Original Article

An Observational Study on the Special Characteristics of Cardiovascular Manifestations of Systemic Lupus Erythematosus in North Eastern India

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Introduction : Systemic Lupus Erythematosus (SLE) is a multisystem autoimmune disease with high prevalence of Cardiovascular abnormalities detectable with high-sensitivity imaging modalities. Introduction of Echocardiography has disclosed a higher prevalence of clinically silent patients with cardiac abnormalities.

Aims and Objectives : To study the Cardiovascular manifestations and Echocardiographic changes in patients of Systemic Lupus Erythematosus.

Materials and Methods : A total of 82 Systemic Lupus Erythematosus patients aged more than 12 years were selected as per 2012 Systemic Lupus International Collaborating Clinics (SLICC) criteria. Clinical and Echocardiographic findings were evaluated.

Results : In our study, median age was 25.5 years and mean age 27.33±10.96 years. The most common Cardiovascular Manifestation was Hypertension in 22 (26.82%) patients amongst whom 15 (18.29%) patients had Echocardiographic evidence of Left Ventricular Hypertrophy. Pericardial disease was detected in 17(20.73%) cases clinically whereas Echocardiographic evidence was present in 26(31.71%) cases.Valvular abnormality was detected clinically in 9(10.97%) out of 82 cases although Echocardiography showed evidence in 31(37.8%) cases. Cardiomyopathy was found in 6.09% cases. Two (2) out of 8 male patients have evidence of Cardiomyopathy. It is also found to be more prevalent in female patients in ethnic groups. Hypertriglyceridemia and increased Very low-density lipoprotein (VLDL) were the most common lipid abnormality detected amongst SLE patients. No significant antibody association was seen in patients with Cardiovascular manifestations unlike Anti ds Deoxyribonucleic Acid (DNA) in Lupus Nephritis.

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Key words **: Systemic Lupus Erythematosus, Cardiovascular manifestations, Echocardiography, Pericardial effusion, Valvular abnormality.**

Systemic Lupus Erythematosus (SLE) is an Autoimmune disease that involves multiple organs of the body and has variable clinical presentations. The cells and organs undergo damage mediated by tissue binding autoantibodies and immune complexes. Prevalence frequencies of SLE range from 20 to 240 per 1,00,000 persons and reported incidence rates range from 1 to 10 per 1,00,000 person-years[1]. The prevalence of SLE in India is comparatively low. Only 3 cases of SLE were detected in a population survey of 91,888, giving a point prevalence of 3.2 per 100,000[2]. Demographic data has showed significant variations in the clinical manifestations of SLE between Eastern and Western parts of India[3].

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Editor's Comment :

- Cardiovascular manifestations mostly remained silent in SLE.
- Echocardiography picked up evidence of cardiovascular disease in patients who were clinically silent.
- High index of suspicion and early use of Echocardiography may aid diagnosis and reduce mortality and morbidity in Systemic Lupus Erythematosus.

The description of cardiac involvement in SLE was first reported by William Osler in 1895. Cardiovascular manifestations of SLE can be divided into following: valvular and Pericardial Involvement, Myocardial Dysfunction, Conduction Disorders, Accelerated Atherosclerosis and Thromboembolic Disease. Cardiovascular Manifestation showever, remain clinically unnoticed during life in majority of SLE patients[4].

Introduction of two dimensional and Doppler Echocardiography has disclosed a higher prevalence of patients with Cardiac Abnormalities in SLE patients[5].

Hence, this study on special characteristics of

Cardiovascular manifestations in cases of SLE with special reference to 2D Echocardiographic evaluation has been done with following Aims and Objectives.

Aims and Objectives

(1) To study the cardiovascular manifestations in patients of SLE.

(2) To study the association of clinicaland echocardiographic findings in cases of SLE.

