

## Cardiovascular manifestations in patients with Systemic Lupus Erythematosus

Dr.Sangita Subba

Regional Institute of Medical Sciences, Imphal, Manipur, Pin- 795001 India

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### **Abstract:**

**Aim:** The aim was to document cardiovascular manifestations and to correlate it with the titre of Anti ds DNA in patients with SLE, admitted in Medicine ward and those attending Medicine, Rheumatology & Cardiology OPD, RIMS, Imphal, Manipur, India.

**Material and Methods:** 78 patients fulfilling the inclusion Criteria were seen between October 2012 and September 2014, using simple laboratory assessments, serology tests like serum ANA, Anti ds DNA, ECG and 2D transthoracic echocardiography. Clinical evaluation using the revised American College of Rheumatology criteria (1997) was used to confirm the diagnosis of Lupus. The study was recorded in a data based program. Descriptive statistics and analysis was carried out as per need.

**Results:** Out of 78, there were 69(88.5%) women and 9(11.5%) men with a mean age of  $30.98 \pm 1.21$  years. The ECG revealed abnormality in 35 (44.9%) and transthoracic echocardiography revealed that 40 (51.3%) had myocardial dysfunction and 4 (5.1%) had pericardial involvement with variable amount of effusion. The involvement of mitral, aortic and tricuspid valves were found in 43.5%, 23.1% and 17.9% respectively. Single valve involvement was found in 16.77%, double in 24.3% and three valves were involved in 6.4% of cases. The Anti ds DNA titre was strongly positive in 38(48.8%) of patients having cardiac abnormalities.

**Conclusions:** SLE is a multisystem immune disorder predominantly affecting females of younger age. Cardiac involvement is common in patients with Systemic Lupus Erythematosus. The most common abnormality found was cardiac valve involvement. High titre of Anti ds DNA was associated with cardiac abnormalities. So it is practical to do these simple investigations for identification and treatment of patients at risk of developing cardiovascular disease in SLE.

**Keywords:** Cardiac abnormalities, Anti ds DNA, Systemic Lupus Erythematosus.

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### I. Introduction

Cardiovascular disease is a clinically important manifestation and a common cause of death in patients with systemic lupus Erythematosus (SLE). However there are very few data available in Indian subjects with SLE. Antinuclear (ANA) and anti double stranded DNA (Anti ds DNA) antibodies are found in large number of SLE patients but there are limited data available regarding the association between the cardiovascular abnormalities and the titre of Anti ds DNA Antibody level. We conducted a study to detect cardiac abnormalities by transthoracic echocardiography (TTE), and determine its relation with raised antibody titre in our patients under study.

### II. Methods

It was a cross sectional study, carried out for a period of two years from October 2012 to September 2014 involving all the patients of SLE attending medicine, cardiology and rheumatology outpatient department and those admitted under medicine department. Clinical history, physical examination, and rheumatologic and serological analyses were performed on all patients to confirm the diagnoses, and exclude patients with possible rheumatic heart disease and congenital heart disease. TTE was performed either on the same day or on a later date as per the feasibility. 1997 revised "American College of Rheumatology" Criteria were used to diagnose SLE.

#### **Transthoracic Echocardiogram:**

TTE was performed by an experienced echocardiographer on Toshiba, Powervision using 3.5 mHz probe and the morphologic condition of heart valves was analyzed. Thickening of mitral, aortic and tricuspid valves were 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 echo density of pericardium and presence of effusion was determined.

**Statistical analysis**

The observation of the study was recorded in Microsoft excel 2007. Descriptive statistics like mean and percentages were used for describing the data. Chi-square test and t-test were used for test of significance and p-value of less than 0.05 was taken as significant.

All the patients of Systemic Lupus Erythematosus (SLE), both old cases and new, diagnosed by 1997 revised “American College of Rheumatology” criteria and age ≥13 years were included in the study whereas the patients with pre-existing heart disease (Congenital Heart Disease, RHD and IHD) and those unwilling for the study were excluded.

