# Clinical Manifestation and Laboratory Finding of Sclerosis Systemic Patient in Dr. Hasan Sadikin General Hospital Bandung : A Descriptive Quantitative Study

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**Abstract**

**Background:** Systemic sclerosis is a chronic progressive multisystem autoimmune disease in connective tissue, characterized by its heterogeneous clinical manifestation. The purpose of this study is to give information regarding clinical manifestations and laboratory findings of systemic sclerosis patients to establish diagnosis of disease.

**Method:** This study was conducted using descriptive quantitative design in September—October 2016. Data was collected from medical records of patients visiting Rheumatology Clinic Dr. Hasan Sadikin General Hospital from 1 July 2015—30 June 2016 using total sampling method. The collected data were expected to comprise patient's clinical manifestation and laboratory finding.

**Result:** Most of patients had cutaneous 57 (100.0%) and musculoskeletal 40 (70.2%) involvement. Some of the disease manifestations were Raynaud's phenomenon 38 (66.7%), fingertip lesion 33 (57.9%), stiffness in skin 34 (59.6%), and arthalgia 29 (50.9%). Gastrointestinal involvements were present in 29 (50.9%) patients. Renal involvement were determined from urinalysis result showed proteinuria 10 (17.5%) and hematuria 8 (14.0%), found in 24 (42.1%) patients, while pulmonary and cardiac involvements were found in 30 (52.6%) patients, acknowledged from clinical symptoms such as dyspnea 12 (21.1%). Identification of autoantibodies was found in 12 (21.1%) patients, with 10 (17.5%) patients had reactive ANA and 3 (3.5%) had positive anti-Scl70.

**Conclusion:** Most of systemic sclerosis patients had cutaneous involvement. Renal, pulmonary, and cardiac involvement were concluded based on laboratory findings.

**Keywords:** Systemic sclerosis, clinical manifestation, laboratory finding

## Introduction

Systemic sclerosis (SSc) is a chronic progressive multisystem autoimmune disease in connective tissue, characterized by its heterogeneous clinical manifestation. Pathophysiologic processes that occur on this disease are vascular abnormality, fibrosis due to collagen deposits and excessive extracellular matrix and autoimmunity.[1] Based on cutaneous involvement patterns, clinical manifestations and laboratory findings, systemic sclerosis is classified into 2 types: diffuse and limited systemic sclerosis. Cutaneous involvement in diffuse systemic sclerosis extend up to proximal knees and elbows, face and trunk. Raynaud's phenomenon usually follows cutaneous manifestations. Organ involvement such as musculoskeletal, kidneys, heart and lungs often appear. Signs of limited systemic sclerosis are known from the mnemonic CREST syndrome, consisting of calcinosis, Raynaud's phenomenon, esophageal dysmotility, sclerodactyly and telangiectasia.[2]

Ten years survival rate of systemic sclerosis patient has increased significantly from 53% in 1970s to 67% in 1990s.[3] However, this rate is lower than SLE patients, which is 93%.[4] A previous study stated that most frequent cause of death in systemic sclerosis patients is related to heart and lungs involvement.[5] Irreversible organ involvement following disease progression may further complicates the disease, hence the long-term prognosis of systemic sclerosis depends on organ involvement and disease manifestation.

Systemic sclerosis is the third most common patients in rheumatology clinic Dr. Hasan Sadikin General Hospital, after systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA).[6] Most of them often delayed referral, diagnosis, and management of systemic sclerosis from primary health care and district hospital take place. As a consequences, patients come to rheumatology clinic Dr. Hasan Sadikin General Hospital Bandung in severe condition with multiple organ involvement. Delayed referral corresponds with the low education profile of health care provider regarding clinical manifestation and laboratory findings of systemic sclerosis. As a result, a study about clinical manifestations and laboratory findings of systemic sclerosis patient is needed as an important information to help health care providers establish early diagnosis as a way to prevent irreversible organ involvement.

## Method

This study conducted during September–October 2016 at rheumatology clinic Dr. Hasan Sadikin General Hospital Bandung. Medical records of

patients was analyzed and presented descriptively using a retrospective method. Sample was selected using total sampling method. Subjects of this study were patients diagnosed with systemic sclerosis who were treated at rheumatology clinic Dr. Hasan Sadikin General Hospital Bandung during July 1, 2015 to June 20, 2016. After ethical clearance letter had been issued, clinical manifestations and results of supportive examination that the patient took were recorded from their medical records. Afterwards, data were grouped based on cutaneous, gastrointestinal, renal, cardiac and pulmonary involvement. The exclusion criteria of the study was patients who have not been completed data on their medical records and patients with overlap syndrome or mixed connective tissue disease (MCTD).

