAVI (<34 ml/m^2)	<34	36 (79.1)	30.41±15.93 (25)
	>34	9 (20.9)	
	Total	45	

Regarding PASP findings, we report results as the following below. The SPAP was found abnormal in 8 (17.8%) of women. The mean PAP was elevated in 23 (51.1%) of patients. The AT was abnormal in 15 (33.3%) of patients. The LVEF was measured by used the modified Simpson method, which was normal in 40 (88.9%), while it was abnormal in 5 (11.1%) of patients. The EDV4 was abnormal in 14 (31.1%) of patients,

as shown in (Table 8).

Table 8: Echocardiography findings regarding PASP (n=45).

Findings (Normal value) [24]		No (%)	Mean±SD (Median)
SPAP (<36 mmHg)	<36	37 (82.2)	29.33±13.43 (25)
	≥36	8 (17.8)	
Mean PAP (25 mmHg)	<25	22 (48.9)	23.88±8.44 (22.25)
	≥25	23 (51.1)	
AT (≥120 cm/s)	<100	15 (33.3)	109.56±25.6 (106)
	100-120	20 (44.4)	
	>120	10 (22.2)	
LVEF (≥55)	Severe (<30)	0	59.55±5.35 (60)
	Moderate (30-44)	0	
	Mild (45-54)	5 (11.1)	
	Normal (≥55)	40 (88.9)	
EDV4 (46-106 ml)	<46	14 (31.1)	54.1±13.55 (50)
	46-106	31 (68.9)	
ESV4 (14-42 ml)	<14	0	39.91±11.1 (37)
	14-42	29 (64.4)	
	>42	16 (35.6)	

Table 9: LVDD grades frequency and percentage (n=45).

LVD function	No.	%
Normal	27	60
LVDD grade I	11	24.4
LVDD grade II	7	15.6
Total	45	100%

Table 10. Patients' demographics and SLE characteristics related to abnormal Echocardiography parameters.

		E/A ratio	S"	E/e" ratio	E' septal	E' lateral	LAVI	SPAP	Mean PAP	AT	LVEF	EDV4	ESV4
		% (p-value)											
Age	<33 year	2.2	17.7	24.5	2.3	9.1	2.3	28.9	23.8	15.6	0	17.8	22.2
	>33 year	22.2	28.9	31.1	27.2	31.8	18.7	31.1	28.6	35.5	14.3	31.1	33.4
	p-value	0.022	0.34	0.2	0.000	0.003	0.043	0.151	0.104	0.012	0.026	0.03	0.134
BSA	<1.7	7.5	17.5	34.1	9.3	16.3	10.3	35	29.7	27.5	5.4	27.5	30
	>1.7	12.5	22.5	22.7	18.6	23.3	7.7	30	27	22.5	5.4	20	25
	p-value	0.497	0.37	0.54	0.028	0.038	0.47	0.14	0.57	0.376	0.677	0.26	0.37
BMI	Normal	4.5	22.1	6.6	1.5	8.5	3.3	20	12.1	15.7	20	30.2	40
	>25m^2/ Kg	16.3	27.4	32.2	25.3	29.2	40.5	25.2	30.9	18.7	11.2	22.6	30.1
	p-value	0.05	0.09	0.05	0.007	0.04	0.000	0.06	0.05	0.1	0.09	0.05	0.22
Fever		8.9 (0.86)	22.2 (0.2)	28.9 (0.81)	13.6 (0.027)	20.5 (0.1)	4.7 (0.17)	33.3 (0.054)	28.6 (0.22)	26.7 (0.21)	7.1 (0.036)	17.8 (0.07)	22.2 (0.1)

