Comparative Analysis of Clinical Features and Autoantibody Profiles in Systemic Sclerosis Patients Among Jewish and Arab Populations in Israel

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ABSTRACT **Background:** Systemic sclerosis (SSc) is a chronic autoimmune disease characterized by fibrosis of the skin and internal organs. Its expression can vary across ethnic groups.

Objectives: To compare clinical and serological manifestations of SSc between Jewish and Arab patients in Israel.

Methods: We conducted a retrospective single-center study included 100 patients with SSc selected from our rheumatology clinic at Meir Medical Center, comprising 50 Jewish and 50 Arab patients with available complete clinical and laboratory data. Demographic characteristics, disease features, autoantibody profiles, organ involvement, and treatment patterns were collected.

Results: Most clinical, laboratory, and treatment variables did not differ significantly between Jewish and Arab patients. Significant difference was the higher prevalence of skin telangiectasia in Jewish patients (86%) compared to Arab patients (38%) ($P < 0.001$) as well as Raynaud phenomenon and pulmonary hypertension. Other manifestations, including organ involvement and autoantibody prevalence, were similar across the groups.

Conclusions: This study reveals significant similarities in the clinical and serological expression of SSc between Jewish and Arab patients in Israel. The higher prevalence of telangiectasia in Jewish patients suggests a possible ethnic or environmental influence on vascular manifestations. Further research is needed to explore the potential genetic or environmental factors contributing to this difference and to assess if this impacts disease progression or treatment outcomes.

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KEY WORDS: autoantibody profiles, autoimmune disease, skin telangiectasia, scleroderma, systemic sclerosis (SSc)

Systemic sclerosis (SSc) is a systemic autoimmune connective tissue disease characterized by immune-mediated vasculopathy and progressive fibrosis of the skin and internal organs, most commonly affecting the lungs, gastrointestinal tract, heart, and kidneys [1,2]. The global prevalence is estimated at 17–19 per 100,000, with regional variations: higher rates in North America and Australia, and lower rates in Europe and Asia [3-5]. Epidemiological data for Israel are limited, but prevalence is likely to be similar to other high-income countries, approximately 10–20 per 100,000 [4,5]. SSc predominantly affects females, with a female-to-male ratio of approximately 5:1. It is associated with high morbidity and mortality, mainly due to pulmonary complications from interstitial lung disease and pulmonary hypertension [6-8].

SSc was classified according to the 2013 American College of Rheumatology (ACR) and the European Alliance of Associations for Rheumatology (EULAR) criteria, which use a weighted point system to improve sensitivity, particularly in early or limited disease. A total score of ≥ 9 points is required for classification in the absence of an alternative diagnosis, based on features such as skin thickening, fingertip lesions, telangiectasia, abnormal nailfold capillaries, Raynaud phenomenon, pulmonary involvement, and disease-specific autoantibodies [9,10]. Clinically, SSc is categorized into limited and diffuse cutaneous forms: limited disease affects the distal extremities and face, sparing the trunk and proximal limbs, and is associated with long-standing Raynaud phenomenon, digital ulcers, and a higher risk of pulmonary arterial hypertension, with mild internal organ involvement. Diffuse disease involves widespread skin thickening, including the trunk and proximal extremities, with rapid progression and early, severe visceral involvement such as interstitial lung disease, renal crisis, and cardiac complications. Autoantibody profiles aid prognostication: anti-centromere antibodies (ACA) are linked to limited disease, anti-topoisomerase I antibodies (anti-Scl-70) to diffuse disease and interstitial lung involvement, and anti-RNA polymerase III antibod-

ies to rapidly progressive diffuse disease, increased renal crisis risk, and malignancy [8-10].

Although ethnicity and socioeconomic factors are known to influence disease severity and clinical manifestations in autoimmune conditions such as rheumatoid arthritis and systemic sclerosis, direct comparisons between Jewish and Arab populations in Israel are scarce. Previous research has largely focused on differences within Jewish subgroups (Sephardic vs. Ashkenazi) [11], leaving a gap in understanding how systemic sclerosis presents across Israel's main ethnic groups.

