The Role of Plasma Lipoprotein and Carotid Doppler in Detecting Premature Atherosclerosis Among Iraqi Patients with Systemic Lupus Erythematosus

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ABSTRACT:

BACKGROUND:

Cardio vascular involvement is fatal and critical complication of the systemic lupus erythematosus. Serum lipid profile and carotid Doppler studies can be used to evaluate premature atherosclerosis among patients with systemic lupus erythematosus .

OBJECTIVE:

The purpose of this study was to detect premature atherosclerosis among Iraqi patients with systemic lupus erythematosus by estimation of fasting serum lipid profiles and Doppler Carotid studies.

PATIENTS AND METHODS:

Fifty Iraqi patients (45 females and 5 males) who fulfilled the American College of Rheumatology (ACR) 1997 revised criteria for classification of SLE were studied . Another 50 healthy (45 females and 5 males) individuals matched for age and sex were collected from relatives and accompanying persons with patients attending the Rheumatology Clinic and studied serving a control group.

Full history was taken and complete clinical examination was done for all patients and control group .The levels of serum cholesterol , low and high density lipoprotein and triglycerides were estimated and Doppler studies for common carotid arteries were done for individuals in both groups.

The patients were classified according to clinical presentation to four groups:

Group 1: Patients with mucocutaneous and musculoskeletal manifestation only.

Group 2 : Patients with mucocutanous,musculoskeletal manifestation and serositis.

Group 3: Patients with mucocutanous, musculoskeletal, serositis and lupus nephritis without cerebritis.

Group 4: Patients with Mucocutanous , musculoskeletal, serositis and lupus cerebritis without nephritis.

RESULTS:

There were no significant differences in total cholesterol level in group 1 patients compared to control group, but there were significant differences in group 2,3,4 patients compared to control group.There were significant differences in cholesterol, low density lipoproteins (LDL),high density lipoproteins (HDL),and triglyceride (TG) levels between SLE patients compared to control group which is positively correlated with disease duration .There were no significant differences in intimal media thickness(IMT)in group1and2 compared to control group but there were significant differences in IMT in group 3 and 4 compared to control group and the significant differences in IMT were positively correlated with disease duration.

CONCLUSION:

The results showed that SLE patients mostly have hyperlipidemia as well as ultrasonic markers of atherosclerosis.

KEY WORDS : premature atherosclerosis, systemic lupus erythmatous

INTRODUCTION:

Systemic lupus Erythematosus (SLE) is a multi-systemic connective tissue disease characterized by the presence of numerous auto antibodies, circulating immune complexes and wide spread immunological determined tissue damage; the onset is most commonly in the second and third decades with female/male ratio of 9:1[(1)].

The prevalence of SLE is approximately one in two thousands individuals although the prevalence varies with race, ethnicity and socioeconomic status[(2)]. It □s

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prevalence in Iraq was reported as 53.6 patients per 100,000 individuals [3].

Premature atherosclerosis is a recognized complication of systemic lupus erythematosus, **since life expectancy in SLE**is improving, premature atherosclerosis is emerging as an evermore important clinical issue[4],

a**therosclerosis begins** in the pediatric age group, and intervention directed at prevention should begin in childhood as well, possible etiologies include dyslipoproteinemia (DL) from the underlying chronic inflammatory disease or from corticosteroid therapy, vasculitis and hypertension[5]. Dietary therapy is helpful but many patients continue to have significant dyslipoproteinemia after both dietary modification and fish oil supplementation, Lipid lowering drugs may be indicated in this subgroup[6]. Large increase in mortality related to premature atherogenesis with coronary artery disease and stroke have been reported in patients with SLE, The main risk factors for atherosclerosis included not only the classic factors identified in epidemiologic studies such as (advanced age, high cholesterol levels, hypertension, diabetes mellitus and obesity) but also prolong glucocorticoid therapy and long duration of SLE, post-menopausal state and heart failure. SLE per se is an important risk factor[4,5,6].

The prevalence of preclinical cardiovascular disease was determined in women with SLE and control subjects matched for traditional risk factors. Compared with control subjects, patients with SLE had a higher prevalence of carotid atherosclerosis (41% versus 9%, P<0.05) and left ventricular hypertrophy (32% versus 5%, P<0.005), supporting the possibility that chronic inflammation predispose to premature cardiovascular disease in SLE[7].

