



A CROSS-SECTIONAL STUDY OF CARDIAC INVOLVEMENT IN SYSTEMIC LUPUS ERYTHEMATOSUS IN AN TERTIARY CARE CENTRE WITH EMPHASIS ON 2-D ECHOCARDIOGRAPHY

Nephrology

Dr Sourav Sadhukhan	Post Doctoral Trainee, Department Of Nephrology, Institute Of Post Graduate Medical Education & Research, Kolkata.
Dr Prabir Kumar Kundu*	Assistant Professor, Department of General Medicine, R. G. Kar Medical College & Hospital, Kolkata. *Corresponding Author
Dr Sandip Ghosh	Associate Professor, Department of General Medicine, R. G. Kar Medical College & Hospital, Kolkata.
Dr Aniruddha Ray	Professor & Head, Department of General Medicine, R. G. Kar Medical College & Hospital, Kolkata.

ABSTRACT

Introduction: Systemic lupus erythematosus (SLE) is a chronic autoimmune inflammatory rheumatologic disease. Its exact etiology is unknown and it can affect several organs—including skin, joints, kidneys, and many other organs. One of the organs reported to be involved in SLE is heart. The American Heart Association includes patients with SLE, especially women, as a high-risk group for cardiovascular diseases.

Objectives: Find out cardiac involvement in patients of SLE. There is any relationship of cardiac involvement with the disease activity of SLE (SLEDAI-2K)

Material And Methodology:

Study Design: An observational cross-sectional study.

Study settings and timeline: An 18 months Hospital Based study.

Place of study: Department of General Medicine, RGKMCH.

Period of study: 18 Months, from January 2018 to June 2019.

Study population: The patients admitted in inpatients wards of Department of General Medicine and also OPD patients of R G Kar Medical College and Hospital who will fulfill the inclusion criteria.

Results And Analysis: In patients with active disease, 29(53.7%) patients had first presentation. 25(46.3%) patients had first presentation but disease activity was low. Association of first presentation with disease activity was statistically significant ($p=0.0000406378$). In patients with active disease, 36(66.7%) patients had cardiac involvement in any form. In patients with low disease activity, 11(50.0%) patients had cardiac involvement. Association of cardiac involvement with disease activity was not statistically significant ($p=0.2730132774$). Out of total 47 patients with cardiac involvement, 27(57.4%) patients had pericardial involvement.

Summary And Conclusion: Cardiac involvement is frequently seen in systemic lupus erythematosus patients, 61.8% in our study. Pericardium, myocardium, endocardium all can be involved in SLE. Pericardium is most commonly involved. Pulmonary hypertension, valvular abnormality, diastolic dysfunction, systolic dysfunction all are found in SLE. Echocardiography is a non-invasive excellent tool to evaluate the SLE patients for any cardiac involvement and serial screening of the patients. All cardiac manifestations are observed in active SLE patients in higher frequency but only pericardial involvement with disease activity is statistically significant.

KEYWORDS

Cross-sectional Study, Cardiac Involvement, Systemic Lupus Erythematosus and Emphasis on 2-D Echocardiography

INTRODUCTION

Systemic lupus erythematosus (SLE) is a chronic autoimmune inflammatory rheumatologic disease. Its exact etiology is unknown and it can affect several organs—including skin, joints, kidneys, and many other organs. One of the organs reported to be involved in SLE is heart.¹ The American Heart Association includes patients with SLE, especially women, as a high-risk group for cardiovascular diseases.

Pericardium, heart muscle (myocardium), valves, and coronary arteries all can be involved in patients with SLE.

Several cardiac conditions have been reported to be considerable in patients with SLE; these conditions include pericarditis (believed to be the most common cardiac involvement in SLE and reported in 11% to 54% of patients) mitral regurgitation, tricuspid valve thickening and regurgitation, valvular vegetations (eg, Libman-Sacks endocarditis, which can be as prevalent as 11%), myocardial dysfunction, AND coronary arteries diseases.²

Cardiac involvement in SLE was first reported a long time ago. Nonetheless, during the last decade, the application of sensitive imaging methods such as echocardiography has considerably augmented our understanding about the details of cardiac diseases in SLE. Echocardiography is a noninvasive and accessible method and, hence, several studies recently have used this imaging technique to study cardiac structure and function in rheumatologic diseases, especially SLE.