A total of seventy eight patients were studied. All the patients fulfilled the 1997 revised criteria of American Association of Rheumatology for diagnosis of SLE. There were 69(88.5%) females and 9(11.5%) males, with a mean age of 30.98 years and a standard deviation of 1.21 years. Majority of the patients belonged to the age group 25-34 years with female and male percentage of 46.4 and 22.2 respectively in this particular age group. The youngest patient in our study was 13 years old and 70 years being the oldest. Unlike females, males were equally distributed in all the age groups. Most patients were Hindu 62(79.5%), Christian 14(17.9%) and Muslim 2(2.6%) by religion. The distribution of the population from Urban 40(51.3%) and Rural 38(48.7%) areas were more or less equal. Most patients 54(69.3%) accounted for known case of SLE under treatment and 24(30.7%) were new cases diagnosed as per the diagnostic criteria set for the present study.

Abnormal ECG finding in the form of low voltage (6.5%), features of pericarditis (11.5%), sinus tachycardia (6.5%) and features of LVH (16.6%) were detected but it was found to be normal in rest of the patients (55.1%). PA view chest X-ray of the patients also showed cardiomegaly in 28.2% being the most common finding. Features of pericardial effusion were found in 4(5.1%) patients and were confirmed by echocardiography. Two female patients could not undergo chest X-ray as they were pregnant during the study period. Rest of the patients revealed normal Chest radiograph.

Out of 78 cases, 29(37.2%) were found to be hypertensive, the rest were all Normotensive.

Echocardiography revealed abnormal myocardial function in 40(51.3%) cases among which mild systolic dysfunction was the most common finding in 23(29.5%) cases. The rest showed early diastolic dysfunction in 9(11.5%), moderate systolic dysfunction in 6(7.7%) and severe systolic dysfunction in 2(2.6%) cases.

Valvular abnormality was detected in 37(47.4%) patients. There was involvement of a single valve in 13(16.7%), double valves in 19(24.3%) and three valves in 5(6.4%) cases. The commonest valve involved was the mitral valve in 34(43.5%) cases with a mild degree mitral regurgitation (MR) in 21(26.9%), moderate degree MR in 9(11.5%) and severe degree MR in 4(5.1%) cases. There was no mitral Stenosis. There was mild aortic regurgitation in 18 (23.1%) patients but no aortic Stenosis and 14(17.9%) patients showed only mild tricuspid regurgitation.

Anti ds DNA Antibody titre was strongly positive (>200 IU/ml) in 38(48.8%) patients. Only 3% showed negative Anti ds DNA antibody results.

We compared the relationship between Anti ds DNA and all the parameters like ECG, Chest X-ray, LV dysfunction, valve involvement and HTN. It was seen that all these parameters with abnormal findings had higher mean level of Anti ds DNA Antibody level, but the significant findings with a p-value of <0.05 were present in ECG and valvular involvement only.

**Table 1. Sex distribution of the respondents stratified by age**

Age in years	Male	Female	Percentage	Chi-square test
14-24	2 (22.2)	20 (29.0)	22 (28.2)	4.03 p=0.25
25-34	2 (22.2)	32 (46.4)	34 (43.6)	
35-44	2 (22.2)	8 (11.6)	10 (12.8)	
45-54*	3 (33.3)	6 (8.7)	9 (11.5)	
55-64*	0 (0.0)	3 (4.3)	3 (3.8)	
Total	9 (100.0)	69 (100.0)	78 (100.0)	

**\*cells were clubbed for analysis**

Majority of the patients were female which constituted 88.5% as shown in table 1. Males were equally distributed in all the age groups except 55-64 years. But among females younger age group were prevalent.