Hyperlipidemia and particularly if It □s persist during the first three years of disease activity, hypertension and lupus itself are important risk factors for the development of accelerated atherosclerosis[6,7].

AIM OF THE STUDY:

To detect premature atherosclerosis among Iraqi patients with systemic lupus erythematosus by estimation of fasting serum lipid profile and common carotid arteries doppler studies .

PATIENTS AND METHODS:

This was a cross-sectional study carried out at the Department of Rheumatology in Baghdad Teaching Hospital from October 2002 till March 2004.

All together, 50 Iraqi (45 females and 5 males) patients fulfilling the ACR (American College of Rheumatology[8]) were included in this study.

Full history was taken and complete clinical examination was done for all patients and control group .Blood samples were taken from individuals in both groups after an overnight fasting for 12 hours for estimation of serum cholesterol (cholest), low density lipoprotein (LDL), high density lipoprotein (HDL) and triglyceride (TG) levels.

Laboratory investigations and immunological studies including anti-nuclear antibody, anti-double stranded DNA antibody and anti-Smith antibody were done in the Laboratory Teaching Center. The immunological studies were detected by immunofluorescence and ELISA (Enzyme Linked Immunosorbent Assay) technique and high titer level of anti-double strand DNA antibody was included in this study (> 80 I.U./ml). Other investigations were done to patients such as complete blood picture and , erythrocyte sedimentation rate(ESR), blood urea, serum creatinine, general urine examination (GUE), ECG. Brain Magnetic Resonant Imaging (MRI) were done to the patients who presented with clinical lupus cerebritis.

Doppler studies for common carotid artries were done to all patients and controls.

Patients were classified according to clinical presentation in to four sub groups :

Group 1:With mucocutaneous and musculoskeletal manifestation only.

Group 2:With mucocutanous,musculoskeletal manifestation and serositis.

Group 3:Mucocutanous, musculoskeletal, serositis and lupus nephritis without cerebritis.

Group 4:Mucocutanous, musculoskeletal, serositis and lupus cerebritis without nephritis.

Patients and individuals with diabetes mellitus, hypothyroid, hypertension, chronic renal failure, chronic liver failure, familial hypercholesterolemia, obesity, pregnancy , smokers, as well as patients on beta-blockers, thiazide, contraceptive pills and hypolipidemic agents were excluded from the study.

A signed consent was taken from individuals in both groups for inclusion in the study.

Statistical analysis: Data were analyzed by using t-test. P-values less than (0.05) was considered significant.

RESULTS:

Table (1):The demographic distribution of both SLE patients and controls are shown in

	SLE patients n=50 No (%)	Controls n=50 No (%)
1. Age (years) < 20 20-29 30-39 Range (years) Mean age ± SD	 9 (18) 25 (50) 16 (32) 9-39 25.8±6.8	 8 (16) 23 (46) 19 (38) 12-38 26.8±6.4
2. Gender Female (F) Male (M) F / M	 45 (90) 5 (10) 9 /1	 45 (90) 5 (10) 9 /1

Table (2):The lipid profile levels in SLE patients with various clinical presentation and controls:

Lipid profile	Clinical presentation	number	Mean ± SD mg/dl	P-value
Cholesterol (Cholest)	Group – 1	12	172.66 ± 4.2	0.346
	Group – 2	8	230.11 ± 6.8	<0.0005*
	Group – 3	21	244.11 ± 5.7	<0.0005*
	Group – 4	9	268.33 ± 6.4	<0.0005*
	Control	50	165.78 ± 3.2	
Low Density Lipoprotein (LDL)	Group – 1	12	136.66 ± 4.5	<0.0005*
	Group – 2	8	202.50 ± 5.3	<0.0005*
	Group – 3	21	204.40 ± 4.6	<0.0005*
	Group – 4	9	206.11 ± 4.2	<0.0005*
	Control	50	113.14 ± 3.9	
High Density Lipoprotein (HDL)	Group – 1	12	77.91 ± 5.2	<0.0005*
	Group – 2	8	25.11 ± 4.5	0.023*
	Group – 3	21	23.60 ± 4.2	0.025*
	Group – 4	9	21.11 ± 3.8	0.027*
	Control	50	46.11 ± 4.7	
Triglyceride (TG)	Group – 1	12	117.50 ± 3.9	<0.0005*
	Group – 2	8	210.11 ± 4.4	<0.0005*
	Group – 3	21	200.80 ± 4.6	<0.0005*
	Group – 4	9	208.88 ± 4.2	<0.0005*
	Control	50	92.81 ± 5.4	

* P-value <0.05 indicate significance .