Materials and Methods

The study was a hospital based cross sectional study conducted in the Department of Medicine at Gawahati Medical College and Hospital, Guwahati, Assam, for a period of one year extending from 1st June 2018 to 31st May 2019,following clearance from ethics committee. A total of 82 cases of SLE, both male and female, were taken up for the study.Statistical graphs were prepared using Microsoft Excel 2007 and Microsoft Word 2007. Statistical analysis was performed using GraphPad in Stat version 3.00 for Windows 7, Graph Pad Software, San Diego, California USA. (www.graphpad.com). Chi square test was used for analysis. P value<0.05 was taken as statistically significant.

Inclusion Criteria :

(1) SLE patients (as per 2012 Systemic Lupus International Collaraborating Clinic Criteria (SLICC criteria) who were above the age of 12 years

Exclusion Critria :

- Age <12 years
- Comorbidities like Diabetes Mellitus, Hypothyroidism and other autoimmune disorder.
- Sepsis in SLE
- History of alcohol and drug abuse.
- Cardiovascular diseases attributable to other causes like Congenital Cardiac Diseases, Rheumatic Heart Disease, Peripartum Cardiomyopathy, Hemochromatosis, Amyloidosis.
- Pregnancy

Observations and Results

The Median age was 26 years and mean age was 27.94 with a standard deviation of 10.54 years. Maximum number of cases were in the age group of 21-30 years. There were 8 male SLE cases while females were 74 making the Female to Male ratio of 9.25:1. The cases were more prevalent from rural areas (57%) whereas 43% of the patients were from urban areas.

Cardiovascular manifestations were clinically detected in 33 (40.24%) patients. The most common Cardiovascular manifestation was Hypertension, present in 22(26.82%) cases followed by Congestive Cardiac Failure in 15(18.29%) cases and pericardial disease in 17 (20.73%) cases. Valvular Heart Disease were seen in 9 (10.98%) cases, Coronary Artery Disease in 6 (7.32%) cases and Arrhythmia in 4(4.88%) cases.

The most common Echocardiographic finding was Valvular abnormality found in 31(37.8%) cases, followed by Pericardial effusion/ pericarditis in 26 (31.71%) cases and Cardiomyopathy in 05 (6.09%) cases. The other significant abnormalities seen were : Diastolic Dysfunction 20 (24.39%) cases, Left Ventricular Hypertrophy 15(18.29%) cases and Pulmonary Arterial Hypertension 4 (4.87%) cases, Regional Wall Motion Abnormality 7 (8.54%) and Global Hypokinesia 2 (2.44%) cases.

Echocardiography revealed Cardiovascular Disease in 46 (56.10%) cases of which 30 (36.58%) cases were diagnosed clinically and the rest 16 (19.51%) remained clinically silent.

Increased Triglyceride 33 (42.24%) was the most common lipid abnormality in this study amongst SLE patients, followed by Hypercholesterolemia (16 cases (19.51%) and raised VLDL (16 cases- 19.51%). Antinuclear Antibodies (ANA) (96.34%) and Anti ds DNA (47.56%) were among the most common serological markers seen in SLE patients in our study followed by Anti Sm (36.58%), Anti-nucleosome (31.97%), Anti Ribosomal P (31.71%) and Antiphospholipid Antibodies (APLA) was seen in 18.29% cases.

Amongst the 33 patients with Cardiovascular manifestations, 3 (9.09%) patients had no disease activity, 13(39.39%) patients had mild disease activity, 7 (21.21%) patients had moderate disease activity, 5 (15.15%) patients had high disease activity and 5 (15.15%) patients had very high disease activity (Figs 1-6 & Tables 1-4).