**Table 2. Distribution of the respondents by Anti ds DNA level**

Anti ds DNA	Value	Number	Percentage
Negative	< 25 IU/ml	3	3
Borderline positive	25-30 IU/ml	0	0.0
Low positive	30-60 IU/ml	7	8.9
Positive	60-200 IU/ml	30	38.5
Strong positive	>200 IU/ml	38	48.8
Total		78	100.0
Mean ± SD		187.01 ± 135.56	

**Table 3. Relation between Anti ds DNA level with some parameters**

Parameters	Anti ds DNA level Mean ± SD	t-test p-value
<b>ECG</b>		
Normal	154.23 ± 64.74	2.08
Abnormal	191.43 ± 89.82	0.04
<b>X-ray</b>		
Normal	159 ± 128.94	-1.261
Abnormal	205 ± 133.27	0.213
<b>LV dysfunction</b>		
Nil	172 ± 142.10	-0.911
Abnormal	204 ± 127.60	0.384
<b>Valve involvement</b>		
None	148.11 ± 70.45	-53.12
Involved	201.23 ± 98.20	0.007
<b>Hypertension</b>		
Hypertensive	185 ± 107.20	0.418
Normotensive	107 ± 97.11	0.677

Table3. Shows that all the parameters (ECG, X-ray chest, LV dysfunction, valve involvement and hypertension) with abnormal finding had higher mean level of Anti ds DNA Antibody level, but the significant findings were present in ECG and valvular involvement only.

### III. Discussion

The youngest patient in our study was 13 years old and the oldest one was 70 years old females. The most common age group was 25-34 (43.6%) years with the mean age of 30.98 years. In a similar study conducted by Kotokey RK et al <sup>(1)</sup> maximum number of patients belonged to the age group 21–30 years (34.25%).

In our study majority of the patients were females 69(88.5%) which is consistent with study by Hameed S et al <sup>(2)</sup> and Kotokey RK et al <sup>(1)</sup> where the percentage of female patients were 91.6% and 93.15% respectively. In our study, majority of the female patients belonged to the younger age group but male patients were equally distributed in all the age groups. However, this finding is statistically insignificant (p>0.05).

The commonest symptom was fatigue in 81% of cases followed by generalized weakness (46.2%) and SOB (41.0%). Palpitation and orthopnoea were present in 19.2% and 16.7% respectively. In the study by Kotokey RK et al <sup>(1)</sup> fatigue was the most common symptom present in 34.25% cases which was also similar to the study by Trench CM et al. <sup>(3)</sup>

QT prolongation was present in 6.5% of cases. Consistent finding was present in the study by Elkayum U et al <sup>(4)</sup> with abnormal electrocardiogram in 43.8% patients. Their study showed LVH in 6.2% patients, sinus tachycardia in 6.2% and low voltage ECG in 3.1%. In the study by Kotokey RK et al <sup>(1)</sup> abnormal ECG was found in 18% of cases with the commonest finding being low voltage ECG in 8.21% cases.

Moyssakis I et al <sup>(5)</sup> in their study found, 24 out of 38 patients had mitral valve regurgitation in all of them (mild in 18, moderate in 4, and severe in 2), whereas stenosis co-occurred with regurgitation in 9 patients (mild in 6 and moderate in 3), whereas 34% patients had aortic valve involvement; 11 had regurgitation (mild) and 8 had stenosis (mild), coexistent with regurgitation in 6 of them. One patient had mild tricuspid regurgitation. Although in our study we found mitral valve regurgitation in 34(43%) out of 78 patients (mild in 26.9%, moderate in 11.5% and severe in 5.1%) whereas there was no stenosis of mitral valve. The aortic valve regurgitation was mild in 23.1% cases and mild tricuspid valve regurgitation was also seen in our study in 17.9% cases.

Hameed S et al <sup>(2)</sup> in their study found antinuclear antibodies in 90% cases and anti ds DNA antibodies in 71% cases of SLE patients, their study yielded a strong association with anti ds DNA in the younger lupus patients. In our study also we found strongly positive Anti ds DNA Antibody titre in 38(48.8%) cases and there was statistically significant relation between higher Anti ds DNA Antibody titre and the occurrence of valvular lesions with a p-value of (0.007).

