ORIGINAL ARTICLE

# RELATIONSHIP OF CARDIAC INVOLVEMENT WITH DISEASE SEVERITY IN PATIENTS OF SYSTEMIC SCLEROSIS

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**Objectives:** Systemic Sclerosis (SSc) is an autoimmune condition with underlying pathology in the connective tissue and can affect almost any organ system mainly skin, joints, lungs, heart and the abdomen. It usually follows a chronic course of disease. The objective of this study was to determine the relationship of cardiac involvement with the severity of disease course in patients with systemic sclerosis.

**Methodology:** Two hundred patients with a diagnosis of Systemic Sclerosis (SSc) were evaluated for cardiac involvement via history, examination, electrocardiogram and echocardiography. Cardiac involvement was compared across genders, age, duration of disease, and relationship with American College of Rheumatology (ACR) scores.

**Results:** Cardiac abnormalities were detected in 16% of these patients. Mean age of the study population was 38.67 ± 12.73 years including 55.5% males and 44.5% females. The mean ACR score of the study population was 12.8 ± 3. A significant relationship was observed between the degree of cardiac involvement and ACR scores (p=0.001) while that between cardiac abnormality and other confounding factors was non-significant i.e., gender (p=0.630), age groups (p=0.287) and duration since diagnosis (p=0.801).

**Conclusion:** There is a potential association of cardiac dysfunction with how severe the systemic sclerosis is, without a noteworthy impact of age, gender and disease duration.

**Keywords**: cardiac involvement, systemic sclerosis, ACR score

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## INTRODUCTION

Scleroderma originates from the Greek word "scleros", that means hard, thick skin.[1] It manifests itself in various forms ranging from a limited form where only skin[2] and subcutaneous tissues are involved to being a more widespread systemic illness and with such an illness is labelled systemic sclerosis (SSc).[3] Further subdivision of SSc is done based on the extent of skin involvement that could either be Diffuse Cutaneous (dcSSc) and Limited Cutaneous SSc (lcSSc). The limited cutaneous type of SSc is seen more commonly with the CREST syndrome.[4]

As a multisystem connective tissue disorder,[5] SSc may present in various forms,[6] with prominent defects seen in circulation (as Raynaud's phenomenon), effect on the musculoskeletal system or a more serious involvement of the renal, pulmonary,[7] cardiac and gastrointestinal systems causing both widespread fibrotic as well as complications in the vasculature.[8]

On study of populations, scleroderma is prevalent in about 4 to 489 cases per million[9] with true prevalence lying at the higher end of this range mentioned, while the number of new cases each year are about 0.6 to 122/ million persons. The geographical distribution in prevalence varies with higher rates seen in the United States and Australia when compared to Japan or Europe. It is also seen more frequently in Afro-American group.[9]

Cardiovascular disease is a well-known complication in all connective tissue diseases and likely so, involvement of this system in Systemic Sclerosis is also multifold[10] ranging from valvular dysfunction, most commonly Mitral Regurgitation to disturbances in the conduction pathway or simply derangement of the Left Ventricular Function.[11]

When the disease process is more widespread as in Diffuse Systemic Sclerosis, chances of heart failure and pericardial involvement were more commonly noted.[11]

Systemic sclerosis causes myocardial damage by causing repeated focal ischemic injury leading to myocardial fibrosis.[12]

Once cardiac damage is evident, it leads to poor outcome of the disease and so it's perhaps important to identify or be able to predict which patients are likely to develop cardiac disease as part of the multisystem disorder that is Systemic Sclerosis.

It was also observed that often patients had no apparent cardiac symptoms and when worked up revealed to have a high rate of cardiac abnormalities.

While there are studies conducted locally to establish the spectrum of Systemic Sclerosis in our population, less literature is available here to study the impact of this rheumatological disorder on the cardiovascular system.[13]

This study was done to assess the presence of a higher ACR score with the possibility of underlying occult cardiac involvement and so to be able to stratify patients who probably need a more rigorous cardiological work up when presenting to the outdoors.