In this study, we aimed to fill that gap by systematically comparing clinical features, autoantibody profiles, and organ involvement between Jewish and Arab patients with systemic sclerosis. Identifying population-specific patterns may improve disease recognition, inform personalized management, and guide future research on genetic and environmental factors contributing to disease expression.

PATIENTS AND METHODS

STUDY DESIGN AND SETTING

In this retrospective cohort study, we reviewed medical records of adult patients diagnosed with SSc and followed at the Rheumatology Clinic at Meir Medical Center. Patients were stratified by self-reported ethnicity into two groups: Jewish (n=50) and Arab (n=50). Only patients with complete clinical and laboratory records were included. All patients met the 2013 ACR/EULAR classification criteria for SSc.

STUDY POPULATION

Inclusion criteria comprised adults aged ≥ 18 years with a confirmed diagnosis of SSC that met the 2013 ACR/EULAR classification criteria. The exclusion criteria included patients with concomitant autoimmune rheumatic diseases.

VARIABLES COLLECTED

Data were collected from electronic medical records in anonymized form and included demographics (age, sex), clinical features (modified Rodnan skin score, Raynaud phenomenon, organ involvement [lungs, heart, gastrointestinal tract, kidneys], and disease subset [limited vs. diffuse cutaneous systemic sclerosis]), diagnostic assessments (echocardiography, pulmonary function tests, high-resolution CT scans), serological profile (ACA, anti-Scl-70, and anti-RNP antibodies), disease course indicators (number of hospitalizations, complications, and mortality), and disease duration (average disease duration was approximately 10 years for both Jewish and Arab patient groups).

SAMPLE SIZE AND DURATION

The study included 100 patients, divided equally between Jewish and Arab groups (50 each). Data were collected and analyzed over a 6-month period.

STATISTICAL ANALYSIS

Descriptive statistics included demographic, clinical, and serological characteristics. Comparative analyses employed chi-square or Fisher's exact tests for categorical variables, and Student's *t*-test or Mann–Whitney U test for continuous variables, based on data distribution.

ETHICS CONSIDERATIONS

All patient data were anonymized and handled in compliance with ethics standards. The study received approval from the Helsinki Committee at Meir Medical Center. Data were securely stored for a period of 7 years as per institutional guidelines.

RESULTS

The study included 100 patients with systemic sclerosis, equally divided between Jewish (n=50) and Arab (n=50) participants. Females comprised the majority in both groups (Jewish: 45/50 [90%]; Arab: 38/50 [76%]), while males were less frequent (Jewish: 5/50 [10%]; Arab: 12/50 [24%]), with no statistically significant difference between the groups ($P = 0.11$).

Co-morbidities were similarly distributed: diabetes was present in 16% of Jewish and 10% of Arab patients ($P = 0.55$), hypertension in 30% vs. 34% ($P = 0.83$), smoking in 28% vs. 16% ($P = 0.23$), osteoporosis in 12% vs. 4% ($P = 0.27$), and thyroid disease in 22% vs. 12% ($P = 0.29$) for Jewish and Arab patients, respectively.

Regarding autoantibody profiles, ACA were detected in 18% of Jewish and 10% of Arab patients ($P = 0.39$), while anti-Scl-70 antibodies were equally present in both groups (24% each, $P = 1.00$). Other scleroderma-specific antibodies were more frequent among Jewish patients (18% vs. 6%, $P = 0.12$), although the difference was not statistically significant. ANA, anti-Ro, anti-La, IgA, and RF were observed in 34% of Jewish and 20% of Arab patients ($P = 0.18$).

Overall, there were no statistically significant differences in co-morbidities or autoantibody prevalence between Jewish and Arab patients in this cohort [Table 1].

The most common clinical feature in both groups was skin involvement with telangiectasia, present in 86% of Jewish patients (n=43) compared to 38% of Arab patients (n=19), a statistically significant difference ($P < 0.001$). Raynaud phenomenon was reported in 64% of Jewish patients (n=32) vs. 30% of Arab patients (n=15), also showing a significant difference ($P = 0.001$).