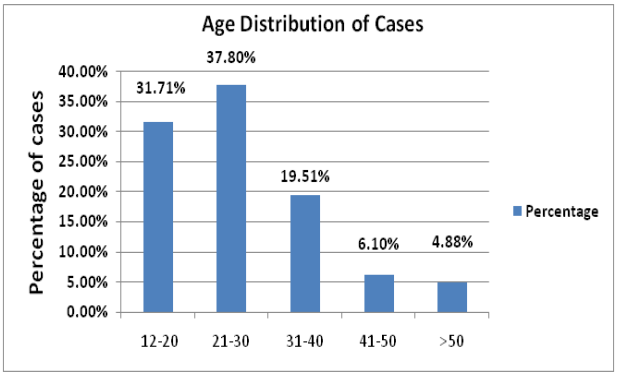

Fig 1 — Bar diagram showing age distribution of cases

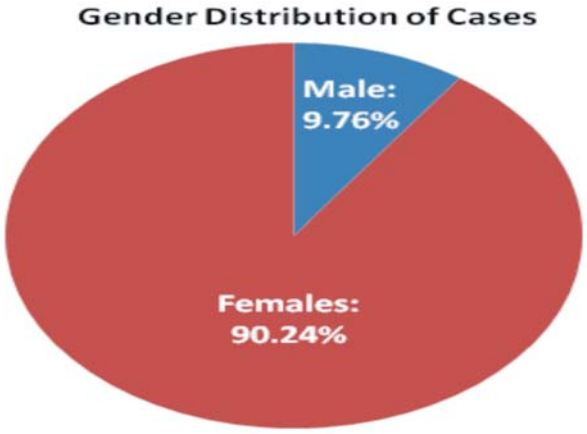

Fig 2 — Pie diagram showing gender Distribution of cases

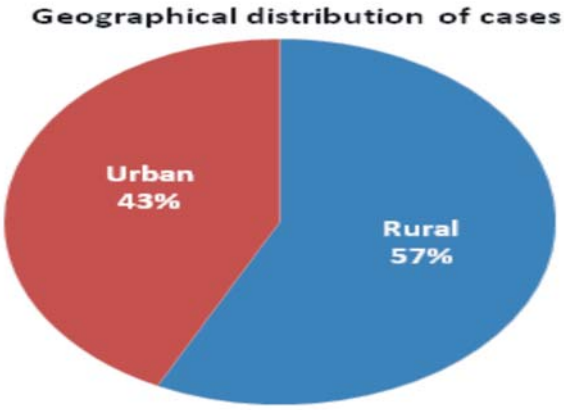

Fig 3 — Pie diagram showing Geographical distribution of cases

Discussion

The Median age was 26 years and mean age was 27.94 with a standard deviation of 10.54 years.

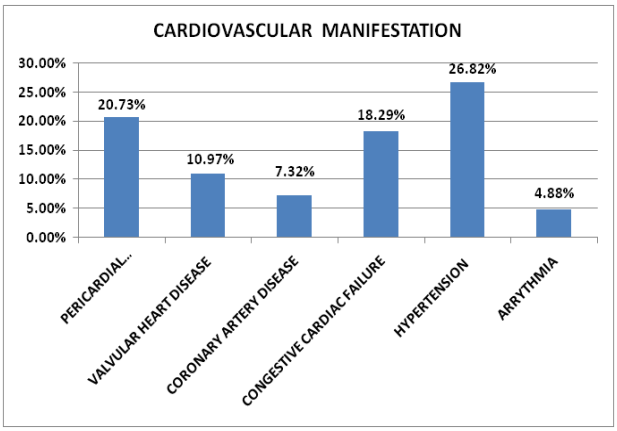

Fig 5 — Bar diagram showing clinical diagnosis of Cardiovascular Manifestation

Maximum number of cases was in the age group of 21-30 years. Other Indian studies which showed similar findings include Malaviya AN, *et al* (1988)[4] and Vaidya S, *et al* (1997)[5] where the peak incidence was seen in the 3rd decade.The Female to Male ratio was 9.25:1.Robert M, *et al* (2006)[6] and Kakati S, *et al* (2017)[7] reported a Female to Male ratio of 11.5:1 and 12:1 respectively.

Most of the cases were rural predominant (57%), more so in tribal populations of Assam. Gergianki I, *et al* (2019) showed that risk of SLE in urban population is 2.08 times more than rural[23].