Most cardiac diseases in SLE may be clinically silent, but they can cause significant morbidity and mortality.³ Identifying these subclinical conditions, in particular myocardial dysfunction and

valvular diseases, confers better management of patients suffering from SLE. In addition, some authors have suggested timely screening with echocardiography to prevent early mortality.¹

The frequencies and types of cardiac involvements are varied among studies, which may be in consequence of the severity of inflammation, diagnostic technique used, side effects of the drug consumed, and many other factors. Given the differences in the literature about the prevalence of cardiac involvement in patients with SLE, we decided to draw upon echocardiography to investigate this topic in our tertiary care hospital.

1. To find out cardiac involvement in patients of SLE.
2. To find out, if there is any relationship of cardiac involvement with the disease activity of SLE (SLEDAI-2K)

MATERIAL AND METHODOLOGY

Study Population: The patients admitted in inpatients wards of Department of General Medicine and also OPD patients of R G Kar Medical College and Hospital who will fulfill the inclusion criteria from January 2018 to June 2019.

Sample Size: (95% level of confidence with 1% margin of error), the study sample size and control sample size is worked out using the statistical formula $N = (Z_{1-\alpha/2})^2 \cdot p \cdot q / L^2$. Where P is the expected proportion of cases from a previous study. And $q = (100 - p)$. $Z_{1-\alpha/2} = 1.96$ (considering 95% confidence level) and $L = \text{precision} (<10, <p)$ taken as 9. The calculated final sample size is minimum of 76.⁴ $P=80, q=20$.

Sample Design: No sampling needed. All patients with Diagnosis of SLE was included in the study.

Inclusion Criteria: Patients newly or previously diagnosed as SLE will be included in this study.

Exclusion Criteria:

- Patient or patient's relative not giving consent.
- Not fulfilling inclusion criteria.
- Coexisting malignancy, cardiovascular disease, other coexisting autoimmune disease.

Data Collection: All the cases, diagnosed as per the SLICC Criteria for SLE, was included after a written, informed consent. The clinical history, examination and investigations were recorded. The past medical records were reviewed for any cardiac abnormalities, electrocardiograms, chest radiographs, 2D-echocardiography reports, flares, and treatment administered.

Besides the routine investigations, 2-D echocardiography was done in all patients who had not done it before. Serial echocardiography findings were noted if available.

Those with other associated rheumatologic diseases, rheumatic heart disease or congenital heart disease were excluded.

RESULTS AND ANALYSIS

Our study showed that 1(1.3%) patient had ≤ 20 years of age, 44(57.9%) patients had 21-30 years of age, 29(38.2%) patients had 31-40 years of age and 2(2.6%) patients had 41-50 years of age. 75(98.7%) patients were female and 1(1.3%) patient was male. 29(38.2%) out of total 76 patients had first presentation of SLE. Total out of 76 patients 47(61.8%) patients had cardiac involvement. Out of total 76 patients, 18(23.7%) patients had PAH. Out of total 76 patients, 27(35.5%) patients had pericardial effusion. Out of total 76 patients 17(22.4%) patients had diastolic dysfunction. Out of total 76 patients only 3(3.9%) patients had systolic dysfunction. Out of total 76 patients 11(14.5%) patients had ≥ 1 valvular involvement. Out of total 76 patients 6(7.9%) patients had RWMA. Out of total 76 patients, 54(71.1%) patients had active SLE and 22(28.9%) patients do not have active SLE. Among the patients with active SLE, 1(1.9%) patient had ≤ 20 years of age, 37(68.5%) patients had 21-30 years of age, 15(27.8%) patients had 31-40 years of age and 1(1.9%) patient had 41-50 years of age.

