RESEARCH ARTICLE

Characteristics of systemic sclerosis patients in Nairobi, Kenya : a retrospective study

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Abstract

Objectives: Systemic sclerosis is a rare rheumatologic disorder that has not been well characterized in African populations. No previous studies have been carried out in Kenya, or in the East African region.
Design: A retrospective descriptive study.
Methods: Records of patients at the Kenyatta National Hospital and Nairobi Arthritis Clinic with a diagnosis of systemic sclerosis based on the American College of Rheumatology criteria were recruited into the study. The study covered a ten year period between 2001 and 2011.
Results: A total of 50 patients were identified, with a predilection of the disease to the female gender (M:F 1:4). The mean age of presentation was 41.7 years with a range of 4 years to 70 years. Majority of the patients (82%) presented with diffuse cutaneous systemic sclerosis. Overlap syndromes were documented in eight of the patients. Skin manifestation was the commonest presentation (100%), followed by Raynaud's phenomenon (64%), pulmonary disease (56%) and esophageal disease (54%). Antinuclear antibodies were present in 67% of the patients tested. Of the patients tested for anti- SCL-70 autoantibodies, only 28% were positive. Most of the patients (80%) were on immunosuppresants whereas 54% were on proton pump inhibitors/ prokinetics.
Conclusion: Patients in Nairobi with systemic sclerosis have similar characteristics as cases described elsewhere in Africa.

Key words: Systemic sclerosis, Scleroderma, Kenyatta National Hospital, Nairobi Arthritis Clinic

Introduction

Systemic sclerosis is an autoimmune disease of unknown etiology which is characterized by vasculopathy, thickening of the skin, internal organ involvement especially gastrointestinal system, lungs, kidney and heart as well as development of autoantibodies[1-3].

The etiology of the disease is not well understood, but possible triggers have been described. These include viruses such as cytomegalovirus and retroviruses, environmental triggers such as silica and industrial fumes, gadolinium contrast agent and some cytotoxic medications used in cancer treatment [4].

There are four main subtypes of the disease depending on the extent of fibrosis and internal organ involvement. In limited cutaneous systemic sclerosis, scleroderma is limited to the skin distal to the elbow and has minimal internal organ manifestation. The diffuse cutaneous form is widespread; skin thickening can involve the whole body including the face. It is associated with more internal organ disease. Localized scleroderma, also called morphea, is limited to the skin with no internal organ disease. Systemic sclerosis sine scleroderma has purely internal organ fibrosis with no features of scleroderma.

Very few studies have been carried out on the African continent on systemic sclerosis, and none in Kenya or the East African region. The estimated prevalence of the disease ranges from 50 to 300 cases per 1 million persons[5]. Females are more predisposed to developing the disease as compared to males, with a male: female ratio of between 1:3 and 1:14[2]. Studies carried out in North America have shown increased cases of systemic sclerosis in African Americans compared to Caucasians [6,7].

The hallmark of systemic sclerosis is thickening of the skin (scleroderma). Internal organ fibrosis occurs mainly in the lungs, gastrointestinal system, kidneys, muscle, joints and the heart. Vasculopathy

presents as pulmonary arterial hypertension, Raynaud's phenomenon, digital ulcers, acro-osteolysis and renal disease. Other clinical presentations include calcinosis cutis and arthritis. It is these clinical presentations that result in the high morbidity and mortality of the disease.

A study carried out in 30 countries (24 European, 6 non- European), involving 3656 patients was undertaken between 2004 and 2006. The male to female ratio was 1:6. Diffuse cutaneous systemic sclerosis was present in 36.9% while limited cutaneous disease was present in 63.1%. Patients with localized scleroderma were excluded from this study. Autoantibodies against SCL-70, which is highly specific for the disease, were positive in 36.4% of the patients[8].

A South African study carried out in Johannesburg in a black population, involving 63 patients found the mean age of onset at 36.1 years, with a male: female ratio of 1:4.6. Of the 63 patients, 13 had been exposed to silica from gold mines, a possible trigger factor of the disease in susceptible individuals. Raynaud's phenomenon was the most common symptom, occurring in 90% of the patients, with 98% of the patients having antinuclear autoantibodies[9]. Another study, also carried out in South Africa, found antinuclear autoantibodies in 96% of the 160 patients[10]. Studies done elsewhere have also implicated silica in the pathogenesis of systemic sclerosis[11-15].

A study undertaken in Nigeria and involving 14 patients showed a predilection of the female gender, with a male: female ratio of 1:6. Diffuse cutaneous was the commonest variant in 57.1% of the study patients. Raynaud's phenomenon was present in only 14.3% of the patients. Antinuclear antibodies were positive in 64.3% of the patients[16]. A study that reviewed the cause of death in systemic sclerosis from 1972 to 2002 in an American centre found that from 1972 to 1976 the commonest cause of death was scleroderma renal crisis. The trend declined and at the end of the study period (1997-2001), pulmonary disease, either pulmonary fibrosis or pulmonary arterial hypertension, was the commonest cause of death. This was attributed to better management of scleroderma renal crisis by use of dialysis services and drugs such as angiotensin converting enzyme inhibitors[17]. A study evaluating the radiological hand involvement in systemic sclerosis in 120 patients found that arthritis, distal phalange resorption, flexion contractures and extra articular calcification were the commonest radiological findings [18].

