

Research Article

Assessment of Pulmonary Artery Hypertension in Patients with Limited and Diffuse Systemic Sclerosis

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Abstract

Objective: To assess the pulmonary artery hypertension in patients with limited and diffuse Systemic Sclerosis upon presentation.

Material and methods: This cross sectional study was conducted at Department of Rheumatology & Immunology, Shaikh Zayed Hospital, Lahore from 05-02-2108 to 04-10-2018. Total 61 patients with systemic sclerosis having age between 18-56 years either male or female and with duration of systemic sclerosis 1-20 years were selected. Pulmonary hypertension was assessed in selected patients.

Results: Mean age of the patients was 32.49 ± 8.88 years and mean duration of systemic sclerosis was 4.00 ± 3.92 years. Out of 61 patients of systemic sclerosis, pulmonary hypertension was observed in 18 (30%) patients. Pulmonary hypertension was found in 11 (31.43%) patients of limited systemic sclerosis and in 7 (26.92%) patients of diffused systemic sclerosis. Pulmonary hypertension was found in 5 (83.33%) male patients and in 13 (23.64%) female patients. Pulmonary hypertension was significantly ($P = 0.0070$) associated with gender.

Conclusion: Results of present study showed a higher percentage of PAH. Development of PAH is not significantly associated with type of SSC. No association of PAH with age and duration of disease was found. Most of female patients were victim of SSC as compared to male patients, but male patients were found with significantly higher rate of PAH.

Key words: Pulmonary artery hypertension, Systemic Sclerosis, Right heart catheterization, Connective tissue

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Introduction

Systemic Sclerosis (SSc) is an autoimmune disease which consists of mainly three disease

manifestations all proved by the American College of Rheumatology (ACR) classification of 2013.¹ Fibrosis of skin and internal organs, production of certain

auto antibodies and vasculopathy.¹ Systemic Sclerosis is classified into limited and diffuse scleroderma. Diffuse Systemic Sclerosis involves the face, limbs and trunk and more severe in disease progression and limited Systemic Sclerosis only confined to face and limbs and relatively not as severe in its organ involvement.²

Pulmonary Arterial Hypertension (PAH) is defined as sustained mean arterial pressure to be greater than 25mmHg at rest and more than 30mmHg during exercise.³ Pulmonary Arterial Hypertension in systemic sclerosis occurs mainly due to vasculopathy and interstitial lung disease.⁴ In literature, reported prevalence of Pulmonary Hypertension is upto 26% in cases of SSc.⁵ In cases of Systemic Sclerosis, Pulmonary Arterial Hypertension is a major cause of mortality and morbidity, if left untreated 1 year survival is 50%.⁶ Pulmonary Hypertension in early stage of the disease is usually asymptomatic and therefore remains undiagnosed. Due to the debilitating effects of pulmonary hypertension on the outcome of disease, its early detection should be the practice by Rheumatologists.⁴ Pulmonary Arterial Hypertension prevalence in limited Systemic Sclerosis is more as compared to Diffuse Systemic Sclerosis where it is usually secondary to fibrosis of the lung interstitium or cardiac involvement.⁷

Right heart catheterization, although, is helpful in differentiating between pre capillary and post capillary pulmonary hypertension as well as predicting the reversibility of it, however, it is an invasive, expensive and not easily reproducible technique but still taken as gold standard for diagnosing pulmonary hypertension.⁸ But the echocardiography has now been proved to be reliable noninvasive and inexpensive source to diagnose Pulmonary Hypertension. Doppler Echocardiography covers all these aspects and therefore becomes an effective screening tool method.⁹

Reported sensitivity and specificity of Doppler echocardiography is 87% and 79% with 91% and 70% positive and negative predictive values respectively.⁹ These values are comparable to the Right heart catheterization. Echocardiography is useful in finding out mean arterial pressure through calculations involving its findings during the procedure which include Tricuspid regurgitation velocity, septal

movement, Inferior Vena cava diameter, Right atrial pressure and ventricular dilatation. Many aids also help affirm the absence or presence of Pulmonary Arterial Hypertension which include clinical examination, Pulmonary Function Tests, ECGs and High Resolution Computed Tomography scans chest.¹⁰⁻¹¹

Literature review shows abundance of the data on this topic however almost all research work has been done in other countries. The prevalence of pulmonary hypertension in systemic sclerosis has been evaluated time to time which shows different figures and it's been observed that it's prevalence in this particular disease has decreased over time. The rationale of this study is that available data regarding frequency of Pulmonary Arterial Hypertension in Systemic Sclerosis is variant and it is also varied in different population in addition to this there is dearth of the data in Pakistan. To fill the gap we have planned to conduct this study on Pakistani population. Therefore this study will not only create local data but also draw the attention of the treating physicians dealing with Systemic Sclerosis to diagnose this lethal complication of the disease earlier. Furthermore, some practical recommendations could be made for early targeted and more intensive therapy to decrease the risk of future cardiovascular disease events.