We found that among the patients with SLE with low disease activity, 7(31.8%) patients had 21-30 years of age, 14(63.6%) patients had 31-40 years of age and 1(4.5%) patient had 41-50 years of age. Association of age in years with disease activity (ACTIVE DISEASE) was statistically significant ($p=0.0209$). In patients with active disease, the mean age (mean $\pm$ s.d.) of patients was 28.6667 ± 4.9868 years. In patients with low disease activity, the mean age (mean $\pm$ s.d.) of patients was 32.3636 ± 5.1505 years. Distribution of mean age with disease activity was statistically significant ($p=0.0049$). In patients with active disease, 29(53.7%) patients had first presentation. 25(46.3%) patients had first presentation but disease activity was low. Association of first presentation with disease activity was statistically significant ($p=0.0000406378$). In patients with active disease, 36(66.7%) patients had cardiac involvement in any form. In patients with low disease activity, 11(50.0%) patients had cardiac involvement. Association of cardiac involvement with disease activity was not statistically significant ($p=0.2730132774$). Out of total 47 patients with cardiac involvement, 27(57.4%) patients had pericardial involvement.

Our study showed that out of total 47 patients with cardiac involvement, 17(36.2%) patients had diastolic dysfunction. Out of total 47 patients with cardiac involvement, 3 (6.4%) patients had systolic dysfunction. Out of total 47 patients with cardiac involvement, 18(38.3%) patients had PAH. Out of total 47 patients with cardiac involvement, 6 (12.8%) patients had RWMA. In patients with active disease, 13(24.1%) patients had PAH. In SLE patients with low disease activity, 5(22.7%) patients had PAH. Association of PAH with disease activity was not statistically significant ($p=0.8632686559$). In patients with active disease, 24(44.4%) patients had pericardial involvement. In patients with low disease activity, 3(13.6%) patients had pericardial involvement. Association of pericardial involvement with disease activity was statistically significant ($p=0.02255$). In patients with active disease, 12(22.2%) patients had DIASTOLIC DYSFUNCTION. In patients with low disease activity, 5(22.7%) patients had Diastolic dysfunction. Association of diastolic dysfunction with SLE disease

activity was not statistically significant ($p=0.7982884773$).

We showed that in patients with active disease, 2(3.7%) patients had systolic dysfunction. In patients with low disease activity, 1(4.5%) patient had systolic dysfunction. Association of systolic dysfunction with disease activity was not statistically significant ($p=0.6322535577$). In patients with active disease, 10(18.5%) patients had valvular involvement. In patients with low disease activity, 1(4.5%) patient had valvular involvement. Association of valvular involvement with disease activity was not statistically significant ($p=0.2259910195$). In PATIENTS WITH active disease, 4(7.4%) patients had RWMA. In patients with low disease activity, 2(9.1%) patients had RWMA. Association of RWMA with disease activity was not statistically significant ($p=0.8241972743$). The mean SLEDAI-2K SCORE (mean $\pm$ s.d.) of patients was 8.6447 ± 6.6907 . The mean duration of DS (mean $\pm$ s.d.) of patients was 18.5132 ± 24.0330 months. Among the patients who had no cardiac involvement 11(37.9%) patients had first presentation. Among the patients who had any cardiac involvement, 18(38.3%) patients had first presentation. Association of first presentation of disease with cardiac involvement was not statistically significant ($p=0.9744$). Multiple cardiac involvements were found in 28 patients out of total 47 patients with cardiac involvement (59.6%). Multiple cardiac involvement was found in 23 patients with active SLE (82.1%) and 5 patients (17.9%) with low disease activity.

DISCUSSION

In patients with active disease, 29(53.7%) patients had first presentation. 25(46.3%) patients had first presentation but disease activity was low. Association of first presentation with disease activity was statistically significant ($p=0.0000406378$). The possible explanation of this may be due to the overt manifestations of SLE of multiple organs when the patients were admitted or came to OPD first time.