In our study, Cardiovascular manifestations were clinically detected in 40.24% patients. Study conducted in different parts of India like Madhavan R, (1983), Malaviya AN (1985), Vaidya S (1997), Paul BJ (2003) and Seigal R (2011) found Cardiovascular manifestations of 9.2% of 54 patients, 5% of 101 patients, 11.8% of 220 patients, 5.3% in 75 patients

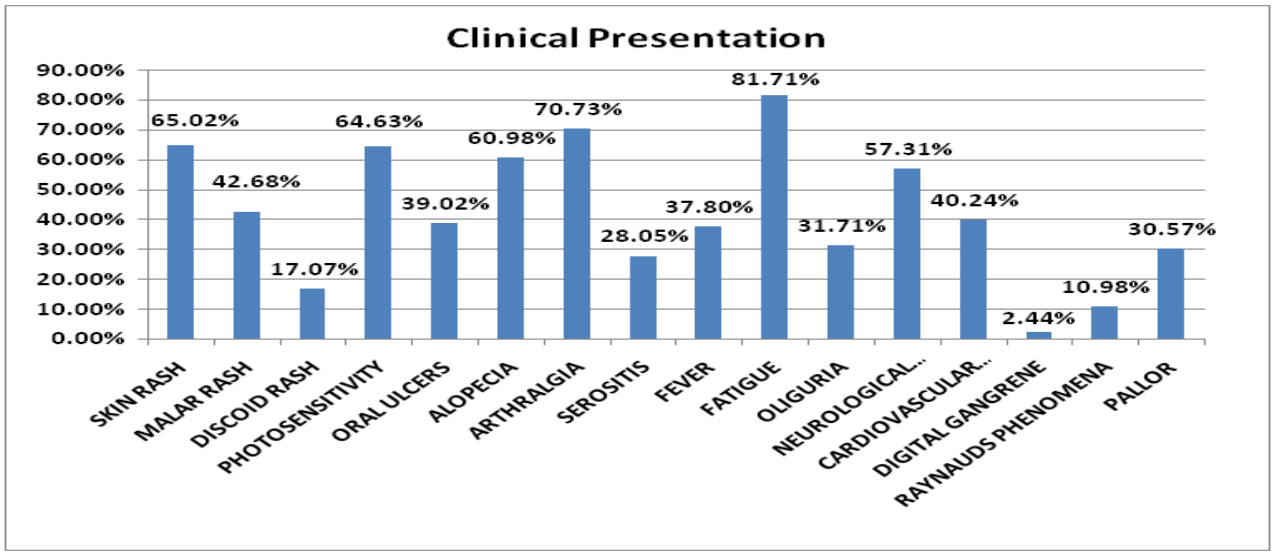

Fig 4 — Bar diagram showing clinical presentations of cases

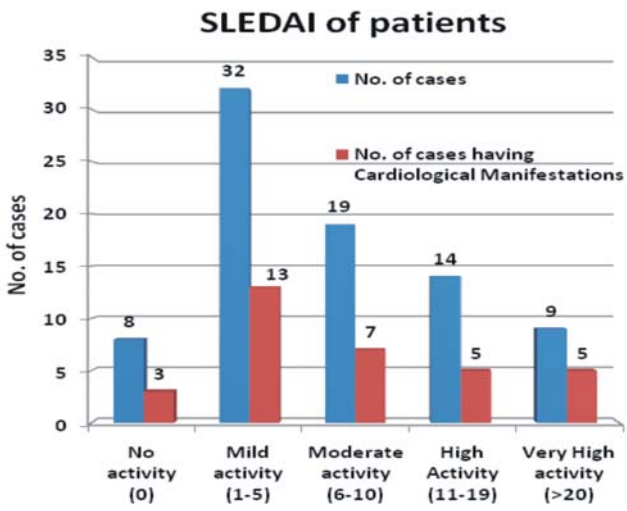

Fig 6 — Clustered Bar diagram showing SLEDAI of patients

and 6.7% of 60 patients respectively in patients of Systemic Lupus Erythematosus (SLE). However, a study by Harvey AN, *et al* (1954) found 55% out of 130 patients showed Cardiovascular involvement at some stage of their illness. Moder K G eta (1999) stated Cardiovascular involvement in 50% cases of SLE.

