Prevalence of Abnormal Ankle –Brachial Index in Iraqi Patients with Systemic Lupus Erythematosus

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ABSTRACT:

BACKGROUND:

Accelerated atherosclerosis is a well-recognized complication of systemic lupus erythematosus (SLE). Its etiology is a multifactorial and several methods may be used to detect the presence and severity of peripheral arterial disease (PAD).

OBJECTIVE:

To assess ankle brachial index (ABI) in Iraqi patients with SLE, and to evaluate predictors of this relationship.

PATIENTS AND METHODS:

Forty three Iraqi SLE patients and 50 healthy controls were included in this study. Full history was taken and complete clinical examination was done for all individuals in both groups. Disease characteristics [age, sex, body mass index (BMI), duration of disease, SLE disease activity index (SLEDAI), smoking history, family history, hypertension, hyperlipidemia, thrombosis, Raynaud's phenomenon and drugs used] were also documented. Laboratory analysis included complete blood count, general urine examination, serum lipid profile, fasting blood sugar, thyroid function tests, anti-double stranded deoxyribonucleic acid (anti-ds-DNA), complements components and anti-phospholipid anti-bodies. Individuals in both groups were assessed using the ABI. The ABI was measured using a contour wrapped 12cm cuff attached to a mercury sphygmomanometer and 5-10 MHz Doppler in the arms and legs; a ratio of ≤0.9 was considered abnormal. Abnormal ABI was categorized as mild, moderate and severe.

RESULTS:

Seven (16%) Iraqi SLE patients have abnormal ABI compared with 0% of controls (P=0.010). All patients were of mild abnormal ABI(P=0.003).There was significant association between abnormal ABI and: sex, smoking history, and cyclophosphamide therapy (P=0.000, P=0.001, P= 0.020 respectively) but there was no significant association between abnormal ABI; and other patients' characteristics[age, BMI, duration of disease, SLEDAI, family history, hypertension, thrombosis, Raynaud's phenomenon, or drugs used (steroid, mycophenolate mofetil, hydroxychloquin, non-steriodal anti-inflammatory drugs and statins)] (P=0.579, P=0.754, P=0.823, p=0.148, P=0.655, P=0.233, P=0.655, P=0.241, P=0.512, P=0.335, P=0.315, P=0.655 , P=0.185) respectively.

CONCLUSION:

Mild abnormal ABI occurs with high frequency (16%) in Iraqi SLE patients. Males, smoking history, and cyclophosphamide therapy are significant predictors.

KEY WORDS: Anke brachial index(ABI), systemic lupus erythematosus(SLE), abnormal ABI in SLE

INTRODUCTION:

Systemic lupus erythematosus (SLE) is a relapsing-remitting autoimmune disease with wide ranging organ involvement and clinical symptoms varying from mild and transient symptoms to death. [1]

Accelerated atherosclerosis is now recognized as a significant cause of morbidity and mortality in SLE, Urowtiz et al [2] were the first to observe this, and the diagnosis of SLE remains one of many risk factors of atherosclerosis [3], so identifying subclinical atherosclerosis or vascular changes is gaining considerable attention.

Ankle brachial index (ABI) is an as an easy, reliable and non-invasive measure of the presence and severity of peripheral arterial disease (PAD) [4]. Measurement of ABI allows the identification of

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both symptomatic and asymptomatic patients with PAD. Therefore, ABI is widely recommended for PAD screening [5].

Recently published guidelines by the American Heart Association and the American College of Cardiology [6] have suggested that the ABI should be considered for the purposes of cardiovascular risk assessment.

The aim of the study was to assess the prevalence of abnormal ABI in 43 Iraqi SLE patients and compared to 50 healthy controls.

PATIENTS AND METHODS:

PATIENTS

A cross-sectional study was conducted on 43 Iraqi patients with SLE who were seen at the Rheumatology Unit, Department of Medicine in Baghdad Teaching Hospital and Kidney Transplantation Centre in Surgical Specialized Hospital from January 2010 to July 2010.

The diagnosis of SLE was made using the criteria developed by the American College of Rheumatology [7,8]. For comparative purposes, 50 healthy control individuals were selected from healthy individuals that did not have symptoms of SLE and were not taking any medications.

All patients were screened clinically for conventional atherosclerotic risk factors (weight, height, smoking status, and family history of ischemic heart diseases) and by notes review (diabetes, nephrotic syndrome, history of thrombosis, presence of Raynaud's phenomenon, current or past steroid treatment), disease duration, activity index using (SLEDAI: SLE disease activity index) [9] and drugs used in the management of SLE patients. Patients were excluded from the study if they had other causes that might be implied in atherosclerosis like diabetes mellitus, hypothyroidism, nephrotic syndrome, rheumatoid arthritis and other connective tissue diseases.