## METHODOLOGY

This descriptive study was conducted at Jinnah Hospital, Lahore from 11-03-2020 to 31-12-2020. The sample size with a margin of error of 5% was calculated as 200, keeping a confidence interval of 95%, considering the frequency of cardiac involvement in patients of systemic sclerosis to be 15%[14]. The study was conducted after being approved by the Institutional ethical review board. The patient management was done according to the standard protocols defined by the hospital. An informed consent was signed by the participants.

Consecutive patients of both genders, aged between 15-65 years diagnosed with SSc for at least 6 months based on the clinical and immune criteria were enrolled in the study. Patients with other autoimmune conditions and with rheumatic heart disease, ischemic heart disease or other cardiac illnesses diagnosed before the appearance of SSc clinical features were excluded.

A specifically designed proforma was used to identify the features of SSc and a formal cardiac assessment was done by clinical evaluation, electrocardiography and trans-thoracic echocardiography. Cardiac involvement was labelled if any of the electrocardiographic or echocardiographic evidence were detected as outlines in Figure 1. ACR scores were calculated for all patients.

The collected data was analysed with the SPSS (Statistical Package for Social Sciences) version 20.0. The presence of cardiac involvement was compared among genders, and groups according to age, duration of disease and ACR scores were calculated. Pearson's chi-square test was used as the statistical tool to check the associations considering significance at a p-value of ≤ 0.05.

**Electrocardiographic features:**

- PR interval > 200 msec
- Right Bundle Branch Block (Qrs > 120msec and "RSR" pattern in V1)
- Left Bundle Branch Block (Qrs > 120 msec and "M" pattern in V6)

**Echocardiographic features:**

- Pulmonary Hypertension ( Mean pulmonary artery pressure > 40mmHG assessed via doppler imaging)
- Valvular involvement including Aortic / Mitral and Tricuspid Regurgitation
- Left Ventricular systolic dysfunction. EF < 50%
- Diastolic dysfunction of at least grade II.
- Pericardial involvement

**Figure 1: Electrocardiographic and echocardiographic features of cardiac involvement in SSc.[15]**

## RESULTS

Mean age of the study population was 38.67 ± 12.73 years including 55.5% males and 44.5% females. The mean ACR Score was 12.8 ± 3.0 (range: 9 to 28). Cardiac involvement was seen in 32 (16.0%) patients (figure 1). There was significant positive relationship between cardiac involvement and ACR scores (p = 0.001). No significant association was found between cardiac involvement and gender (p = 0.630), age groups (p = 0.287) and disease duration (p = 0.801) (Table 1).

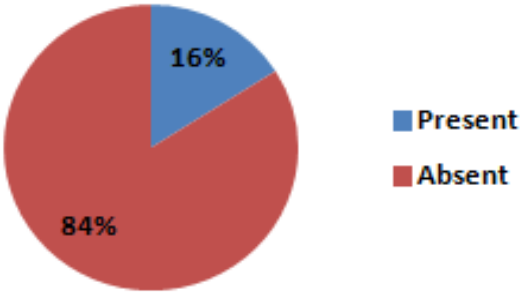


**Figure 2: Overall frequency of cardiac involvement in patients with systemic sclerosis**

**Table 1: Cardiac involvement in patients with scleroderma and association with ACR score**

| | Total (N) | Cardiac Involvement | | p-values |
|---|---|---|---|---|
| | | Detected | Not detected | |
| **Gender** | | | | |
| Males | 89 | 13 (14.6%) | 76 (85.4%) | 0.63 |
| Females | 111 | 19 (17.1%) | 92 (82.9%) | |
| **Age** | | | | |
| < 40 years | 117 | 16 (13.7%) | 101 (86.3%) | 0.287 |
| ≥ 40 years | 83 | 16 (19.3%) | 67 (80.7%) | |
| **Duration since diagnosis of systemic sclerosis** | | | | |
| < 9 months | 79 | 12 (15.2%) | 67 (84.8%) | 0.801 |
| ≥ 9 months | 121 | 20 (16.5%) | 101 (83.5%) | |
| **American College of Rheumatology (ACR) scores** | | | | |
| < 15 | 168 | 0 (0%) | 168 (100%) | 0.001 |
| ≥ 15 | 32 | 168 (100%) | 0 (0%) | |

