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Impact of systemic sclerosis on foot skin hydration: A case-control study

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ABSTRACT

Introduction: Systemic sclerosis (SSc), or scleroderma, is a connective tissue disease characterized by excessive collagen production, leading to microvascular damage, fibrosis, and dysfunction of the skin and internal organs. The skin of the foot, due to its weight-bearing function and exposure to mechanical forces, may undergo alterations, contributing to the development of ulcers and other podiatric complications. However, little is known about foot skin hydration in patients with SSc. This study aims to assess the hydration level of the stratum corneum in the foot skin of patients with SSc.

Materials and methods: A case-control study was conducted at the Clinical Rheumatology Unit of the Regional University Hospital of Málaga (Spain). Participants included 47 patients diagnosed with SSc and 52 age- and sex-matched controls. Hydration measurements were performed at ten points on the foot using the Corneometer 825® device. Sociodemographic and clinical data, including smoking habits, were also collected.

Results: No significant differences were found in total foot hydration between the SSc and control groups ($p = 0.254$ for the right foot, $p = 0.835$ for the left foot), although a trend towards lower hydration was observed in the feet of affected patients. Differences were identified in specific areas of the foot, with lower hydration levels in the arch and the medial and lateral heel regions. In the medial arch of the right foot, the SSc group showed significantly lower hydration ($p = 0.006$). No significant associations were found with age, body mass index (BMI), physical activity, or water intake, but an association with smoking habits was observed in SSc patients; non-smokers had higher foot hydration levels compared to former and current smokers ($p = 0.06$).

Conclusion: Patients with systemic sclerosis present reduced hydration in specific areas of the foot, particularly in the medial arch. Smoking may negatively influence foot skin hydration. Further research is needed to explore these findings and their implications for podiatric care in patients with SSc.

1. Introduction

Systemic sclerosis (SSc), or scleroderma, is a connective tissue disease characterized by excessive collagen production, leading to microvascular and macrovascular damage, fibrosis of the skin, and internal organ involvement [1–3]. The countries with the highest incidence rates include Spain (29.23, 17.76–42.60 per 100,000 person-years), Italy (24.45, 20.64–28.82 per 100,000 person-years), Poland (22.23, 19.24–25.63 per 100,000 person-years), and the United Kingdom (19.88, 17.18–22.91 per 100,000 person-years) [4].

Musculoskeletal involvement is common in SSc and is associated with significant disability and substantial psychosocial and economic burdens [5]. The hands, particularly the metacarpophalangeal and proximal interphalangeal joints, are the most frequently affected [6,7]. Foot problems include Raynaud's phenomenon, which can sometimes progress to tissue loss or ulceration, subcutaneous calcinosis, skin thickening, callus formation, tendinopathy, foot ulcers, joint space narrowing, bone demineralization, joint subluxation, marginal erosions,

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and degenerative changes [8–10]. However, few studies have investigated the prevalence of foot-related problems and their potential disability impact [10–12].

The pathogenesis of SSc involves early vasculopathy, dysfunction of both the innate and adaptive immune systems, and ultimately, abnormal connective tissue formation [13].

In general, the skin of the foot, due to its weight-bearing function and exposure to mechanical forces, may undergo specific alterations that contribute to ulcer formation and other podiatric complications [14,15]. Several studies have demonstrated that assessing skin hydration is a useful indicator in the evaluation of both dermatological and systemic diseases [16]. In SSc patients, the presence of structural skin changes characteristic of the disease may be associated with a deficit in skin hydration. However, to date, these changes have not been specifically studied in the skin of the foot.

This study aims to provide novel insights into the hydration level of the stratum corneum in the foot skin and its potential impact on podiatric health, contributing to the development of more targeted care strategies for this population.

2. Materials and Methods

2.1. Study design

A case–control study was conducted following the guidelines of the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) [17]. This study was conducted in accordance with the Declaration of Helsinki and received approval from the Ethics Committees of the University of Malaga (CEUMA-91-06-05-2015-H) and the Andalusian Health Service (PEIBA ARC000118-07-2022).

2.2. Participants

Participants were recruited from the Podiatry Service of the Clinical Rheumatology Unit at the Regional University Hospital of Málaga, Spain. They were thoroughly informed about the study and signed an informed consent form prior to participation. Data collection was performed by a foot specialist with over five years of clinical experience, and all data were pseudonymized to ensure confidentiality.

Inclusion criteria for the case group were patients aged 18 years or older with a confirmed diagnosis of systemic sclerosis (SSc) according to the *American College of Rheumatology (ACR)* criteria [18,19].