METHODS:

Ankle brachial index (ABI) was calculated using the following formula [10-12]

$$ABI = \frac{\text{Highest each ankle pressure}}{\text{Highest brachial pressure}}$$

Then we use the lowest ABI value of the left and right limbs to stratify patient's risk. Interpretation of ABI[13-15]: Normal ABI: $\geq 0.91 - \leq 1.30$; An ABI ≤ 0.90 is diagnostic of PAD (mild PAD: 0.70- 0.90 , moderate PAD: 0.41-0.69, severe PAD or Critical Limb Ischemia: ≤ 0.4, Non-compressible: ≥ 1.3).Blood sample was obtained for measurement of haemoglobin, white blood cells, platelets, serum lipid profile, fasting blood sugar , and lupus serology anti-double stranded-DNA (anti-ds-DNA), complements components and antiphospholipid antibodies. Urine examination was done for measurement of protein, white blood cells, red blood cells and cellular casts. A signed consent was taken from the individuals in both groups for admission in the study. Ethical approval was obtained from the Ethics Committee of Baghdad University, College of Medicine, Medical Department.

Statistical analysis:

statistical analysis was done using analysis package for social science version 17 (SPSS V17). Association between discrete variables was measured by Chi square test and Fisher Exact test where appropriate. Difference between continuous variables was measured by t-test. Findings with P-values < 0.05 considered significant.

RESULTS:

Forty three patients with SLE, 39 females (90.7%) and 4 males (9.3%), their mean age (30.9+-11.1) years, and 50 control group, 45 females (90%) and 5(10%), their mean age (33.1+-11.2) years were included in this study .The age and sex of patients and control groups are shown in Table 1 (P-value=0.358 and 0.881 respectively) indicating no statistical difference between both groups.

Ankle-brachial index (ABI) was abnormal in 7(16%) patients, and normal in 36(84%), patients while it was normal in all 50(100%) healthy individuals of control group (p-value=0.010) which is statistically highly significant as shown in Table 2.

The abnormal ABI was mild in all 7 patients (P-value=0.003) which is statistically highly significant as shown in Table 3.

We found that there is highly statistical significant association between abnormal ABI and: male sex, and smoking history of patients (P-value=0.00 and P-value=0.001 respectively) and statistical significant association with cyclophosphamide therapy (P-value=0.020) as shown in Table 4.

We found that there is no statistical significant association between abnormal ABI and other SLE patients characteristics (age, BMI, duration of disease, disease activity index (SLEDAI), family history hypertension, hyperlipidemia, thrombosis, Raynaud`s phenomenon and other medication), as shown in Table 4.

Table 1: Demographic characteristics of 43 SLE patients and 50 controls

Variables	Patients = 43	Controls = 50	p-value
Age (years) Mean ± SD	30.9 ± 11.1	33.1 ± 11.2	0.358 ns
Sex Male n. (%) Female n. (%)	 4 (9.3) 39 (90.7)	 5 (10) 45 (90)	 0.881 ns

ns, not significant; SD, standard deviation; n, number; %, percent

Table 2: Comparison of Ankle Brachial Index (ABI) in 43 patients and 50 controls.

Study group	ABI Abnormal (≤ 0.9) n. (%)	Normal (> 0.9) n. (%)	p-value
Patients =43	7(16.0)	36(84)	
Controls = 50	0(0.0)	50(100.0)	0.010 *

*, P- value is significant; n, number; %, percent.

Table 3: Distribution of ABI severity in 43 SLE patients and 50 controls.

Severity	Patients n=43(100.0%)	Controls n=50(100.0%)	P-value
Normal ABI (>0.9)	36(84.0)	50(100.0)	
Mild (0.7_0.9)	7(16.0)	0(0.0)	0.003 **
Moderate (0.4_0.6)	0(0.0)	0(0.0)	
Severe (<0.4)	0(0.0)	0(0.0)	

**, highly significant; n, number; %, percent

Table 4: Association between abnormal ABI in 43 SLE patients and patients` characteristics
ABI, ankle brachial index.