Joints pain		17.8 (0.17)	40 (0.049)	51.1 (0.79)	20.5 (0.008)	31.8 (0.1)	14 (0.042)	55.6 (0.066)	47.6 (0.08)	44.4 (0.11)	9.5 (0.07)	44.4 (1)	51.1 (0.8)
Chest pain		2.2 (0.84)	11.1 (0.04)	4.4 (0.26)	2.3 (0.03)	2.3 (0.032)	2.3 (1)	8.9 (0.051)	9.5 (0.15)	6.7 (0.3)	0	6.7 (1)	8.9 (0.87)
Dyspnea		11.1 (0.48)	20 (0.25)	15.6 (0.14)	13.6 (0.041)	18.2 (0.19)	14 (0.16)	20 (0.012)	16.7 (0.035)	22.2 (0.32)	9.5 (0.09)	13.3 (0.2)	15.6 (0.13)
SLE duration	0-36	6.8	25	32.5	10.3	17.9	9.5	45.5	41.5	25	2.4	31.8	36.4
	>36	18.2	20	25	12.8	15.4	11.9	15.9	12.2	25	9.8	18.2	20.5

Discussion

Systemic Lupus erythematosus (SLE) is a severe autoimmune disease with varying incidence, prevalence, disease activity, and prognosis based on race and ethnicity. It can cause myocarditis, pericarditis, endocarditis, valvular lesions, and defects in the conduction system. Cardiovascular involvement in SLE is rare but can be associated with significant morbidity and mortality. Echocardiography is a sensitive technique for detecting cardiac abnormalities in SLE patients. The study analyzed young females with a mean age of 32.58±10.14 years. The most common symptom was joint pain, followed by arthralgia and skin and mucous membrane manifestations. The study found that patients below 36 months of disease duration were 62.2%, while those above 36 months were 37.8%.

We were recorded different pre-exciting conditions in different proportions as HTN, VHD, CKD, and IHD. About 26.7% of patients have CKD, which was a commonly presented condition. Al-Mukhtar et al. reported pre-exciting conditions in (44.6%) of patients, included cerebrovascular accidents (CVA), transient ischemic attaches TIAs, unilateral blindness, seizures, migraine, psychosis, and depression. They also recorded that renal impairment was present in 18 patients (32.1%), while abnormal renal deposits was found in 16 patients (28.5%) [30]. Mohammad et al. [13] reported renal diseases was the most frequent co-exciting clinical finding in 66.1% of patients. Higher percent of renal disorder was reported by the Maha et al. study [14], as 60% of patients.

In our study, the active SLE present with arthritis was found in 82.2% of patients, whereas nephritis was found in 37.8% of patients. These findings were inconsistent with other studies in Egypt by Mohammad et al.

[34]; they mention that those who suffered from arthritis was 33.9%, whereas Maha et al. study [32] reported 68% of patients have arthritis. In Iran, Mirfeizi et al. [15], recorded 17 (37.8%) of patients had active arthritis.

In our study, most of the patients received drugs between 1-10 years duration (60% of them). The hydroxychloroquine (Q) plus corticosteroids (CS) was mostly used to control SLE in 82.2%. In our study, those patients with LVDD I that received hydroxychloroquine were 9 (50%), while those with LVDD II were 5 (27.8)%, with statistically significant differences (p-value= 0.01).Regarding parameters of LV function, LVDD grade I was found in 24.4%, whereas grade II was presented in 15.6% of patients. LA dilation was found in 20.9% of women. Mean LVEF measured by the modified Simpson method was 59.55±5.35, and it was mildly abnormal in 5 (11.1%) of patients. Low S' (peak systole velocity) was figured in (46.7%) of the patients.

These findings were much higher than the results of a previous study in Egypt by Maha et al., which recorded that 10% of patients had LVDD grade I and 2% had grade II LVDD, the mean LVEF was equal to 63.3 ± 6.7; in Mirfeizi et al. study, the mean LVEF was 57.21±4.90.

Conclusion

Concluded that cardiac involvement in patients with SLE is common and is a significant source of morbidity and mortality, and all parts of the heart can be affected, including the pericardium, endocardium, myocardium, valves, conduction system, and coronary arteries

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