Cervera R et al <sup>(6)</sup> in their study found high prevalence of cardiac disturbances 57% cases. Valvular abnormalities constituted mainly mitral and aortic dysfunctions (44%) as the most common finding. In addition, pericardial effusion was a common echocardiographic finding in 27% cases, but significant pericardial disease was found in only 7% patients. In our studies also we found similar findings with valvular abnormalities involving mitral valve in 34(43.5%) and aortic valve in 18(23.1%) cases, nevertheless pericardial effusion was found in only 4 (5.1%) cases.

In the present study 41(47.4%) patients had valvular involvement. This finding is consistent with study by Hameed S et al <sup>(2)</sup> where valvular involvement was found in 43 % of cases. This finding is also consistent with study by Tessier JB et al <sup>(7)</sup> where the main abnormality was the mitral valve (37.3%), whereas in the study by Kotokey RK et al <sup>(1)</sup> tricuspid regurgitation was found more than mitral valve.

In the present study, Severe mitral regurgitation was found in 4(5.1%) of cases. All the valves (mitral, aortic and tricuspid) were involved in 5(6.4%) cases. Tricuspid and aortic valve abnormality was found in 17.9% and 23.1% respectively but only in mild form. The commonest valve involved was mitral valve followed by aortic valve and tricuspid valve. Hameed S et al <sup>(2)</sup> in their study found 14% patients in whom all the three valves were involved although they found mild mitral regurgitation as the most common valve abnormality in 26.9%.

In the present study virtually half of the SLE patients (48.8%) under study had strongly positive Anti ds DNA Antibody level. Higher Anti ds DNA Antibody level was observed in patients with abnormal ECG, Chest X-Ray, LV dysfunction and Valvular involvement however only ECG and Valvular abnormality showed statistical significance with the high level of Anti ds DNA Antibody . Hameed S et al <sup>(2)</sup> in their study also found majority of cases having high ANA and Anti ds DNA level but in their study there was no association with cardiac abnormalities as in case of our studies.

#### **IV. Conclusion**

The study was carried out to study the cardiovascular manifestations in patients with Systemic Lupus Erythematosus and to find if any relation exists between the cardiovascular manifestations and the level of Anti ds DNA as such cases are not uncommon in this part of the north east region of India.

The study incorporated 78 patients and most of them were females from the age group 25-34 years. Majority of the patients were Hindus by religion and presented with fatigue followed by shortness of breath and generalized weakness.

Our study suggests that there are no major clinical differences between male and female patients with SLE in contrast to many studies. However the studies suggest that differences between male and female patients also depend on ethnicity hence future studies will need to consider both ethnicity and gender to understand these differences.

Twenty nine (37.2%) patients had hypertension. ECG was abnormal in 44% of the patients. Cardiomegaly was the most common abnormal finding on Chest X-ray. Mild systolic dysfunction was the most common myocardial abnormality in 2D TT Echocardiography. Features of pericardial effusion were found in 5.1% of cases. Mild mitral regurgitation was present in 21(26.9%) cases, mild tricuspid regurgitation in 14(17.9%) cases and mild aortic regurgitation in 18(23.1%) cases.

SLE is associated with increased risk of CVDs. Echocardiography is the modality of choice for the diagnosis of valvular pathology. Though 2D Transthoracic Echocardiography (TTE) used in this study is considered standard method to diagnose valvular pathology but studies using Trans Esophageal Echocardiography (TEE) is superior to trans-thoracic Echocardiography in that it gives more clear and precise image. However owing to the need for sedation and/or localized numbing medication in order to make the patient more comfortable during the procedure which is distressing for both the patient as well as the physician, it was not done in our setting.

However, there were certain limitations in our study like there was no follow up which might have missed the cardiovascular abnormality that might have developed in later course of the disease. Also, majority of the patients 54(69.3%) under study were a known case of SLE under treatment with steroids which might have altered the cardiovascular changes in them.

Electrocardiographic changes are often non specific but at times are very useful as a tool to suspect cardiovascular abnormality that may be underlying

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