Table(3)A: Levels lipid profiles among 30 SLE patients with disease duration < 5 years compared to controls:

Lipid profile	Group	Number	Mean mg/dl ± SD	P-value
Cholesterol	Patient	30	205.73 ± 6.8	0.035*
	Control	50	165.78 ± 5.6	
LDL	Patient	30	182.16 ± 4.8	0.024*
	Control	50	113.14 ± 3.9	
HDL	Patient	30	46.11 ± 3.2	0.003*
	Control	50	40.33 ± 4.4	
TG	Patient	30	173.11 ± 6.2	0.021*
	Control	50	92.81 ± 5.4	

* P-value < 0.05 indicate significance .

Table(3)B: Levels of lipid profile among 20 SLE patients with disease duration ≥ 5 years compared to controls:

Lipid profile	Group	Number	Mean mg/dl ± SD	P-value
Cholesterol	Patient	20	266.72 ± 5.6	0.021*
	Control	50	165.78 ± 4.9	
LDL	Patient	20	197.51 ± 6.2	0.023*
	Control	50	113.14 ± 5.4	
HDL	Patient	20	46.11 ± 2.4	0.002*
	Control	50	30.25 ± 3.8	
TG	Patient	20	198.11 ± 5.6	0.022*
	Control	50	92.81 ± 4.7	

* P-value < 0.05 indicate significance .

Table(3)C: levels of lipid profile levels in SLE patients of the less than 5 years duration and those with 5 years duration and above :

Lipid profile	Disease duration group	Number	Mean mg/dl ± SD	P-value
Cholesterol	< 5 years	30	205.73 ± 6.4	0.019*
	≥ 5 years	20	266.75 ± 5.5	
LDL	< 5 years	30	182.16 ± 4.8	0.003*
	≥ 5 years	20	197.51 ± 4.3	
HDL	< 5 years	30	40.33 ± 3.2	0.002*
	≥ 5 years	20	30.25 ± 2.8	
TG	< 5 years	30	173.11 ± 5.8	0.004*
	≥ 5 years	20	198.11 ± 4.9	

- P-value < 0.05 indicate significance .

Table (4):The intimal media thickness of common carotid arteries with evidence of atheromatus plaque in 50 SLE patients with various clinical presentation compared to 50 healthy controls are shown in:

Clinical presentation	Number	Mean IMT mm ± SD	P-value	Atheromatus plaque
Group – 1	12	0.47 ± 0.24	0.839	0
Group – 2	8	0.52 ± 0.13	0.164	0
Group – 3	21	0.78 ± 0.12	0.001*	1
Group – 4	9	0.89 ± 0.23	0.002*	2
Control	50	0.46 ± 0.12		0

* P-value < 0.05 indicate significance .

DISCUSSION:

In this study aimed to investigate the presence of ultrasonic marker as well as lipid profile levels for subclinical atherosclerosis in SLE patients without history of atherosclerosis or its complications.

The data failed to show significant differences in the cholesterol level between SLE patients in group – 1compared to control group, this result is different from the finding in other studies[9], which might be attributed to limited patients number, while data confirmed the presence of significant differences in cholesterol levels between patients in groups 2, 3 and 4 compared to control group. These results are in agreement with the finding of others[9,10].

Data reported the presence of significant differences in LDL, HDL and TG levels between SLE patients compared to control group. These results are similar to the findings in other series[912].

There were significant differences in the cholesterol, LDL, HDL and TG levels between patients whose disease duration were < 5 or ≥ 5 years compared to control group, these results are in agreement to the findings in other studies[9-12].

We failed to show significant difference in the IMT of common carotid arteries between patients in Group – 1 and Group – 2 compared to control group, which are similar to the findings in other studies[13].

The finding of significant differences in the IMT of common carotid arter**ies** between patients in Group –3 and Group – 4 compared to control group, are in agreement with the findings of others [13,15].

CONCLUSION:

Our findings indicate that Iraqi SLE patients mostly have hyperlipidemia which is a risk factor of premature atherosclerosis.

RECOMMENDATIONS

I recommend after initial diagnosis of SLE to estimate fasting serum lipid profile levels as a baseline then afterwards to do these investigations every year to detect premature atherosclerosis in order to treat patients early and to prevent serious complications.

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