Ischemic digital ulcers were observed in 20% of Jewish patients (n=10) and 12% of Arab patients (n=6), with no statistically significant difference ($P = 0.41$). Esophageal dysmotility was more frequent in Arab patients (14%, n=7) compared to Jewish patients (2%, n=1), although this finding did not reach statistical significance ($P = 0.06$). Gastroesophageal reflux was present in 54% of Jewish patients and 38% of Arab patients ($P = 0.16$), while dysphagia occurred in 58% vs. 46%, respectively ($P = 0.32$). Intestinal involvement was rare in both groups (Jewish: 4%, Arab: 6%, $P = 1.0$).

Cardiac involvement, including ischemic heart disease (32% vs. 20%, $P = 0.39$), systolic dysfunction (4% vs. 6%, $P = 1.0$), diastolic dysfunction (18% vs. 10%, $P = 0.39$), heart rhythm disorders (12% vs. 6%, $P = 0.49$), and peripheral artery disease (4% vs. 2%, $P = 1.0$), did not differ significantly between the groups.

Pulmonary complications were common. Interstitial lung disease was present in 42% of Jewish and 34% of Arab patients ($P = 0.54$). Pulmonary hypertension was significantly more frequent in Jewish patients (30%, n=15) compared to Arab patients (12%, n=6, $P = 0.049$).

Hematological and renal involvement, including anemia (30% vs. 14%, $P = 0.09$), thrombocytopenia (46% vs. 32%, $P = 0.22$), chronic renal failure (6% vs. 12%, $P = 0.49$), and renal crisis (4% vs. 10%, $P = 0.44$), were observed at low frequencies with no significant differences between groups. Myositis was rare in both populations (6% vs. 2%, $P = 0.62$).

In summary, telangiectasia, Raynaud phenomenon, and pulmonary hypertension were significantly more prevalent in Jewish patients, whereas other organ involvements did not differ significantly between Jewish and Arab patients [Table 2].

Analysis of treatment patterns revealed that most medications were used at similar rates between Jewish and Arab patients. Specifically, the use of antiplatelet drugs, anticoagulation therapy, proton pump inhibitors or H2 blockers, immunosuppressants (e.g., mycophenolate mofetil, methotrexate, hydroxychloroquine), iloprost, and calcium channel blockers did not differ significantly between the groups (all $P \geq 0.283$). The only exception was the use of angiotensin-converting enzyme (ACE) inhibitors, which was significantly more common in Jewish patients (34%) compared to Arab patients (14%, $P = 0.035$).

Regarding disease course indicators, the proportion of patients experiencing more than two hospitalizations per year was similar between Jewish and Arab patients (8% vs. 10%, $P = 1.00$). Mortality was low in both groups, with one Jewish patient and four Arab patients dying during the study period. The difference was not statistically significant ($P = 0.362$).

Table 1. Patient characteristics by ethnicity, including co-morbidities, exposure to sclera, and autoantibody presence

Number of participants	Total (N=100)	Arab ethnicity (n=50)	Jewish ethnicity (n=50)	*P*-value
Female	83	38 (76%)	45 (90%)	0.1102
Male	17	12 (24%)	5 (10%)	0.1102
Diabetes	13	5 (10%)	8 (16%)	0.552
Hypertension	32	17 (34%)	15 (30%)	0.8303
Smoking	24	8 (16%)	14 (28%)	0.2274
Osteoporosis	8	2 (8%)	6 (12%)	0.2687
Thyroid gland disease	17	6 (12%)	11 (22%)	0.2869
Antibodies				
Anti-centromere	14	5 (10%)	9 (18%)	0.3873
Anti SCL70	24	12 (24%)	12 (24%)	1.000
Other scleroderma antibodies	12	3 (6%)	9 (18%)	0.1212
ANA, anti-RO, anti-LA, IGA, RF	27	10 (20%)	17 (34%)	0.1765