Operational Definition

Systemic Sclerosis those patients who fulfill the American College of Rheumatology ACR 2013 classification CRITERIA of Systemic Sclerosis.

- Limited Systemic Sclerosis: disease limited to limbs and face.
- Diffuse Systemic Sclerosis: disease involving limbs, face and trunk.

Pulmonary Arterial Hypertension sustained mean arterial pressure to be greater than 25mmHg at rest and more than 30mmHg during exercise.

Methods

This cross sectional study was conducted at Department of Rheumatology & Immunology, Shaikh Zayed Hospital, Lahore from 05-02-2018 to 04-10-2018. Total 61 patients with systemic sclerosis having age between 18-56 years either male or female and with duration of systemic sclerosis 1-20 years were

selected by using non-probability consecutive sampling technique.

Patients with Mixed Connective Tissue Disease (MCTD) or Overlap Syndrome, patients with known lung or heart pathology due to other reason like COPD, Valvar heart disease were excluded from the study.

Study was approved by ethical committee of the institution and written informed consent was taken from every patient.

All the selected patients were taken to cardiology department for echocardiography to assess the Pulmonary Hypertension. Trans Thoracic Echocardiography was performed by a senior cardiologist of SZH Lahore to measure the mean pulmonary arterial pressure at rest. Findings were entered in pre-designed proforma in term of pulmonary hypertension (Yes/No). Demographic profile of all the patients was also entered on proforma.

All the collected data was entered in SPSS version 18 and analyzed. Mean and SD of age and duration of systemic sclerosis was calculated. Frequencies and percentages were calculated for categorical data like pulmonary hypertension, type of systemic sclerosis and gender. Stratification of data in relation to age, duration of systemic sclerosis, type of systemic sclerosis and gender was done. Post stratification chi-square test was applied to see the effect of these on outcome variable i.e. pulmonary hypertension. P value ≤ 0.05 was considered as statistically significant.

Results

In present total 61 patients with systemic sclerosis were selected. Mean age of the patients was 32.49 ± 8.88 years and mean duration of systemic sclerosis was 4.00 ± 3.92 years.

Out of 61 patients of systemic sclerosis, pulmonary hypertension was observed in 18 (30%) patients. (Fig. 1)

Distribution of patients was done according to type of systemic sclerosis. Total 35 (57.38%) patients were found with limited systemic sclerosis and 26 (42.62%) were found with diffuse systemic sclerosis.

Pulmonary hypertension was found in 11 (31.43%) patients of limited systemic sclerosis and in 7 (26.92%) patients of diffused systemic sclerosis. After applying chi-square test, statistically insignificant ($P = 0.7814$) association of pulmonary hypertension with type of systemic sclerosis was observed. (Table 1)

Patients were divided into two equal age groups i.e. age group 18-38 years and age group 39-56 years. Total 47 (77.05%) patients belonged to age group 18-38 years and 14 (22.95%) patients belonged to age group 39-56 years. Pulmonary hypertension was noticed in 13 (27.66%) patients and 5 (35.71%) patients respectively in age groups 18-38 years and 39-56 years. Chi-square test showed insignificant association between pulmonary hypertension and age groups with p value 0.7394. (Table 2)

Out of 6 (9.84%) male patients, pulmonary hypertension was found in 5 (83.33%) patients. Female patients were 55 (90.16%) and pulmonary hypertension was seen in 13 (23.64%) female patients. Pulmonary hypertension was significantly ($P = 0.0070$) associated with gender after applying chi-square test. (Table 3)

Duration of systemic sclerosis was from 1-20 years. Two groups were made according to duration of systemic sclerosis i.e. 1-10 year duration group and 11-20 years duration group. Out of 58 (95.08%) patients of 1-10 years group, pulmonary hypertension was seen in 16 (27.59%) patients. Total 3 (4.92%) patients belonged to 11-20 years duration group and pulmonary hypertension was found in 2 (66.67%) patients. Chi-square test was applied and insignificant association of pulmonary hypertension with duration of systemic sclerosis was noted with p value 0.2055. (Table 4)

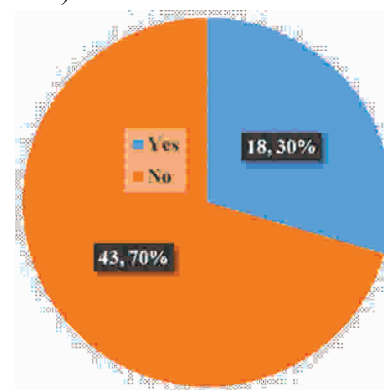


Fig. 1: Frequency of PH in Cases of Systemic

Table 1: Association of Pulmonary Hypertension with Type of Systemic Sclerosis

| Type of systemic sclerosis | Pulmonary Hypertension | | Total | P value |
|----------------------------|------------------------|------------|------------|---------|
| | Yes (%) | No (%) | | |
| Limited | 11 (31.43) | 24 (68.57) | 35 (57.38) | 0.7814 |
| Diffused | 7 (26.92) | 19 (73.08) | 26 (42.62) | |
| Total | 18 | 43 | 61 | |