## Result

Total participants who fulfilled inclusion were 57 patients. Table 1 showed characteristic of systemic sclerosis patients in rheumatology clinic Dr. Hasan Sadikin General Hospital. The table showed that most of systemic sclerosis patients was female 56 (98.2%) with age range from 31−40 years 19 (33,3%).

**Table 1.** Characteristics of SSc patients at rheumatology clinic Dr. Hasan Sadikin Bandung General Hospital in July 2015−June 2016

| Characteristics | Frequency (n=57) | Percentage (%) |
|---|---|---|
| Sex | | |
| Female | 56 | 98.2% |
| Male | 1 | 1.8% |
| Age | | |
| <20 years | 1 | 1.8% |
| 20-30 years | 9 | 15.8% |
| 31-40 years | 19 | 33.3% |
| 41-50 years | 17 | 29.8% |
| 51-60 years | 5 | 8.8% |
| >60 years | 6 | 10.5% |

Table 2 showed the distribution of clinical manifestation in involved organ on patients with systemic sclerosis at rheumatology clinic Dr. Hasan Sadikin General Hospital Bandung. The table showed that all 57 subjects are patient with cutaneous involvement (100.0%). Raynaud's phenomenon was found in 38 (67.9%) patients.

**Table 2.** Distribution of clinical manifestations on organs involved in SSc patients at rheumatology clinic Dr. Hasan Sadikin General Hospital Bandung in July 2015−June 2016

| Clinical Manifestation | Frequency (n=57) | Percentage (%) |
|---|---|---|
| Skin | n = 57 | 100.0% |
| Raynaud's Phenomenon | 38 | 66.7% |
| Fingertip lesion | 33 | 57.9% |
| Telangiectasia | 9 | 15.8% |
| Calsinosis cutis | 21 | 36.8% |
| Sclerodactyly | 25 | 43.9% |
| Hardened skin | 25 | 43.9% |
| 0Skin stiffness | 34 | 59.6% |
| Painful skin | 26 | 45.6% |
| Itchy skin | 16 | 28.1% |
| Mask-face | 8 | 14.0% |
| Fish mouth | 22 | 38.6% |
| Salt and pepper appearance | 19 | 33.3% |
| Gastrointestinal | n = 29 | 50.9% |
| Nausea | 14 | 24.6% |
| Difficulty in swallowing | 13 | 22.8% |
| Epigastric pain | 6 | 10.5% |
| Diarrhea | 4 | 7.0% |
| Musculoskeletal | n = 40 | 70.2% |
| Swelling fingers | 14 | 24.6% |
| Arthalgia | 29 | 50.9% |
| Myalgia | 13 | 22.8% |
| Joint stiffness | 10 | 17.5% |
| Muscle contracture | 2 | 3.5% |
| Knee pain | 6 | 10.5% |
| Back pain | 4 | 7.0% |
| Renal | n=24 | 42.1% |
| Pulmonary and cardiac | n=30 | 52.6% |

Table 3 showed multiple of organ involvements in systemic sclerosis patient. Most patients (40.4%) had combination of skin, musculoskeletal, and gastrointestinal organ

**Table 3.** Distribution of multiple organ involvements in SSc patients at rheumatology clinic Dr. Hasan Sadikin General Hospital Bandung in July 2015−June 2016

| Multiple Organ Involvements | Frequency (n=57) | Percentage (%) |
|---|---|---|
| Skin only | 13 | 22.8% |
| Skin and musculoskeletal | 16 | 28.1% |
| Skin and gastrointestinal | 5 | 8.8% |
| Skin, musculoskeletal, and gastrointestinal | 23 | 40.4% |

Table 4 showed the distribution of constitutional symptoms which appeared on systemic sclerosis patients at rheumatology clinic Dr. Hasan Sadikin General Hospital. The table showed that the most frequent constitutional symptoms experienced by patients were easy fatigability 12 (21.1%) and weakness 11 (19.3%).

**Table 4.** Distribution of constitutional symptoms in SSc patients at rheumatology clinic Dr. Hasan Sadikin General Hospital Bandung in July 2015−June 2016

| Constitutional Symptom | Frequency (n=57) | Percentage (%) |
|---|---|---|
| Easily fatigue | 12 | 21.1% |
| Weakness | 11 | 19.3% |
| Hair fall | 6 | 10.5% |
| Epistaxis | 4 | 7.0% |
| Weight loss | 8 | 14.0% |

Renal, cardiac and pulmonary involvement in patients with systemic sclerosis can be assessed from clinical manifestations and/or supporting examination. Examinations which usually carried out were routine urinalysis, serum creatinine, plain chest x-ray, chest CT scan, spirometry and echocardiography. Table 5 showed the distribution of clinical manifestations and

laboratory findings of systemic sclerosis patients with renal, cardiac and pulmonary involvement at Dr. Hasan Sadikin General Hospital.

