

## ECHOCARDIOGRAPHIC EVALUATION OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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### ABSTRACT

**Objective:** Cardiac disease occurs in various forms and is a common cause of death in systemic lupus erythematosus. The objective was to detect cardiac abnormalities by transthoracic echocardiography and determine their association in SLE patients.

**Methods:** We conducted a transthoracic echocardiographic study in 48 inpatients with systemic lupus erythematosus. Clinical and serological evaluation to confirm the diagnosis of lupus was done in all patients.

**Results:** There were 44 women (91.6%) and 4 men with a mean age of 26 years. Anti ds DNA was positive in 34 patients (68.75%). Transthoracic echocardiography revealed abnormality in 28 patients (58.33%). Of these, 16 patients (57%) had pericardial involvement with variable amount of effusion. Twelve patients (43%) had some valvular involvement and some degree of myocardial systolic dysfunction was found in 12 patients (43%). Only 4 patients (14%) had all three abnormalities. Anti ds DNA was positive in 71% of patients with cardiac abnormalities.

**Conclusions:** Cardiac involvement is common in patients with systemic lupus erythematosus. Serological abnormalities had an association with cardiac abnormalities, and were found to be more prevalent in young patients.

**KEY WORDS:** Echocardiography, Cardiac abnormalities, Systemic lupus erythematosus.

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### INTRODUCTION

Cardiovascular disease is a clinically important manifestation and is a common cause of death in patients with systemic lupus erythematosus (SLE). Both idiopathic and drug

induced lupus have cardiac manifestations. However, there is diversity in literature about the most prevalent cardiac abnormality.<sup>1-6</sup> Antinuclear (ANA) and anti double-stranded DNA (anti ds DNA) antibodies are present in a large number of SLE patients but are not known to have any association with cardiac involvement. We conducted a study to detect cardiac abnormalities by transthoracic echocardiography (TTE), and determine its association with antibody profile in our population of lupus patients.

### METHODS

**Patients:** Between 2002 and 2005, we studied 48 patients. Thirty of these were admitted to the department of dermatology because of systemic illness or skin manifestations. Others were admitted to medical wards and cardiology department. Clinical history, physical examination, and rheumatologic and serological

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analyses were performed on all patients to confirm the diagnoses, and exclude patients with possible rheumatic heart disease. TTE was performed during the same admission.

**Transthoracic Echocardiogram:** TTE was performed by an experienced echocardiographer on Toshiba, Powervision using 3.5 mHz probe. As the patients were generally young and thin, good echocardiographic images were obtained. The morphologic condition of heart valves was analysed. Thickening of mitral, aortic and tricuspid valves was looked for. The presence of severity of regurgitation and stenosis was evaluated with color flow mapping and Doppler echocardiography. Heart chambers diameter, ventricular wall movement, left ventricular function, presence of spontaneous intracavitary thrombus, thickness and echodensity of pericardium and presence of effusion was determined.

**Statistical Analysis:** Frequencies were calculated, and means for continuous variables. Echocardiographic outcomes were compared with antibody profile with reference to age groups. Chi squared test was applied for comparison on SPSS for windows. P value of less than 0.05 was considered to indicate statistical significance.

## RESULTS

Forty eight patients were studied. All the patients fulfilled the criteria of American Association of Rheumatology for diagnosis of SLE. There were 44 women (91.6%) and 4 men in the study, with a mean age of 26 years (range 11 to 60). An echocardiographic abnormality was detected in 28 patients (58.33%), and it was commoner in younger age group (Table-I). In younger age group (11-35), only 35% (14/40) patients had normal echocardiography. In older age group (36-60), 75% (6/8) patients had normal echocardiograms.

**Antibody Profile:** All the patients had the more specific antibody, the anti double-stranded DNA antibody (anti ds DNA) checked. It was positive in 34 patients (68.75%). In patients with cardiac abnormalities it was positive in 20 patients (71%). Serological abnormalities, both ANA and anti ds DNA were found to be more prevalent in younger age group ( $p < 0.001$ ), and those with cardiac abnormalities (Table-II).

**Abnormalities of the heart detected by TTE:** Following results of TTE, patients were divided into four groups for sake of analysis; normal echocardiogram (N), myocardial abnormality (myocardial), pericardial involvement (pericardial) and valvular involvement (valvular). Twenty patients (41.67 %) had a normal echocardiogram and 28 patients (58.33%) had a cardiac abnormality. Of these, 12 patients (43%) had some degree of myocardial systolic dysfunction. Pericardial involvement with some degree of effusion was the commonest abnormality and was found in 16 patients (57%). Twelve patients (43%) had valvular involvement. Valvular thickening (3 mm) was the commonest valve abnormality and was equally frequent on mitral and aortic valves. Two patients had mitral valve prolapse, and two patients had annular calcification of the mitral valve (4.1%). The regurgitation was moderate to severe in 3 out of 6 patients. Stenotic lesions were not found in our population. Four patients had moderate pulmonary hypertension. Only 4 patients (14%) had all three abnormalities, and all of them were women. In the age group comparison, all the cardiac abnormalities were prevalent in younger patients (Table-I).

## DISCUSSION

In our study, there was predominance of women and young patients, which is consistent with previous data.<sup>7-9</sup> ANA, anti ds DNA

Table-I: Age group distribution of echocardiographic abnormalities.