The most common Cardiovascular manifestation was Hypertension present in 26.82% cases. Hypertension was noted in 22%[10] and 30.4%[14] patients in different studies. The findings of these studies are almost consistent with the findings of our study. Few studies showed lower incidence of Hypertension in 14% and 4% of patients of SLE[10,13].

Congestive Cardiac Failure was present in 18.29% cases. Other studies reported Congestive Cardiac Failure in 7% and 5-31.0% patients of SLE[8,14]. Pericardial effusion was clinically detected in 20.73% cases in our study. In a study in Spain pericardial effusion was clinically detected in less number of cases (7%)[3]. However, it was detected in higher number of cases (25.4%)in a meta-analysis by Chen J, *et al* (2006)[15].

Valvular Heart Disease was present in 10.98% cases in our study. Clinically important valvular disease was found to be present in16.7% and 13-65.0% cases of SLE which was slightly higher in comparison to our study[12,14].

The prevalence of Cardiovascular events like Myocardial Infarction, cardiac sudden death or Angina was reported in 8.3% in the Baltimore Lupus Cohort and 8.9% by Urowitz MB, *et al* (1976)[16]. However, our study showed Coronary Artery Disease in 7.32% cases.

Arrhythmia was found in the current study of 4.88% cases comparable to 3-16.0% cases in other studies[14].

In the present study Echocardiographic changes were found in 56.10% cases. Studies by Cujec B, *et al* (1991), Cervera R, *et al* (1992) and Meriem D, *et al* (2018), showed similar observations[3,18,19]. In one study16.7% cases of valvular disease were diagnosed clinically although Echocardiography revealed valve involvement in 40.1% patients[12]. However, in our study Valvular Heart Diseaase was diagnosed clinically in 10.98% patients and Echocardiography showed evidence of Valvular Heart Diseaase in 37.80% patients.

Echocardiographic evidence of pericardial effusion/ Pericarditis was seen in 31.71% cases of our study

Table 1 — *Showing Echocardiographic diagnosis cardiovascular diseases*

Echocardiographic Findngs	No of cases (percentage of cases) n=82
Valvular abnormality	31 (37.80%)
Pericardial effusion	26 (31.71%)
Cardiomyopathy	05 (6.09%)
Regional Wall Motion Abnormality	7 (8.54%)
Global Hypokinesia	2 (2.44%)
Pulmonary Arterial Hypertension	4 (4.87%)
Diastolic Dysfunction	20 (24.39%)
Left ventricular Hypertrophy	15 (18.29%)

Table 2 — *Cardiovascular manifestations found clinically and on Echocardiography*

Echocardiographic findings	Clinically evident	Clinically silent	Total
Positive	30 (36.58%)	16 (19.51%)	46 (56.10%)
Negative	3 (3.66%)	33 (40.24%)	36 (43.90%)
Total	33 (40.24%)	49 (59.75%)	82
P value is < 0.01(CI 95%)			

Table 3 — *Lipid Profile of patients*

Lipid	No of cases (Percentage of cases %) [n=82]
Dyslipidaemia	43 (52.44%)
Hypercholesterolaemia	16 (19.51%)
Hypertriglyceridaemia	33 (42.24%)
Raised LDL	12 (14.63%)
Raised VLDL	16 (19.51%)
Decreased HDL	10 (12.19%)

Table 4 — *Antibodies in SLE patients*

Antibody	No of cases (percentage of cases %) [n=82]
ANA	79 (96.34%)
Anti-ds DNA	39 (47.56%)
Anti Sm	30 (36.58%)
Anti RNP	19 (23.17%)
Anti Ro (SS-A)	9 (11.67%)
Anti La (SS-B)	6 (7.31%)
Anti Histone	12 (14.63%)
Anti nucleosome	27 (31.97%)
Anti Ribosomal-P	26 (31.71%)
Antiphospholipid (APLA)	20 (18.29%)
Direct Coombs test	13 (15.85%)

which was in concordance with results obtained in other studies which showed presence of pericardial effusion in 27%[5] and 38%[21] cases.