SSc = Systemic sclerosis, ACR = American College of Rheumatology

## DISCUSSION

Systemic sclerosis is an autoimmune connective tissue disorder[16] that can cause many severe complications of major organ systems[17,18] including cardiac diastolic dysfunction (16%) that is associated with mortality exceeding that of Pulmonary Hypertension.[18,19] Diastolic dysfunction is considered a precursor for Heart failure (HFpEF).[19] Other cardiovascular manifestations include increased Pulmonary artery pressure (pulmonary hypertension)[20] assessed by right heart catheterization (15%), a reduced forced vital capacity - <70% of the predicted value (15%), FVC less than 80% predicted (17%). Pulmonary arterial hypertension (PAH) poses an independent risk factor for mortality in those with systemic sclerosis (SSc).[21] Muscle inflammation; myositis (13%), joint inflammation (12%), Overlap with Sjogren (13%) and digital ulcers (15%) with complications of ulcers and hospitalizations (13%).

Renal crisis due to scleroderma was not a common occurrence and was seen in almost 12% of the cases.[22] The prevalence of rhythm and conduction disturbances in SSc has been estimated to be 60.9% according to the data previously available and these patients were relatively older and had a higher prevalence of pulmonary arterial hypertension, valvular disease and chamber enlargement.[23]

In another study it was revealed that cardiac involvement in systemic sclerosis patients is variable and difficult to determine because of the diversity of manifestations. However, when clinically manifested cardiac involvement is considered to be an important prognostic factor. Microvascular involvement seems to be a constant occurrence because of structural changes and vasospasm while there are contradictory opinions about acceleration of the atherosclerosis process. Considering all these factors screening for subclinical cardiac involvement via modern diagnostic tools does provide an interesting opportunity to make an early diagnosis and initiate prompt treatment.

Our study aims to determine if the severity of systemic sclerosis has an impact on the cardiovascular system so that patients with a higher ACR score can be investigated more rigorously and perhaps earlier. The limitations of the study are that it is a cross sectional single centre study, and perhaps a bigger sample size or a multi-centre study may achieve a better association between the aforementioned and future work might be needed to be done in this direction.

## CONCLUSION

Cardiac involvement in patients of SSc is potentially linked with the severity of SSc without significant impacts of age, gender and disease duration. The take home message from our study is that attempts should be made to stratify patients with diagnosed systemic sclerosis into having a mild or severe disease course both clinically as well as objectively using ACR scores. Patients with suspected extensive systemic involvement must be subjected to non- invasive diagnostic options including ECG, Echocardiography to determine the cardiac dysfunction. Out-patient department follow ups must include some emphasis on trying to determine the involvement of organ systems that have an impact on the prognosis.

## AUTHORS' CONTRIBUTION:

ND: Concept and design, data acquisition, interpretation, drafting, final approval, and agree to be accountable for all aspects of the work. WQ, MI: Data acquisition, interpretation, drafting, final approval and agree to be accountable for all aspects of the work.

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## REFERENCES


1. Khanna D, Distler JH, Sandner P, Distler O. Emerging strategies for treatment of systemic sclerosis. J Scleroderma Relat Disord. 2016;1(2):186-93.
2. Dyavannanavar V, Malkud S. Cutaneous manifestations of systemic sclerosis. J Pakistan Assoc Dermatologist. 2020;30(4):558-62.
3. Denton CP, Hughes M, Gak N, Vila J, Buch MH, Chakravarty K, et al. BSR and BHPR guideline for the treatment of systemic sclerosis. Rheumatology. 2016;55(10):1906-10.
4. Asano Y. Systemic sclerosis. J Dermatol. 2018;45(2):128-38.
5. Hussain MA, Rahim MR, Alam MN, Haque MR. Association of plasma D-dimer concentration with systemic sclerosis. J Pakistan Assoc Dermatologists. 2018;28(3):301-5.