Table 2. Disease characteristics and multi-organ involvement

Number of participants	Total (N=100)	Arab ethnicity (n=50)	Jewish ethnicity (n=50)	*P*-value
Skin involvement telangiectasia	62	19 (38%)	43 (86%)	< 0.001
Raynaud phenomenon	57	15 (30%)	32 (64%)	0.001
Ischemic digital ulcer	16	6 (12%)	10 (20%)	0.413
Esophageal dysmotility	8	7 (14%)	1 (2%)	0.059
Gastric antral vascular ectasia	46	19 (38%)	27 (54%)	0.160
dysphagia	52	23 (46%)	29 (58%)	0.316
Intestine involvement	5	3 (6%)	2 (4%)	1.000
Ischemic heart disease	26	10 (20%)	16 (32%)	0.387
Systolic dysfunction	7	4 (8%)	3 (6%)	1.000
Diastolic dysfunction	14	5 (10%)	9 (18%)	0.387
Heart rhythm disorder	9	3 (6%)	6 (12%)	0.487
Peripheral artery disease	5	2 (4%)	3 (6%)	1.000
Interstitial lung disease	38	17 (34%)	21 (42%)	0.536
Pulmonary hypertension	21	6 (12%)	15 (30%)	0.049
Anemia	22	7 (14%)	15 (30%)	0.091
Thrombocytopenia	39	16 (32%)	23 (46%)	0.218
Chronic renal failure	9	6 (12%)	3 (6%)	0.487
Renal crisis	7	5 (10%)	2 (4%)	0.436
Myositis	4	1 (2%)	3 (6%)	0.617

Table 3. Medications, number of hospitalizations, and mortality

Number of participants	Total (N=100)	Arab ethnicity (n=50)	Jewish ethnicity (n=50)	*P*-value
Anti-platelets drugs	18	9 (18%)	9 (18%)	1.00
Anti-coagulation drug	8	4 (8%)	4 (8%)	1.00
Proton pump inhibitors	45	22 (44%)	23 (46%)	1.00
ACE inhibitors	24	7 (14%)	17 (34%)	0.035
Calcium channel blockers	32	13 (26%)	19 (38%)	0.283
Mycophenolate mofetil	17	9 (18%)	8 (16%)	1.00
Methotrexate	13	5 (10%)	8 (16%)	0.552
Hydroxychloroquine	18	7 (14%)	11 (22%)	0.434
Iloprost	20	13 (26%)	7 (14%)	0.211
Anti-depressant	27	9 (18%)	18 (36%)	0.071
> 2 hospitalizations per year	9	5 (10%)	4 (8%)	1.00
Death	5	4 (8%)	1 (2%)	0.362

ACE = angiotensin-converting enzyme

Causes of death were heterogeneous and included heart failure, complications from poorly controlled diabetes, and major organ involvement related to systemic sclerosis [Table 3].

DISCUSSION

SSc is a complex multiorgan autoimmune disease characterized by progressive fibrosis of the skin and internal

organs, along with widespread vascular abnormalities. Its clinical presentation is highly heterogeneous, ranging from limited cutaneous involvement to rapidly progressive diffuse disease with early visceral complications. Morbidity and mortality are largely driven by pulmonary manifestations, particularly interstitial lung disease (ILD) and pulmonary hypertension [1-3].

Increasing evidence indicates that ethnicity plays a significant role in shaping disease phenotype, severity, autoantibody profile, and long-term outcomes for SSc patients. Ethnic differences in SSc have been well documented in large multiethnic cohorts, demonstrating variations in organ involvement, autoantibody distribution, and survival [12,13]. Arab patients have exhibited shorter median survival times compared to European-descent white and East Asian patients. They exhibit higher rates of severe organ involvement in some studies [13]. Differences in serological profiles, such as the prevalence of ACA and anti-Scl-70, further support the influence of ethnicity on disease expression and prognosis [14].

In our study, we compared clinical characteristics, serological profiles, organ involvement, and treatment patterns of Jewish and Arab patients with SSc who were treated at a single tertiary care center in Israel. All participants met the 2013 ACR/EULAR classification criteria, ensuring diagnostic consistency and allowing a reliable comparison between ethnic groups.

The principal finding of our study is the overall similarity in clinical, serological, and therapeutic characteristics between Jewish and Arab patients with SSc. The notable exception was a significantly higher prevalence of vascular manifestations among Jewish patients, including telangiectasia, Raynaud phenomenon, and pulmonary hypertension. In contrast, fibrotic organ involvement, including interstitial lung disease, was comparable between groups, suggesting that ethnic or environmental factors may preferentially influence vascular pathology rather than fibrotic disease processes.