Diastolic dysfunction was detected in 24.39% cases compared to 16% cases in a study by Cujec B, *et al* (1991)[18].

Cardiomyopathy was found in 6.09% cases. Left Ventricular Hypertrophy was noted in 18.29% cases in Echocardiography which is comparable to14% obtained in a study by Cujec B, *et al* (1991)[18]. Pulmonary Arterial Hypertension was present in 4.8% cases, comparable to otherstudies showing its presence in 10.1%, 10% and 8.5% cases of SLE[12,19,20]. In the present study Regional Wall Motion Abnormality was found in 8.54% cases and Global Hypokinesia was present in 2.44% cases compared to2.8% and 4% patients in other studies[12,18].

Hypercholesterolaemia was present in 16 (19.51%) cases and hypertriglyceridaemia was present in 33 (42.24%) cases. Raised VLDL, raised Low-density Lipoprotein (LDL) and decreased High-density Lipoprotein (HDL) were present in 16 (19.51%) cases 12 (14.63%) cases and 10 (12.19%) cases respectively. In a study at a tertiary teaching hospital of Eastern India by Dakua S, *et al* (2017), Hypercholesterolemia was found in 23 (22.7%), Hypertriglyceridemia in 55 (54.4%), raised LDL-C in 24 (23.7%) cases.

ANA positivity was 96% in our study. Malviya AN *et al*, Paul BJ, *et al*, Saigal R, *et al*, Sharma M, *et al* found similar findings in their study. APLA association in SLE was found to be 18.29% cases positive in our study however, a study by Bourre- Tessier J, *et al* (2011) found APLA in 32.7% of cases.

Amongst the patients with Cardiovascular manifestations,9.09% patients had no disease activity, 39.39% patients had mild disease activity, 21.21% patients had moderate disease activity, 15.15% patients had high disease activity and 15.15% patients had very high disease activity. A study by Mohamed AA, *et al* (2019), reported that there were no significant associations between the Echocardiographic features and the SLEDAI scores, a finding which is consistent with our study[20]. However, in a study by Cervera R, *et al* (1992), active disease was found in 56%, of whom 67% had Echocardiographic abnormalities[3].

Conclusion

In the present study, most of the patients presented with fatigue, arthralgia, skin rash, alopecia, photosensitivity. The study revealed pre-ponderance of disease amongst rural population, more specifically in tribal population. Echocardiographic evidence of cardiovascular disease was found in more than fifty percent of patients whereas only forty percent of the patients were diagnosed clinically. Most common cardiovascular findings detected clinically were Hypertension, Pericardial Effusion, Congestive Cardiac Failure Andvalvular Heart Disease. However, Echocardiography Revealed Valvular Abnormality, Pericardial Disease, Cardiomyopathy, Diastolic Dysfunction, Left Ventricular Hypertrophy, Pulmonary Artery Hypertension, Regional Wall Motion Abnormality and Global Hypokinesia in decreasing order respectively. A special observation was made that dilated cardiomyopathy were found in 2 out of 8 male patients andalso found in female patients in ethnic groups. Hypertriglyceridemia followed by Hypercholestero-laemia and increased VLDL were the most common lipid abnormalities detected amongst SLE patients.No significant antibody association was seen in patients with Cardiovascular Manifestations unlike Anti ds DNA in Lupus Nephritis.APLA association is seen in Coronary Artery Disease.

Limitations :

Our study had a small sample size and duration of study was short. It was a cross- sectional observational study and patients were not followed up. Hence no definite inference was concluded from this study. A large longitudinal prospective epidemiological study is required to arrive at a definite conclusion.

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Conflict of Interest : None

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