**Tabel 5**. Distribution of clinical manifestations and laboratory findings on renal, cardiac, and pulmonary involvement in SSc patients at rheumatology clinic Dr. Hasan Sadikin General Hospital Bandung in July 2015−June 2016

| Organ Involvement | Frequency (n=57) | Percentage (%) |
|---|---|---|
| Renal Involvement | n=24 | 42.1% |
| Clinical manifestation | | |
| Dysuria | 6 | 10,5% |
| Oligouria | 2 | 3,5% |
| Laboratory findings | | |
| Urinalysis | | |
| Proteinuria | 10 | 17,5% |
| Hematuria | 8 | 14,0% |
| Bakteriuria | 3 | 5,3% |
| Increased creatinine serum | 4 | 7,0% |
| Pulmonary and Cardiac Involvement | n=30 | 52,6% |
| Clinical manifestation | | |
| Dyspnea | 12 | 21,1% |
| Dyspnea with edema in lower | 2 | 3,5% |
| extremities | 7 | 12,3% |
| Dyspnea with cough | 5 | 8,8% |
| Cough | 2 | 3,5% |
| Palpitation | | |
| Laboratory findings | | |
| Plain chest x-ray | 2 | 3,5% |
| Cardiomegaly | 5 | 8,8% |
| Cardiomegaly without pulmonary | 2 | 3,5% |
| edema | 1 | 1,8% |
| Suspected ILD | | |
| Idiopathic pulmonary fibrosis | 3 | 5,3% |
| CT Scan | | |
| ILD appearance | 2 | 3,5% |
| Spirometry | 4 | 7,0% |
| Mild restrictive | | |
| Moderate restrictive | 2 | 3,5% |
| Echocardiography | 1 | 1,8% |
| Pulmonary hypertension | | |
| Diastolic dysfunction | | |

Table 6 showed the distribution of autoantibody test result on systemic sclerosis patients at Dr. Hasan Sadikin General Hospital Bandung. The tests included antinuclear antibody (ANA) and anti-Scl70.

**Table 6**. Distribution of autoantibody test in SSc patients at rheumatology clinic Dr. Hasan Sadikin General Hospital Bandung in July 2015−June 2016

| Autoantibody | Frequency (n=57) | Percentage (%) |
|---|---|---|
| Autoantibody test | n=12 | 21.1% |
| ANA | | |
| Reactive | 10 | 17.5% |
| Speckled pattern | 2 | 3.5% |
| Nuclear pattern | 3 | 5.3% |
| Homogenous type | 3 | 5.3% |
| Not-specified | 2 | 3.5% |
| Non-reactive | 2 | 3.5% |
| Anti-Scl70 | | |
| Positive | 3 | 5.3% |
| N/A | 45 | 78.9% |

## Discussion

It was obtained from this study that most patients with systemic sclerosis were female 56 (98.2%) with age range from 31-40 years 19 (33.3%). This result corresponded with previous study conducted by Pagalavan dan Ong in Malaysia, where most systemic sclerosis patients were 31−40 years old female.[7]

All systemic sclerosis patients showed cutaneous involvement as disease manifestation. This result suited to previous study which stated that even though clinical manifestations in systemic sclerosis were heterogeneous, most patients had cutaneous involvement.[8] Systemic sclerosis patients which showed clinical manifestation and positive laboratory findings on organs without any cutaneous involvement were called systemic sclerosis sine scleroderma (ssSSc). On a study conducted by Marangoni, et al., in Brazil, it was found that among 947 systemic sclerosis patients, there were only 79 (8.3%) patients with ssSSc.[9]

Based on Le Roy vascular hypothesis, dysfunctional blood vessel was an initial pathophysiologic process in systemic sclerosis marked by Raynaud's phenomenon.[10] The result of this study revealed that the most frequent clinical manifestation found on skin was Raynaud's phenomenon (66.7%). This result corresponded with a previous study conducted by Pagalavan and Ong in Malaysia, where 38 (83.6%) patients with systemic sclerosis experienced Raynaud's phenomenon.[7] Hanitsch in Germany published a higher rate; 1160 (96.7%) patients experienced Raynaud's phenomenon.[11]

This study revealed that 9 (15.8%) patients experienced telangiectasia and 21 (36.8%) patients experienced cutaneous calcinosis. This result was different with the study by Pagalavan and Ong in Malaysia, where 28 (45.9%) patients experienced telangiectasia and 7 (11.5%) patients experienced calcinosis cutis.[7] The result might be affected by the type of systemic sclerosis experienced by patients, calcinosis cutis was more frequently found in limited systemic sclerosis.[12]