Telangiectasia, a marker of chronic microvascular damage and a weighted component of the ACR/EULAR classification criteria, was markedly more prevalent among Jewish patients. This finding is consistent with prior reports linking vascular manifestations to limited cutaneous SSc and ACA positivity, whereas fibrotic complications are more strongly associated with anti-Scl-70 and seronegativity [15-17]. Although disease subset distribution did not differ significantly between groups in our cohort, subtle differences not reaching statistical significance may still contribute to the observed disparity in vascular features.

Several mechanisms may underlie the increased vascular involvement observed among Jewish patients. Ethnic variability in vascular biology, endothelial dysfunction, angiogenic repair capacity, and genetic susceptibility may influence the severity and clinical expression of microvascular damage. Environmental factors, including sun exposure, occupational exposures, and lifestyle differences, may also affect the development or clinical detection of vascular manifestations. Importantly, the increased burden of vascular features occurred despite similar healthcare access, supporting a biological or environmental contribution beyond differences in medical care or autoantibody status alone.

Pulmonary hypertension was also more frequent among Jewish patients, further supporting the predominance of vascular involvement in this group. This finding may partly explain the higher use of ACE inhibitors observed among Jewish patients, reflecting either greater pulmonary vascular or cardiovascular involvement, or differences in clinical management related to vascular disease burden.

Al-Sheikh et al. [12] reported poorer prognosis among Arab patients with SSc-associated ILD. No significant ethnic differences were observed in ILD prevalence, overall organ involvement, hospitalization rates, or mortality in our current cohort. However, differences in study design, cohort size, disease severity at presentation, and follow-up duration may account for these discrepancies. Moreover, the single-center design of our present study, conducted in a tertiary referral hospital, may reduce disparities related to referral patterns, disease monitoring, and access to specialized care.

Although Israel has a universal healthcare system, socioeconomic factors such as health seeking behavior, disease awareness, referral timing, and adherence to follow-up may still influence disease outcomes. Nevertheless, the similarity in treatment strategies, hospitalization rates, and survival observed in this cohort suggests that, within a specialized tertiary care setting, access to care and disease management were relatively comparable between Jewish and Arab patients.

Our findings indicate that while ethnic background may influence specific vascular manifestations of systemic sclerosis, it does not appear to translate into substantial differences in fibrotic organ involvement or short to midterm clinical outcomes when patients are managed in a specialized tertiary care environment. These results underscore the importance of considering ethnicity as a modifier of disease expression particularly vascular in-

volvement rather than as a determinant of overall disease severity.

LIMITATIONS

This study has several limitations. Its retrospective, single-center design, and modest sample size may limit the generalizability of the findings. The sample size was determined pragmatically based on data availability and feasibility within the retrospective design, rather than on formal power calculation. Therefore, selection bias cannot be entirely excluded. In addition, the lack of genetic data prevent exploration of underlying biological mechanisms contributing to ethnic differences. Despite these limitations, the study provides valuable insights into the clinical and serological characteristics of Jewish and Arab patients with SSc. Larger prospective studies with randomized or consecutive sampling are needed to validate these results.

CONCLUSIONS

Jewish and Arab patients with SSc show broadly similar clinical, serological, and therapeutic profiles, with ethnic differences observed mainly in vascular manifestations. Future studies incorporating genetic, molecular, and longitudinal data are warranted to better understand the mechanisms underlying these ethnic variations and their clinical implications.

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The tragedy in the lives of most of us is that we go through life walking down a high-walled lane with people of our own kind, the same economic situation, the same national background and education and religious outlook. And beyond those walls, all humanity lies, unknown and unseen, and untouched by our restricted and impoverished lives.

Florence Luscomb (1887–1985) American architect and women's suffrage activist

Writers, like teeth, are divided into incisors and grinders.

Walter Bagehot (1826–1877), English journalist, businessman, and essayist, who wrote extensively about government, economics, literature and race