Age group (n = number)	Echo abnormality (Normal)	Echo abnormality (Myocardial)	Echo abnormality (Pericardial)	Echo abnormality (valvular)
11-35 (40)	14	12	14	12
36-60 (8)	6	0	2	0
P value	> 0.1	<0.01	<0.01	<0.01

Table-II: Association of cardiac abnormalities with antibody profile in lupus patients.

<i>Echo abnormality</i>	<i>ANA positive (n=number)</i>	<i>p</i>	<i>Anti ds DNA positive</i>	<i>p</i>
Normal	11-35 (4) 36-60 (0)	>0.1	11-35 (10) 36-60 (4)	>0.1
Myocardial	11-35 (6) 36-60 (0)	<0.05	11-35 (8) 36-60 (0)	<0.02
Pericardial	11-35 (4) 36-60 (0)	>0.1	11-35 (8) 36-60 (0)	<0.02
Valvular	11-35 (6) 36-60 (0)	<0.05	11-35 (10) 36-60 (0)	<0.005
Age	11-35 (16) 36-60 (0)	<0.001	11-35 (30) 36-60 (4)	<0.001

antibodies and echocardiographic abnormalities were also commoner in the younger age group. Libman-Sacks endocarditis has specially been described to occur in younger age group.<sup>10</sup>

Antinuclear and anti double-stranded DNA antibodies are present in a large number of SLE patients but not known to have any association with cardiac involvement. Over 90% of lupus patients are known to have ANA, although, presence of high titres of ANA are not diagnostic of SLE. Anti ds DNA antibodies are present in 50% to 70% of lupus patients, and commoner in glomerulonephritis patients. However, in our study anti ds DNA antibodies were detected in a higher number of lupus patients, both with and without echocardiographic abnormalities as compared with ANA. One probability was laboratory error as all tests were done by latex method in case of ANA as compared to anti ds DNA where ELISA was used. This would however mean that value of ANA as a screening test for SLE is lost in our setting as many ANA negative cases were anti ds DNA positive.

ANA negative SLE is also recognized as a distinct entity in which cutaneous involvement is usually the predominant feature but organ involvement is less than expected. Over 60% have anti Ro antibodies and about one third have anti La antibodies. About 10% of such patients eventually become ANA positive with time.

In previous studies presence or nature of cardiac disease was not associated with the activity or severity of Lupus.<sup>1</sup> There are various explanations for this finding. The disease activity in various organ systems may be present at different times. Similarly, there is lack of association of cardiac involvement with usual diagnostic serology (ANA, anti dsDNA

antibodies). However, our study yielded a strong association with anti ds DNA in the younger lupus patients.

Antiphospholipid antibodies (APLAs), which are independently present of lupus activity, in primary antiphospholipid syndrome (PAPS) have been strongly associated with cardiac involvement.<sup>11</sup> Primary antiphospholipid syndrome (PAPS) is identified by the presence of anticardiolipin antibodies in the absence of SLE and has high association with valve disease (35%-50%). Antiphospholipid antibodies (APLAs) are present in over 20% of lupus patients, and have association with thrombosis, valvular thickening, valvular endocarditis, and coronary artery disease.<sup>12,13</sup> Our study was limited as our patients did not have anticardiolipin antibodies checked because of lack of laboratory facility. Pericarditis has been described as the most common cardiac problem and various imaging and autopsy series have demonstrated pericardial involvement in more than 60% patients with SLE. In our study also pericardial involvement was the commonest (57%) cardiac abnormality.

However, studies using transesophageal echocardiography (TOE) have shown valvular disease to be the commonest cardiac abnormality (61%).<sup>1</sup> It is explained by the higher sensitivity of TOE in detecting valvular abnormalities. Valvular thickening, vegetations (Libman-Sacks), and valvular insufficiency are the common valvular abnormalities.

Coronary arteritis and atherosclerotic disease also occur with high incidence, but often difficult to differentiate clinically. Similarly, when cardiac dysfunction occurs, it is difficult to ascribe it to myocarditis, coronary artery disease, coronary arteritis or valvular dysfunction. Pulmonary hypertension is also a common

problem in SLE.<sup>14</sup> Pulmonary embolism can also occur. Aortitis is rare. The other imaging modalities like stress echocardiography, MRI, CT scan may help in improving the detection of these abnormalities.<sup>15,16</sup>

The possibility of the selection bias affecting the results can not be ruled out. Most of the patients were admitted in department of dermatology, without signs and symptoms of cardiac disease, and unlikely to have transthoracic echocardiographic abnormality. Majority of young patients in our population might have affected the results as well. The higher prevalence of valve disease has previously been seen in studies including older patients. The possibility of a single operator bias can also not be eliminated. There was no follow up study, and the possibility of cardiac abnormalities undergoing change along with the fluctuating course of disease activity could not be excluded. The effect of treatment on the prevalence and extent of cardiac abnormalities can also not be excluded.

Most patients with lupus and cardiac disease have no cardiac symptoms. A high index of suspicion is required for detection of presence of cardiac disease, as asymptomatic cases with cardiac involvement are widely reported.<sup>17</sup> A careful cardiac examination should be the primary screening method, but TTE can be helpful as a non-invasive, easily available diagnostic tool for detection of such cases. However, there will always be possibility of having other vascular problems in lupus patients despite normal echocardiographic studies.

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