Total out of 76 patients 47(61.8%) patients had cardiac involvement in any form. This finding is similar to many other studies in literature like by D'Cruz D, et al.³ according to this study prevalence of cardiac involvement in SLE is estimated to be more than 50%. Also finding of our study almost similar to a transversal, descriptive study of SLE patients in the Internal Medicine department at the Military Hospital of Tunis between January 2016 and June 2018. Where out of total 80 patients of SLE Forty two patients (52.5%) had cardiac involvement. In a controlled, prospective study by Doherty NE III, et al. in which echocardiography was used, pericardial involvement (pericardial effusion or thickening) was detected in 37% of patients with SLE. Similar to our finding of pericardial involvement in out of total SLE patients (35.5%)⁶

In an analytic cross-sectional study conducted in IRAN, 50 patients with SLE underwent transthoracic 2D, color Doppler, and tissue Doppler imaging echocardiography Left ventricular (LV) systolic dysfunction was diagnosed in 9 (18%) patients and LV diastolic dysfunction was seen in 8 (16%) patients.

In a study "Echocardiography abnormalities in a cohort of Chinese patients with systemic lupus erythematosus--a retrospective analysis of eighty-five cases." By Yu XH1, Li YN.⁷ The left ventricle showed decreased compliance in 10.29%, impaired relaxation in 14.12% i.e almost 24% similar to finding in our study (22.4%).

An analytic type of cross sectional study, conducted in Dhaka, Bangladesh from July 2008 to June 2009. Showed out of total 50 SLE patients the prevalence of diastolic dysfunction to be 72%.⁸

In a study Left ventricular systolic function, evaluated by two-dimensional echocardiographic ejection fraction, was preserved in all patients (EF: 60 $\pm$ 5%). Left ventricular diastolic function, as expressed by echo-Doppler transmitral flow indices of left ventricular filling, was subclinically impaired in 23 patients of 75 patients (30.6%) almost similar to prevalence of diastolic dysfunction in our study.

Different Studies in literature by Galve E, et al⁹ found prevalence of valvular dysfunction to be 3-18% almost similar to our study finding.

However, Study by Omdal R, Lunde P, Rasmussen K et al. By Transesophageal and trans thoracic echocardiography and Doppler-examination in systemic lupus erythematosus showed valvular lesions

in 40–50% of cases with the transthoracic echocardiography (TTE) and in 50–60% with transesophageal echocardiography (TEE). This seems to be more than what we have found in our study.¹⁰

Similar result was found by a study done to determine the incidence and spectrum of morphologic and functional cardiac abnormalities in systemic lupus erythematosus (SLE) and to relate these findings to the disease activity and duration, with a clinical cardiovascular examination and M-mode, 2-D Doppler echocardiogram. No association was found between activity, duration of the disease and prevalence of cardiac abnormalities.

Association of pericardial involvement with disease activity by SLEDAI-2K score was statistically significant ($p=0.02255$). This is similar to a study by Nurhay Abdurahman, et al¹¹, where Of the 36 patients with SLE, 17 patients were found with active SLE and 19 with inactive SLE. This study showed that the PE was more frequently found in active SLE ($P < 0.01$) and constituted independent risk factors.

Association of PAH with disease activity was not statistically significant ($p=0.8632686559$). This is similar to a study by Johnson SR, et al.¹² conducted in Canada, which showed disease activity, organ involvement were not associated with PAH.

Association of diastolic dysfunction with SLE disease activity was not statistically significant ($p=0.7982884773$) which was similar to Analysis by Wislowska M¹³. This revealed no statistically significant correlation between SLEDAI values and LV diastolic function parameters.

SUMMARY AND CONCLUSION

Cardiac involvement is frequently seen in systemic lupus erythematosus patients, 61.8% in our study. Pericardium, myocardium, endocardium all can be involved in SLE. Pericardium is most commonly involved. Pulmonary hypertension, valvular abnormality, diastolic dysfunction, systolic dysfunction all are found in SLE. Echocardiography is a non-invasive excellent tool to evaluate the SLE patients for any cardiac involvement and serial screening of the patients. All cardiac manifestations are observed in active SLE patients in higher frequency but only pericardial involvement with disease activity is statistically significant.