A study which evaluated cardiac involvement by using cardiac MRI in 52 systemic sclerosis patients found an abnormality in 75% of them. These included pericardial effusion, altered ejection fractions of the right or left ventricle and ventricular kinetic abnormalities[19]. Systemic sclerosis is a poorly understood and rarely studied disease in the African population. Few studies have been carried out in Africa, with majority done in South Africa [9-14,15] and the rest in Nigeria[16,20,21]. Kenyatta National Hospital is a tertiary referral and teaching hospital situated in Nairobi, Kenya; and is one of two in the country. It is the only public hospital with a rheumatology clinic, which has been in operation for one year, having been started in February 2010. Prior to the inauguration of this clinic, patients were seen in the general medical outpatient clinics. The rheumatology clinic is run under the auspices of qualified rheumatologists who review patients attending the clinic together with the registrars/residents from internal medicine attached to the unit. Nairobi arthritis clinic, a private rheumatology clinic based in Nairobi caters for a large number of patients with rheumatologic disorders including systemic sclerosis. These two rheumatology centers serve as the catchment area for the whole country due to the paucity of rheumatologists in Kenya.

Patients and methods

Patient's records covering a 10 year period between January 2001 and August 2011 were reviewed and those fulfilling the American College of Rheumatology criteria for systemic sclerosis were recruited into the study. Clinical presentation, age, gender, organ involvement, laboratory and radiological investigations, treatment modalities were documented.

Results

A total of 55 patients were identified. Five patients were excluded from the final analysis as they had localised scleroderma/morphea. The mean age at diagnosis was 41.7 years with a range of 4 to 70 years. Only one patient was aged less than 18 years. Female patients were 44 while 11 were male (M:F 1:4) (Table 1).

Table 1: Demographics

Female	44 (80%)
Male	11 (20%)
Mean age	41.7 years
Age range	4 years- 70 years

Majority of the patients (41) presented with diffuse cutaneous systemic sclerosis. Nine patients had limited cutaneous disease and no patient with systemic sclerosis sine scleroderma was identified. Fourteen of the patients had an overlap of scleroderma with another connective tissue disease (Tables 2, 3).

Table 2: Clinical variants

Diffuse cutaneous	41 (82%)
SSc sine scleroderma	0
Limited cutaneous	9 (18%)

Table 3: Overlap syndromes

Syndrome	No.
SLE/ Diffuse cutaneous	5
SLE/ Localised cutaneous	2
Rheumatoid arthritis/ Diffuse cutaneous	2
Sjogrens / Diffuse cutaneous	2
Dermatomyositis/ Diffuse cutaneous	3

The commonest clinical presentation was skin manifestation which was present in all the patients. Raynaud's phenomenon was present in 32 of the patients. In the rest of the patients, the information in the patient records did not indicate that symptoms of Raynaud's were not present or it was that they were not asked for. Therefore the actual incidence of Raynaud's phenomenon may have been higher. Esophageal involvement; either from symptoms or confirmed by barium studies was present in 27 of the patients. Pulmonary involvement was present in 20 of the patients, with the 18 having pulmonary fibrosis both radiologically and on pulmonary function test and 10 having pulmonary arterial hypertension on echocardiogram (Table 4).

One patient with diffuse cutaneous systemic sclerosis and rheumatoid arthritis presented with rapidly progressive glomerulonephritis which was managed successfully with intravenous cyclophosphamide. The other patient with scleroderma renal disease presented with protenuria and was managed with ACE inhibitors. Three deaths were documented, with all three patients having died from severe pulmonary disease and the attendant cor pulomonale.

Table 4: Clinical features

Feature	No.	(%)
Skin involvement	50	100
Raynaud's phenomenon	32	64
Pulmonary involvement	28	56
Pulmonary fibrosis	18	36
Pulmonary arterial hypertension	10	20
Esophageal involvement	27	54
Myopathy	16	32
Cardiac	11	22
Calcinosis	5	10
Acro-osteolysis	3	6
Scleroderma renal crisis	2	4
Arthritis/ arthalgia	8	16
Alopecia	4	8
Sicca symptoms	2	4
Vasculitis	1	2
Telengectasia	1	2

Various autoantibodies were carried out in the patients. Antinuclear antibody (ANA) test was carried out in 40 of the patients and was positive in 27 of the patients. Antibody to SCl-70 was carried out in 23 patients and was positive in six patients only (Table 5).