Inclusion criteria for the control group were patients aged 18 years or older, able to walk at the time of evaluation, and without active dermatological conditions or any condition that could interfere with skin hydration measurement (e.g., psoriasis, eczema, or ichthyosis).

Exclusion criteria (applied to both groups) included foot amputations, open wounds, active infections, or a history of recent surgery in the evaluated area. Both groups were matched by age and sex.

2.3. Sample size calculation

The sample size was calculated considering a 1:1 case–control design, with a 95 % confidence level ($Z = 1.96$) and 80 % statistical power ($\beta = 0.20$). Given that SSc is a rare disease globally (~18.87 per 100,000 inhabitants, reaching ~45.4 per 100,000 in adult women), the expected difference in skin hydration between SSc patients and controls was based on previous studies. A prevalence of dry skin in 71 % of SSc patients was assumed, compared to 32 % in healthy individuals, yielding an estimated Odds Ratio (OR) of 5.0. Applying the standard formula for unpaired case-control studies, the minimum sample size was determined to be 25 cases and 25 controls.

2.4. Evaluation procedure

The study collected sociodemographic and clinical variables, including age, sex, Body Mass Index (BMI), duration of SSc (cases group), medical history, smoking habits, physical activity, previous dermatological treatments, and foot surgeries. BMI, body fat percentage, and water percentage were measured using a Tanita BC-545 N® scale.

Additionally, variables related to foot care habits were recorded, such as daily use of moisturizing creams, foot washing frequency, and daily water intake, assessed through a participant interview.

All measurements were conducted in a controlled environment, with room temperature and humidity levels recorded using a digital hygrometer (ThermoPro TP50®). Stratum corneum hydration (SCH) assessment was performed using a Corneometer 825® (CM 825; Courage & Khazaka, Cologne, Germany) at ten anatomical foot points, following a protocol used in previous studies [20,21]. Distal areas of the first, third, and fifth toes, plantar areas of the first, third, and fifth metatarsal heads, foot arch, medial and lateral plantar heel áreas and dorsal foot región. The Corneometer 825 is one of the most widely used methods for assessing SCH levels. It is a portable, non-invasive device that quantitatively and reproducibly measures epidermal hydration at a depth of 10–20 μm [22,23]. It uses the dielectric constant of water ($\varepsilon r = 81$) to detect capacitance changes related to skin water content. Each foot region was measured three times, and the mean value was calculated to reduce measurement error. The same measurement order (ten points) was followed in all participants to minimize bias. Subsequently, the average hydration level for each region (forefoot, midfoot, and rearfoot) and total plantar foot hydration was calculated. All measurements were performed by the same evaluator to ensure consistency and reduce interobserver variability.

Table 1
Sociodemographic and clinical characteristics of the case and control groups.

Sociodemographic and Clinical Characteristics	With SSc (Case Group) n = 47	Without SSc (Control Group) n = 52
Sex n (%)		
Male	1 (2.1)	12 (23.1)
Female	46 (97.9)	40 (76.9)
Age (years) md ± sd	59.64 ± 9.14 (37–76)	57.77 ± 8.23 (43–77)
Body fat percentage md ± sd	32.39 ± 7.53 (15.5–32.39)	32.50 ± 9.16 (11.6–51.2)
Body water percentage md ± sd	48.74 ± 5.19 (37.2–60.2)	48.81 ± 5.97 (36.7–62.8)
BMI (kg/m^2) md ± sd	24.27 ± 3.80 (17.5–37.3)	26.11 ± 5.64 (18.9–43.1)
Daily water intake (liters) md ± sd	1.37 ± 0.54 (0.5–2.5)	1.48 ± 0.55 (0.5–3)
Disease duration (years) md ± sd	13.96 ± 11.61 (2–46)	–
Smoking habit n (%)		
Current smoker	6 (12.8)	6 (11.5)
Ex-smoker	13 (27.7)	22 (42.3)
Never smoked	28 (59.6)	24 (46.2)
Physical activity n (%)		
Sedentary lifestyle	24 (51.1)	12 (23.1)
Physically active	23 (48.9)	40 (76.9)
Foot surgery n (%)		
Yes	3 (6.4)	5 (9.6)
No	44 (93.6)	47 (90.4)

2.5. Statistical analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS®) v. 28. Qualitative variables were described using frequency distributions (counts and percentages), while quantitative variables were expressed as means and standard deviations. The mean and range (minimum and maximum values) were calculated for the different foot regions.

