Article published online: 2022-07-07

Original Article

Demographic Characteristics and Clinical Manifestations of Systemic Sclerosis in Benghazi, Libya

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Abstract

Background: Systemic sclerosis (SSc) is a rare, heterogeneous autoimmune disease characterized by skin fibrosis, vasculopathy, and internal organ involvement. This study aims to determine the frequency of clinical manifestations of SSc among Libyan patients in Benghazi. **Patients and Methods:** Thirty patients (28 females) attended the Rheumatology Clinic at Benghazi Medical Center between January 2016 and December 2019. They were diagnosed to have SSc according to American College of Rheumatology/European League Against Rheumatism 2013 revised classification criteria and were classified into diffuse cutaneous systemic sclerosis (dcSSc) and localized systemic sclerosis (lcSSc) disease subsets. **Results:** We reviewed the data of the 30 patients, including 28 (93.3%) females and 2 (6.7%) males (female: male ratio 14:1); the mean age at diagnosis was 40.5 ± 21.5 years (17–62 years). Twenty-four (80%) patients were diagnosed as dcSSc, whereas 6 (20%) were diagnosed as lcSSc. On diagnosis, patients with dcSSc were comparatively younger than those with lcSSc. The frequency of musculoskeletal manifestations and organ involvement was more frequent among patients with dcSSc ($P = 0.001$). All the thirty patients had rheumatoid factor and anti-nuclear antibody positivity. Anti-Scl-70 was only positive in the dcSSC subset in all patients of dcSSc only, whereas anti-centromere Ab was positive in all patients of lcSSc only. **Conclusions:** This is the first study to assess the clinical manifestations of SSc in the Libyan population. Our disease cohort showed similarity to what was published in other cohorts with regard to the age at the time of diagnosis, gender, and autoimmune profile.

Keywords: Benghazi, diffuse, epidemiology, Libya, localized, rheumatology, systemic sclerosis

Introduction

Systemic sclerosis (SSc) is a rare, heterogeneous autoimmune disease characterized by skin fibrosis, vasculopathy, and internal organ involvement. Because of the low prevalence of SSc in the population, providing clinical

Access this article online

Quick Response Code:

Website: www.ijmbs.org

DOI: 10.4103/ijmbs.ijmbs_36_20

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Submitted: 02-Apr-2020 **Revised:** 13-Jun-2020
Accepted: 14-Jun-2020 **Published:** 27-Jun-2020

How to cite this article: Elbraky FM, Amailaf IA, Alsaeiti KD. Demographic characteristics and clinical manifestations of systemic sclerosis in Benghazi, Libya. Ibnosina J Med Biomed Sci 2020;12:118-22.

trials and comprehensive observations may be challenging.[1] The estimated prevalence derived from population-based studies is between 1 and 2/10,000 people.[2] Higher rates have been reported in the USA, Australia, and Eastern Europe, and lower rates have been reported in Northern Europe and Japan.[3] These differences can be explained by ethnic differences.[4,5] Significant differences in the prevalence and specificity of autoantibodies and clinical features in SSc patients depending on race and ethnicity have been reported. Hence, we aimed to study the frequency of SSc-related autoantibodies and associated clinical features in Libyan patients.

Patients and Methods

Thirty patients (28 females and two males) attending the Rheumatology Clinics at Benghazi Medical Center between January 2016 and December 2019 were included in the study. They were diagnosed as having SSc clinically and those who fulfilled the American College of Rheumatology/European League Against Rheumatism 2013 revised classification criteria were divided into diffuse cutaneous SSc (dcSSc) and localized cutaneous SSc (lcSSc) disease subsets for SSc.[6] The patients were classified according to Leroy 2001[7] into limited cutaneous SSc and dcSSc, and patients with localized scleroderma (morphea and linear disease) were excluded from the study population.

Patients' data were obtained through medical records through chart review. Data collection included age, gender, disease duration at the time of presentation, clinical characteristics, cutaneous manifestations, musculoskeletal manifestations, and organ involvement. Autoimmune profiling included rheumatoid factor (RF), antinuclear antibodies (ANAs), and anti-Scl-70 antibody.

Data were analyzed using the Statistical Package for the Social Sciences (SPSS) 17.0 (SPSS Inc. Chicago, IL, USA). Descriptive statistics of the different variables were presented either as frequencies and percentages or as means ± standard deviation. Frequency tables were analyzed using the Chi-square test, and *P* values were used to assess the significance of correlation between the categorical variables. In all cases, $P < 0.05$ was considered statistically significant.

Results

Thirty patients with an established diagnosis of SSc were enrolled in this study, including 28 (93.3%) females. The mean age at the time of diagnosis was 40.5 ± 21.5 years, with a wide range of 17–62 years. Twenty-four (80%) patients were diagnosed as dcSSc, whereas 6 (20%) patients had lcSSc. On diagnosis, patients with dcSSc were comparatively younger than those with lcSSc ($P = 0.03$). The demographic and clinical manifestations of dcSSc and lcSSc are shown in Table 1.