Table 5: Autoantibody profile

Antibody	No.	(%)
Antinuclear	27/40	67.5
Anti- SCL- 70	6/23	28.6
Anti- ds-DNA	4/16	25
Anti- CCP	0/8	
Rheumatoid factor	7/27	25.9
Anti- SM	2/28	7.1
Anti- SSA	3/29	10.3
Anti- SSB	2/29	6.9
Anti- JO1	2/27	7.4
Anti- RNP	4/28	14.3

Table 6: Treatment modalities

Modality	No.	(%)
Acetylsalicylic acid/ antiplatelet agent	18	36
PPI/H^2 blocker	27	54
Calcium channel blocker	31	62
Prokinetic agent	6	12
Sildenafil	2	4
Immunosuppressants	40	80
Methrotrexate	20/40	50
Cyclophosphamide	9/40	22.5
Mycophenolate mofetil	5/40	12.5
Azathioprine	5/40	12.5
Hydroxychloroquine	4/40	10
Prednisone	20/40	50

Treatment modalities in the patients varied according to the presenting symptoms and extent of organ involvement. Twenty seven of the patients were on a proton pump inhibitor (PPI)/ H2 receptor blocker, 31 were on a calcium channel blocker, 18 were of acetylsalicylic acid and 40 were on immunosuppressant therapy, either in combination or as a single agent (Table 6).

Discussion

Systemic sclerosis/ scleroderma is a rare condition with an estimated prevalence of 50 to 300 cases per 1 million persons and an incidence ranging from 2.3 to 22.8 cases per 1 million persons per year[2,5] with an increased incidence reported amongst blacks [6,7.] The mean age of at diagnosis was 41.7 years; compared to 40.3 years in the Nigerian series[16] and 36.1 years in the South African study[9] .The male to female ratio was 1:4 which is comparable to South African data (M:F 1:4.6)[9] and Nigerian study M:F 1:6[16]. The youngest patient in our study was a four year old male who presented with localized scleroderma with negative autoantibody profile, while the oldest were three patients aged 70 years.

Diffuse cutaneous was the commonest clinical variant, occurring in 74%, with no cases being described with systemic sclerosis sine scleroderma. A Nigeria study[16] had 57% of their patients presenting as diffuse cutaneous while a South African study[9] had 65% of the patients presenting as diffuse cutaneous. Patients with systemic sclerosis sine

scleroderma may have presented to other specialties such as gastroenterologists or chest physicians depending on the predominant organ involved. This may account for the absence of this variant at our rheumatology clinic. Similarly, patients with localized forms of scleroderma may have presented to the dermatology clinic and thus lead to underreporting in our series.

Skin involvement was the commonest manifestation (100%), followed by with Raynauds phenomenon at 58% and esophageal disease was present in 49% of the patients. The relatively lower incidence of Raynaud's compared to other largely western studies[8] may be due to hotter climate and darker skin pigmentation leading to underreporting in our population. Nigerian study documented Raynaud's in only two patients (14%). The South African study, which was carried out in blacks, reported occurrence of raynaud's in 90% of their patients[9]. The lower incidence of Raynauds may also be attributed to the retrospective nature of the study.

Antinuclear antibody was done in 21 patients and was positive in 67%. Anti- SCL-70 autoantibody, which is specific for scleroderma was, present in only 4 out of the 14 patients tested (28%). All the patients with antibodies to SCL-70 had the diffuse cutaneous variant. Anti- SCL-70 antibodies are more common in the diffuse cutaneous variant and are associated with severer forms of the disease. Two of these patients had severe lung restrictive patterns on pulmonary function tests, two had esophageal dysmotility whereas one had peripheral gangrene. One of the mortalities reported in our case series had anti- SCL-70 antibodies.

Two patients presented with diffuse cutaneous systemic sclerosis after having been diagnosed to have breast cancer and subsequently underwent mastectomy followed by radiation and chemotherapy consisting of cyclophosphamide, methrotrexate and 5-florouracil. One patient developed the disease three years after the diagnosis of breast cancer. In this patient the autoantibodies done were all negative. The other patient developed diffuse cutanoeus disease 10 years after the diagnosis of cancer. In this patient rheumatoid factor as well as SCL-70 antibodies were positive. Cytotoxic medications have been implicated in the pathogenesis of this disease[4]. Treatment modalities varied depending on the clinical presentation. Fourty nine percent of the patients were on either prokinetic or PPI/H^2 blocker. Immunosuppressants were administered to 72% of the patients , mainly due to internal organ involvement especially pulmonary involvement.

The three deaths reported were as a results of pulmonary involvement (both fibrosis and pulmonary arterial hypertension) and cor pulmonale. The two cases of scleroderma renal crisis were documented in our series were managed successfully with immunosuppressants and angiotensin converting enzyme inhibitors. This is in keeping with data that shows the commonest cause of death currently is as a result of pulmonary involvement[17].

Limitations of the study included loss of follow up of majority of the patients. More than half of the patients had not presented to the clinic in over one year. Some of these patients may have succumbed to their disease in peripheral health facilities. This is a recurrent problem in most of the outpatient clinics due to a variety of reasons such as lack of financial resources and residing far from the hospital. There was a limitation of the investigations carried out due to financial constraints. Being a retrospective study, some data may have been missing from the patients' records. It is hoped that this study will provide vital information for a rare disease, which has not been studied much in the African population and that it will serve as a reference for future studies.

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