Musculoskeletal involvement as the main cause of disability was frequently found on systemic sclerosis.[13] From the study result, it was revealed that 40 (70.2%) systemic sclerosis patients had a musculoskeletal involvement. The most frequently found manifestation was arthalgia 29 (50.9 %). This result was suitable with the previous literature which stated that the most common clinical manifestation on musculoskeletal involvement was arthalgia.[14] This result corresponded with the study by Pagalavan and Ong in Malaysia which reported that arthalgia/arthritis were frequently found (49.2%).[7]

There were 29 (50.9%) systemic sclerosis patients in this study with gastrointestinal involvement. The most manifestation which frequently found was difficulty in swallowing 13 (22.8%). This result corresponded with previous study which stated that gastroesophageal reflux and dysphagia were the frequent manifestations of systemic sclerosis on patients.[15] The other common complaint were nausea 14 (22.8%). These gastrointestinal manifestations were one factor which might cause malnutrition on systemic

sclerosis patients. Baron, et al reported 18% patients were at risk for malnutrition.[16]

On this study, the most frequent constitutional symptoms reported by systemic sclerosis patients were fatigue (21.1%) and weakness (19.3%). This result suited to previous study by Sandusky, et al., in USA which stated that 76% subjects experienced fatigue, while 61% of those patients stated that this was one of the most physically and socially disturbing symptoms.[17]

Renal involvement on systemic sclerosis patients can be assessed from clinical features or from supporting examination. On this study, there were 24 (42.1%) patients with renal involvement; 8 (14.0%) patients with clinical symptoms such as dysuria (10.5%) and oliguria (3.5%), while the rest of them had abnormal supporting examination test result. The supporting examinations conducted were routine urinalysis and serum creatinine level. Abnormalities found on patients from those test were proteinuria (17.5%), hematuria (14.0%) and bacteriuria (5.3%). Albuminuria could be used as vasculopathy marker, which was one of the pathophysiologic processes on systemic sclerosis.[18] On this study, increasing creatinine serum level was found on 4 (7.0%) patients. The increasing creatinine serum level did not completely describe a renal dysfunction, since renal dysfunction could also occur on patients with normal creatinine serum level.[18]

There were 30 (52.6%) patients on this study showed cardiac and pulmonary involvement marked by clinical manifestations and supporting examination. On this study, there were 12 (21.1%) patients with dyspnea, 2 (3.5%) patients with dyspnea and edema on extremities and 7 (12.3%) patients with dyspnea and cough. Meanwhile, a study by Hanitsch in Germany reported 390 (32.5%) patients had dyspnea.[11] Patients with dyspnea needed further observation and screening for pulmonary hypertension. The most frequent pulmonary manifestations and the main cause of death on 60% systemic sclerosis patients were interstitial lung disease (ILD) and pulmonary hypertension.[19] From plain chest x-ray and chest CT scan, respectively there were 2 (3.5%) and 3 (5.3%) patients with interstitial lung disease, while from echocardiography there were 2 (3.5%) patients with pulmonary hypertension. Systolic and diastolic dysfunction are early signs of heart problems on patients with systemic sclerosis.[20] On this study, there were 1 (1.8%) patients presented with diastolic dysfunction from echocardiography.

One of the pathophysiologic process occur on systemic sclerosis is the synthesis of autoantibody. The number and level of this autoantibody fluctuates depending on the disease activity, hence it could be used as diagnostic markers and determine prognosis of systemic sclerosis.[2] There were 10 (17.5%) patients on this study had positive ANA (antinuclear antibody) test result while 3 (5.3%) patients with positive anti-Scl70. This result was different from Pagalavan and Ong in Malaysia who stated that there were 51 (83.6%) patients with positive ANA and 21 (34.4%) patients with positive anti-Scl70 test result. This difference because not all patients who were treated at rheumatology clinic Dr. Hasan Sadikin General Hospital had autoantibody tests.[7]

## Conclusion

From 57 sample, it could be concluded that most systemic sclerosis patients had cutaneous involvement, renal, pulmonary, and cardiac involvement based on laboratory findings.

This study was a retrospective study that evaluated history taking and supporting examination test result on medical records. Most of the medical records had not been on computerized system, hence there could still be a possibility that there were mistakes in interpreting the writings on the medical records. On the other hand, not all patients took autoantibody test hence their records were not reported.

Recommendation from this study is demographic data on medical records could be completed. The medical records should also comprise the recordings of all examination the patient took to help clinician establish the diagnosis of the patient.

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