Both types of scleroderma had evidence of cutaneous involvements such as Raynaud's phenomenon, skin thickening distal to the elbow joint, and sclerodactyly. On the other hand, hyperpigmentation was seen only in patients with dcSSc (20, 8%). The dcSSc subgroup was associated with more cutaneous manifestations than the limited cutaneous SSc ($P = 0.03$). Other cutaneous manifestations are listed in Table 2.

Table 1: Demographic manifestations of the systemic sclerosis patients

Variables	Diffuse systemic sclerosis	Limited systemic sclerosis	Total
Number of patients (%)	24 (80)	6 (20)	30 (100)
Age (mean±SD)	39±22	41.2±20.8	40.5±21.5
Disease duration (mean±SD)	8.5±4	9.5±4	9±4.5
Female, *n* (%)	24 (100)	4 (66.7)	28 (93.3)
Male, *n* (%)	0	2 (33.3)	2 (7.3)

SD: Standard deviation

Table 2: Cutaneous manifestations of the systemic sclerosis

Cutaneous manifestations	Diffuse systemic sclerosis (24 patients), *n* (%)	Limited systemic sclerosis (6 patients), *n* (%)
Skin thickening	24 (100)*	6 (100)**
Sclerodactyly	24 (100)	6 (100)
Hyper/depigmentation	21 (87.5)	0
Telangiectasia	20 (83)	3 (50)
Digital ulcer	13 (54)	3 (50)
Nail fold changes	12 (50)	4 (66)
Alopecia	7 (29)	0
Calcinosis	6 (25)	3 (50)
Vasculitic lesion	5 (20.8)	0

*Proximal to elbow, **Distal to elbow

Musculoskeletal manifestations were more frequent among patients with dcSSc than those with lcSSc ($P = 0.001$). For instance, 24 dcSSc patients had polyarthralgia and eight dcSSc patients had polyarthritis, tendon friction rub, myopathy, and myositis, whereas three lcSSc patients only had polyarthralgia.

The frequencies of organ involvement among patients were statistically significantly higher among patients with dcSSc when compared to lcSSc, and those include scleroderma renal crises, interstitial lung disease (ILD), and pulmonary arterial hypertension (PAH) ($P = 0.02$, 0.03, and 0.001, respectively). The frequencies of other organ involvements are shown in Table 3.

Immunologically, all patients had a positive RF and ANA. Anti-Scl-70 was positive in all patients (100%) of dcSSc only, whereas anti-centromere Ab was positive in all patients (100%) of lcSSc only.

Table 3: Manifestations of organ involvement

	Diffuse systemic sclerosis	Limited systemic sclerosis
Hypertension	8 (33.3%)	0
Scleroderma renal crises	4 (16.6%)	0
Abnormal urinary sediment	3 (12.5%)	0
ILD	8 (20.8%)	0
PAH	5 (16.6%)	1 (16.6%)
Pleural disease	1 (4%)	0
Cardiac manifestations	0	0
Esophageal dysmotiliy	19 (79%)	4 (66%)
Large bowel obstruction	2 (8.3%)	0
Secondary sjogren's syndrome	16 (66.6%)	2 (33%)
Depression	9 (37.5%)	0
Hypothyroidism	4 (16.6%)	1 (16.6%)
Primary biliary cirrhosis	1 (4%)	0

Discussion

We recruited thirty cases in 4 years' duration; this low number of patients recruited in this study is numerically comparable to other studies. Seventy-seven cases and 75 cases were reported in Egypt[8] and Tunisia[9] in 13 and 15 years, respectively. Adelowo and Oguntona[10] reported 14 cases in Nigeria in 5 years, while 35 cases in 10 years were reported from Mali.[11]

The female predominance seen in the present study is comparable to previous cohorts.[12-16] SSc is more common in females, with a very high female-to-male ratio of 3:1.[12] In the present study, we saw a clear female predominance with even a higher female-to-male ratio of 14:1. The female predominance was reportedly lower in some studies from the same Middle East and African series. The female-to-male ratio was 8:1 in Tunisia,[9] 9:1 in Iraq,[13] and 7.4:1 in Qatar.[14] However, lower ratios of 4:1 were reported in other studies from Egypt, South Africa, and Malaysia.[8,15,16] Our high female: male ratio of 14:1 is similar to observations from Japan.[17]