Table: Distribution of Cardiac Inv, PAH, Pericardial Effusion, Diastolic Dysfunction, Systolic Dysfunction, Valvular Involvement, Regional Wall Motion Abnormality and Sledai Group

		Frequency	Percent
Cardiac Inv	No	29	38.2%
	Yes	47	61.8%
	Total	76	100.0%
PAH	No	58	76.3%
	Yes	18	23.7%
	Total	76	100.0%
Pericardial Effusion	No	49	64.5%
	Yes	27	35.5%
	Total	76	100.0%
Diastolic Dysfunction	No	59	77.6%
	Yes	17	22.4%
	Total	76	100.0%
Systolic Dysfunction	No	73	96.1%
	Yes	3	3.9%
	Total	76	100.0%
Valvular Involvement	No	65	85.5%
	Yes	11	14.5%
	Total	76	100.0%
Regional Wall Motion Abnormality	No	70	92.1%
	Yes	6	7.9%
	Total	76	100.0%
Sledai Group	Active	54	71.1%
	Inactive	22	28.9%
	Total	76	100.0%

REFERENCES

1. Barutcu A, Aksu F, Ozcelik F, Barutcu CA, Umit GE, Pamuk ON, et al. Evaluation of early cardiac dysfunction in patients with systemic lupus erythematosus with or without antinuclear antibodies. *Lupus* 2015;24(10):1019-28.

2. Schoenfeld SR, Kasturi S, Costenbader KH. The epidemiology of atherosclerotic cardiovascular disease among patients with SLE: a systematic review. *Semin Arthritis Rheum* 2013;43(1):77-95
3. Qureshi MA, Jamshaid TD, Siddiqui AM. Stroke - A study of clinical patterns and risk factors. *Ann King Edward Med Coll Jun* 2003;9:98-
4. Citrulline dependence of anti-cyclic citrullinated peptide antibodies in systemic lupus erythematosus as a marker of deforming/erosive arthritis. Kakumanu P, Sobel ES, Narain S, Li Y, Akaogi J, Yamasaki Y, Segal MS, Hahn PC, Chan EK, Reeves WH, Satoh M, J Rheumatol. 2009 Dec; 36(12):2682-90.
5. 1 D'Cruz D, Khamashta M, Hughes GRV. Cardiovascular manifestation of systemic lupus erythematosus. In Wallace DJ and Hahn BH, eds. *Dubois' lupus erythematosus*, Philadelphia: Lippincott Williams & Wilkins, 2001: 645.
6. Doherty NE III, Feldman G, Maurer G, Siegel RJ. Echocardiographic findings in systemic lupus erythematosus. *Am J Cardiol* 1988; 61:1144.
7. Yu XH, Li YN. Spectrum of cardiac involvement in systemic lupus erythematosus: echocardiograph, echo-Doppler observations and immunological investigation. (PMID:8506742)
8. Shazzad MN, Islam MN, Ara R, Ahmed CM, Fatema N, Azad AK, Salimulla SM, Haider MS, Haq SA. Echocardiographic assessment of cardiac involvement in systemic lupus erythematosus patients. *Mymensingh medical journal: MMJ*. 2013 Oct 1;22(4):736-41.
9. Galve E, Candell-Riera J, Pigrau C, et al. Prevalence, morphologic types and evolution of cardiac valvular disease in systemic lupus erythematosus. *N Engl J Med*. 1988;319:817-823
10. Omdal R, Lunde P, Rasmussen K et al. Transesophageal and trans thoracic echocardiography and Doppler-examination in systemic lupus erythematosus. *Scand J Rheumatol* 2001; 30: 275-281
11. Abdurahman N, Alwi I, Hakim L, Ismail D, Soelistijo H. Association of disease activity and pericardial effusion on systemic lupus erythematosus patients. *Medical Journal of Indonesia*. 1998 Apr 1;7(2):89-93.
12. Johnson SR, Gladman DD, Urowitz MB, Ibanez D, Granton JT. Pulmonary hypertension in systemic lupus. *Lupus*. 2004 Jul;13(7):506-9.
13. Wislowska M, Dereń D, Kochmański M, Sypuła S, Rozbicka J. Systolic and diastolic heart function in SLE patients. *Rheumatology international*. 2009 Oct 1;29(12):1469-76.