Variables	ABI Abnormal N=7 (100.0%)	Normal N=36 (100.0%)	P-value
Age (year); Mean ± SD	33.0 ± 8.2	30.4 ± 11.7	0.579
Sex; n(%) Male Female	 3(75.0) 4(11.4)	 1(25.0) 35(88.6)	 0.000**
BMI(kg/m^2); Mean ± SD	24.3 ± 3.5	23.8 ± 3.8	0.754
Duration of disease (year); Mean ± SD	5.9 ± 2.34	6.4 ± 6.5	0.823
Activity of disease; n (%) Active Inactive	 5(25.0) 2(8.7)	 15(75.0) 21(91.3)	 0. 148
Smoking; n(%) Current Ex smoker Never	 0(0.0) 2(28.6) 5(71.4)	 0(0.0) 0(0.0) 36(100.0)	 0.001 **
Family history; n (%)	0 (0.0)	1(100.0)	0.655
Hypertension; n (%)	4(25.0)	12(75.0)	0.233
Hyperlipidemia; n (%)	0 (0.0)	0 (0.0)	***
Thrombosis; n (%)	0 (0.0)	1(100.0)	0.655
Raynaud's Phenomenon; n(%)	2(28.5)	19(52.7)	0.241
Medication; n (%) Steroid Mycophenolate mofetil Cycophosphamide Hydroxychloroquin NSAIDS Statins	 5(13.2) 2(28.6) 4(40.0) 1(7.7) 0(0.0) 1(50.0)	 33(86.8) 5(71.4) 6(60.0) 12(92.3) 1(100.0) 1(50.0)	 0.512 0.335 0.020* 0.315 0.655 0.185

**, P- value is highly significant, * P- value is significant ; n, number, %,percent ,

DISCUSSION:

In the present study we observed a significant association between abnormal ABI and SLE patients. Possible explanation is that in SLE there is vascular inflammation which is mediated by immune complexes that may result in atheroma [12].

Up to the best of our knowledge this is the 1st cross sectional study investigating ABI in Iraqi SLE patients.

Mortality due to coronary artery disease accounts for up to 30% of all deaths in patients with SLE [13]. There has been a dramatic change in the approach to studying cardiovascular disease. The ABI measurement can be conducted at low cost, using simple techniques and is non-invasive and it is an easy, quick, and accurate. Furthermore, only minimal training is required to use the technique. It can be used as a primary prevention tool in routine screening of cardiovascular status in the community [14-18] and has high patient acceptability.

In attempting to prevent initial cardiovascular events in SLE patients, a reasonable strategy would be to target and treat patients with asymptomatic subclinical atherosclerosis and controlling its risk factor using anti-platelet drugs and encouraging lifestyle changes such as stopping smoking, diet, exercise and controlling of disease activity [12].

In the present study, abnormal ABI was observed in 7(16%) SLE patients compared to 0 (0%)

control, (P-value =0.010) which may indicate a significant association between abnormal ABI and SLE patients. This agreed with other studies done by Theodoridou A et al [12], and Lijmer JG et al [(19)]. The prevalence of abnormal ABI in SLE was less in comparison to its prevalence in rheumatoid arthritis (25%) [(20)], in antiphospholipid syndrome (23%) [(21)], and in primary Sjogren's syndrome (20%) [(22)].

Mildly abnormal (0.7-0.9) ABI form is the only detected form among our SLE patients compared to controls (P=0.003) which may indicate a highly statistical significant difference between patients and controls. There were no other reports to compare with.

Male sex showed significant association with abnormal ABI in SLE patients which contrasted with another study done by Theodoidou A et al [(12)]. This might be explained because most of the males have abnormal ABI in our study although their number is small[(3(75%) abnormal ABI versus 1(25%)normal ABI in comparison to females although their total number was more[4(11.4%) abnormal ABI versus 35(88.6) normal ABI].

Smoking history showed significant association with abnormal ABI in SLE patients which is in agreement with by Theodoidou A et al [(12)].

Other SLE patients characteristics (age, BMI ,duration of disease, family history, hypertension, hyperlipidemia , thrombosis ,Raynaud`s phenomenon and medications (except cyclophosphamide) are not significantly associated with abnormal ABI .This agreed with other studies done by Newman AB et al [(16)] , Satish et al [(22)] , and Khudhir ZM [(23)]. Possible explanation is that immune-inflammatory disease influences early atherosclerosis independently of the traditional risk factors, and for cyclophosphmide the result might be related to the severity of the disease and renal involvement.

A number of limitations of the current study must be pointed out. The small number of patients and being a cross-sectional study might limit the cause and effect relationship between abnormal ABI and SLE. Despite these limitations, our findings call attention to use ABI as a simple, noninvasive technique for the detection of accelerated atheroma in young patients with SLE.

CONCLUSION:

Mild abnormal ABI occurs with high frequency (16%) in Iraqi patients with SLE. Males, smoking history, and cyclophosphamide therapy are significant predictors.

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