6. Cutolo M, Soldano S, Smith V. Pathophysiology of systemic sclerosis: current understanding and new insights. Expert Rev Clin Immunol. 2019;15(7):753-64.
7. Bergamasco A, Hartmann N, Wallace L, Verpillat P. Epidemiology of systemic sclerosis and systemic sclerosis-associated interstitial lung disease. Clin Epidemiol. 2019;11:257.
8. Denton CP, Khanna D. Systemic sclerosis. Lancet. 2017;390(10103):1685-99.
9. Chifflot H, Fautrel B, Sordet C, Chatelus E, Sibilia J. Incidence and prevalence of systemic sclerosis: a systematic literature review. Semin Arthritis Rheum. 2008;37:223.
10. Plastiras SC, Toumanidis ST. Systemic sclerosis: the heart of the matter. Hellenic J Cardiol. 2012;53(4):287-300.
11. Fernández-Codina A, Simeón-Aznar CP, Pinal-Fernandez I, Rodríguez-Palomares J, Pizzi MN, Hidalgo CE, et al. Cardiac involvement in systemic sclerosis: differences between clinical subsets and influence on survival. Rheumatol Int. 2017;37(1):75-84.
12. Distler JH, Feghali-Bostwick C, Soare A, Asano Y, Distler O, Abraham DJ. Frontiers of antifibrotic therapy in systemic sclerosis. Arthritis Rheumatol. 2017;69(2):257-67.
13. Khaliq T, Aziz W, Farooqi A. Spectrum of systemic sclerosis in patients presenting to a tertiary care hospital in Pakistan. Pak Armed Forces Med J. 2014;64(4):591-5.
14. Morelli S, Sgreccia A, Ferrante L, Barbieri C, Bernardo ML, Perrone C, et al. Relationships between electrocardiographic and echocardiographic findings in systemic sclerosis (scleroderma). Int J Cardiol. 1996;57(2):151-60.
15. Bruni C, Ross L. Cardiac involvement in systemic sclerosis: Getting to the heart of the matter. Best Pract Res Clin Rheumatol. 2021;35(3):101668.
16. Asif S, Haroon M, Khan A, Faiq M. AB0093 Clinical And Serological Characteristics Of Systemic Sclerosis: Experience From A Tertiary Care Center In Pakistan. Ann Rheum Dis. 2021;80(Suppl 1):1075-1076
17. Murdaca G, Contatore M, Gulli R, Mandich P, Puppo F. Genetic factors and systemic sclerosis. Autoimmun Rev. 2016;15(5):427-32.
18. Kowal-Bielecka O, Fransen J, Avouac J, Becker M, Kulak A, Allanore Y, et al. Update of EULAR recommendations for the treatment of systemic sclerosis. Ann Rheum Dis. 2017;76(8):1327-39.
19. Denton CP. Advances in pathogenesis and treatment of systemic sclerosis. J Clin Med. 2016;16(1):55.
20. Tennøe AH, Murbræch K, Andreassen JC, Fretheim H, Garen T, Gude E, et al. Left ventricular diastolic dysfunction predicts mortality in patients with systemic sclerosis. J Am Coll Cardiol. 2018;72(15):1804-13.
21. Desbois AC, Cacoub P. Systemic sclerosis: an update in 2016. Autoimmun Rev. 2016;15(5):417-26.
22. Tyndall AJ, Bannert B, Vonk M, Airò P, Cozzi F, Carreira PE, et al. Causes and risk factors for death in systemic sclerosis: a study from the EULAR Scleroderma Trials and Research (EUSTAR) database. Ann rheum dis. 2010;69(10):1809-15
23. Medsger TA, Masi AT, Rodnan GP, Benedek TG, Robinson H. Survival with Systemic Sclerosis (Scleroderma) A Life-Table Analysis of Clinical and Demographic Factors in 309 Patients. Ann Intern Med. 1971;75(3):369-76.


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