The mean age at diagnosis of patients in the present study (40 years) was comparatively lower (36 years) than those of patients reported from Qatar,[14] Egypt,[8] and Tunisia.[9] However, other studies from Japan, Spain, and the USA reported older age at diagnosis (51, 51.2, and 45.5 years, respectively).[18-20] Furthermore, on diagnosis, patients with dcSSc were comparatively younger than those with lcSSc in our cohort. These findings were in contrast to those found in the Tunisian study, which found that patients with lcSSc are of younger age at diagnosis.[9] However, no significant difference in demographic data was observed between the two subtypes in the Egyptian study.[8]

In the current study, 24 patients (80%) had dcSSc and 6 patients (20%) had lcSSc. This is similar to the reported data from various regions such as those reported from Tunisia (80%),[9] Kenya (82%),[21] Nigeria (57.1%),[10] Qatar (52.4%),[14] and Ukraine (72.9%).[1] However, these findings are at contrast to an Egyptian study,[8] which showed a higher frequency of lcSSc (81.3%). A large multicentric European study of 3656 patients with SSc from thirty different countries found that lcSSc is more frequent than the diffuse type.[22] Similarly, a higher frequency of lcSSc was reported evidently in other studies, too.[16,23,24] The difference in the spectrum between studies could be related to ethnic differences between patients in different studies. Another plausible reason could be the delay in making the diagnosis or being evaluated by a rheumatologist, particularly in low-income settings.

Raynaud's phenomenon, skin thickening, and sclerodactyly were evident in all patients in the current study. Raynaud's phenomenon was the most common manifestation among Egyptian patients,[8] Qatar patients (78%),[14] and Spanish study patients (83.6%).[19] Similar results were reported in Malaysia (70%).[16] Lower rates of Raynaud's phenomenon were reported among African populations from Nigeria and Cote d'Ivoire.[10,25] This could be attributed to a warm tropical climate as cold is one of the triggering factors.

All patients with dcSSc reported arthralgia, while arthritis was reported in 33.3% of patients. Studies from Egypt, South Africa, and Malaysia reported higher frequencies of arthritis among scleroderma patients, 40%–68%.[8,15,16]

The differences in the frequencies of organ involvement between dcSSc and lcSSc patients included in the present study were significant for scleroderma renal crisis, ILD, and PAH among the diffuse type ($P = 0.02$, 0.03, and 0.001, respectively). In the current study, ILD was reported in 33.3% of patients with dcSSc. No patient was diagnosed with ILD in the limited subtype, and most studies suggest that ILD is the most frequent organ manifestation of SSc,.[8,9,14,24] ILD was reported in 61.9% of patients, and it was more commonly seen in patients with dcSSc than in patients with lcSSc (45%). The same results were reported in the Egyptian[8] and Spanish[19] studies (78.6% vs. 47.5% and 70% vs. 39.3%, respectively).

Pulmonary hypertension (HTN) was seen in six patients (20%), with five of them (20.8%) being the diffuse type. Similar results were reported in the Qatar cohort[14] (14.7%) with a higher frequency within the diffuse subtype than in the limited subtype (35.7% vs. 9.8%, respectively). Our results are similar to the reported rates from Egypt and South Africa.[8,15]

Autoantibody screening of our patients showed RF and ANA.

Anti-Scl-70 was positive in all patients with dcSSc only. In addition, anti-centromere Ab was positive in all patients of lcSSc only, and there were no significant associations of these autoantibodies with specific organ involvement. The frequency of ANA positivity was slightly lower, i.e., 94.2%, 92.4%, and 86.7% among German,[26] Brazilian,[27] and Indian[28] patients.

Lower frequencies were reported in most studies of both Anti-Scl-70 and anti-centromere Ab in most studies.[26,28,29]

Anti-Scl-70 antibodies were strongly associated with dcSSc subtype,[27] while other studies show a strong association of anti-centromere antibodies with lcSSc.[30]

To the best of our knowledge, this is the first study looking into the clinical characteristics of SSc in the Libyan population. Some limitations are noteworthy. The small number of patients and the single-center design of the study are noted, yet the sample size is comparable to several other studies.

Conclusions

The diffuse SSc subtype is more frequent among Libyan patients than with limited SSc subtype. However, dcSSc is more commonly associated with ILD, pulmonary HTN, and renal crisis compared with lcSSc. Raynaud's phenomenon, skin thickening, and sclerodactyly are reported in all patients of our cohort, and the younger age of patients with lcSSc at diagnosis compared with other studies may have a genetic contribution that needs to be studied thoroughly in future studies. A more extensive multicentric series would be valuable further to elucidate the clinical characteristics of the disease in Libya.

Authors' contributions

All authors contributed to the conception, conduct of the study, data collection and analysis and drafting and review of the manuscript. All authors approved the final version of the article.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

Compliance with ethical principles

The study was conducted according to the Declaration of Helsinki 1975. The study was

approved by the scientific committee of October 7, Hospital ((171.ك.7. All the information was kept confidential, and no individual identifiers were collected.

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