Table 2: Association of Pulmonary Hypertension with Age

| Age Group | Pulmonary Hypertension | | Total | P value |
|--------------|------------------------|------------|------------|---------|
| | Yes (%) | No (%) | | |
| 18-38 | 13 (27.66) | 34 (72.34) | 47 (77.05) | 0.7394 |
| 39-56 | 5 (35.71) | 9 (64.29) | 14 (22.95) | |
| Total | 18 | 43 | 61 | |

Table 3: Association of Pulmonary Hypertension with Gender

| Gender | Pulmonary Hypertension | | Total | P value |
|--------------|------------------------|------------|------------|---------|
| | Yes (%) | No (%) | | |
| Male | 5 (83.33) | 1 (16.67) | 6 (9.84) | 0.007 |
| Female | 13 (23.64) | 42 (76.36) | 55 (90.16) | |
| Total | 18 | 43 | 61 | |

Table 4: Association of Pulmonary Hypertension with Duration of Systemic Sclerosis

| Duration of systemic sclerosis | Pulmonary Hypertension | | Total | P value |
|--------------------------------|------------------------|------------|------------|---------|
| | Yes (%) | No (%) | | |
| 1-10 | 16 (27.59) | 42 (72.41) | 58 (95.08) | 0.2055 |
| 11-20 | 2 (66.67) | 1 (33.33) | 3 (4.92) | |
| Total | 18 | 43 | 61 | |

Sclerosis

Discussion

Development of Systemic Sclerosis is a result of dysfunction in immune system, fibroblasts and endothelium which causes fibrosis of skin and internal organs.¹² Etiology of this disorder is still unknown, it is thought that environmental and genetic factors are responsible for this disorder.

Different organ systems like gastrointestinal, renal, cardiac and pulmonary can be affected by this disorder. Prevalence of pulmonary involvement in Systemic Sclerosis significantly varies and frequently occurs in both limited and diffuse Systemic Sclerosis.¹³ Reported prevalence of pulmonary artery hypertension ranges from 30-60% diagnosed by echocardiography or right heart catheterization.¹⁴⁻¹⁷

The purpose of the present study was to determine the frequency of pulmonary artery hypertension in Systemic Sclerosis cases.

Mean age of the patients of systemic sclerosis was 32.49 ± 8.88 years and mean duration of systemic sclerosis was 4.00 ± 3.92 years. Out of 61 patients of systemic sclerosis, pulmonary hypertension was observed in 18 (30%) patients.

In one study by Niklas et al,¹⁵ mean age of patients of systemic sclerosis was 56.6 ± 13.1 years which is higher than our study. Higher mean age of this study is due to age criteria of the patients. Niklas et al¹⁵ also found pulmonary artery hypertension in 11.6% patients out of 83 patients of systemic sclerosis (58 patients with diffuse SSc and 11 patients of limited SSc) which is much lower than our study.

In present study, total 35 (57.38%) patients were found with limited systemic sclerosis and 26 (42.62%) patients were diagnosed with diffuse systemic sclerosis. Pulmonary hypertension was found in 11 (31.43%) patients of limited systemic sclerosis and in 7 (26.92%) patients of diffused systemic sclerosis. Statistically insignificant ($P = 0.7814$) association of pulmonary hypertension with type of systemic sclerosis was noted.

In one study by Vandecasteele et al,¹⁶ out of 362 patients of systemic sclerosis, limited SSc was found in 23.2% patients, limited cutaneous SSc was noted in 59.9% patients, limited diffuse cutaneous SSc noted in 16.9% patients and prevalence of pulmonary artery hypertension was 2.5%. In another study by Coghlan et al,¹⁷ out of 466 systemic sclerosis patients, 19% patients were found with pulmonary artery hypertension.

Yoo et al¹⁸ reported prevalence of pulmonary artery hypertension as 21.6% in cases of systemic sclerosis. Pulmonary artery hypertension was diagnosed by echocardiography and confirmed on right heart catheterization. In one study by Visovatti et al,¹⁹ out of 244 patients of systemic sclerosis, PAH was found in 25% patients.

Conclusion

Results of present study showed a higher percentage of PAH. Development of PAH is not significantly

associated with type of SSC. No association of PAH with age and duration of disease was found. Most of female patients were victim of SSC as compared to male patients, but male patients were found with significantly higher rate of PAH.

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