Normality was assessed using the Kolmogorov-Smirnov test. Bivariate inferential analysis was conducted to identify associated risk factors, calculating the corresponding odds ratios and applying statistical

Table 2
Comparison of foot hydration in different areas between case and control groups.

Foot Areas	Hydration Case Group n = 47 md ± sd		Hydration Control Group n = 52 md ± sd	
	Right Foot	Left Foot	Right Foot	Left Foot
Tip of the 1st Toe	34.11 ± 16.31 (14.40–77.63)	34.66 ± 15.46 (10.90–74.37)	37.89 ± 16.59 (14.87–94.20)	34.87 ± 14.53 (9.47–86.23)
Tip of the 3rd Toe	48.34 ± 15.98 (23.47–82.13)	42.83 ± 16.15 (13.17–94.40)	46.28 ± 18.53 (10.63–94)	44.57 ± 20.89 (4.23–91.70)
Tip of the 5th Toe	46.99 ± 15.96 (23.23–88.87)	44.84 ± 16.13 (17.97–85.27)	47.87 ± 15.60 (10.93–83.22)	45.76 ± 17.34 (15.57–100.40)
Head of the 1st Metatarsal	19.86 ± 9.92 (5.17–51.30)	21.31 ± 10.84 (6.77–52.53)	21.57 ± 10.99 (5.67–52.37)	18.61 ± 10.15 (7.90–68.37)
Head of the 3rd Metatarsal	17.92 ± 11.10 (4.37–49.13)	17.20 ± 9.52 (4.27–54)	21.57 ± 16.74 (2.53–98.17)	18.09 ± 10.83 (5.10–51.83)
Head of the 5th Metatarsal	20.08 ± 9.86 (4.23–53.83)	20.50 ± 10.84 (4.10–55.23)	19.06 ± 10.36 (2.57–44.93	17.94 ± 9.45 (3.70–46.30)
Foot Arch	15.48 ± 9.56 (0–41.77)	17.58 ± 12.37 (0–62.33)	22.83 ± 13.99 (3.57–87)	19.81 ± 8.87 (3.63–43.37)
Medial Heel Area	11.98 ± 6.00 (3.47–29.10)	13.70 ± 8.62 (2.93–40.57)	15.27 ± 14.46 (3.63–98.23)	14.14 ± 11.22 (2.83–76.14)
Lateral Heel Area	15.59 ± 8.75 (2.90–41.57)	14.82 ± 8.13 (3.97–37.53)	18.09 ± 13.81 (2.53–81.87)	16.15 ± 11.10 (3.70–69.50)
Dorsal Foot	33.50 ± 12.99 (8.33–66.43)	33.49 ± 11.02 (14.07–58.47)	32.88 ± 7.73 (15.43–52.53)	30.88 ± 9.26 (11.23–49.93)
Total Mean Foot Hydration	26.37 ± 7.23 (11.59–42.51)	26.09 ± 7.74 (14.05–45.59)	28.33 ± 9.65 (10.37–61.10)	26.20 ± 8.77 (10.86–50.31)

Table 3
Comparison of the analysis by specific foot areas.

Foot Areas		Right Foot Hydration (md ± sd)	p-value	Left Foot Hydration (md ± sd)	p-value
Tip of the 1st Toe	Case Group	34.11 ± 16.31 (14.40–77.63)	0.128¥	34.66 ± 15.46 (10.90–74.37)	0.847¥
	Control Group	37.89 ± 16.59 (14.87–94.20)		34.87 ± 14.53 (9.47–86.23)	
Tip of the 3rd Toe	Case Group	48.34 ± 15.98 (23.47–82.13)	0.553	42.83 ± 16.15 (13.17–94.40)	0.645
	Control Group	46.28 ± 18.53 (10.63–94)		44.57 ± 20.89 (4.23–91.70)	
Tip of the 5th Toe	Case Group	46.99 ± 15.96 (23.23–88.87)	0.508¥	44.84 ± 16.13 (17.97–85.27)	0.926¥
	Control Group	47.87 ± 15.60 (10.93–83.22)		45.76 ± 17.34 (15.57–100.40)	
Head of the 1st Metatarsal	Case Group	19.86 ± 9.92 (5.17–51.30)	0.479¥	21.31 ± 10.84 (6.77–52.53)	0.215¥
	Control Group	21.57 ± 10.99 (5.67–52.37)		18.61 ± 10.15 (7.90–68.37)	
Head of the 3rd Metatarsal	Case Group	17.92 ± 11.10 (4.37–49.13)	0.250¥	17.20 ± 9.52 (4.27–54)	0.980¥
	Control Group	21.57 ± 16.74 (2.53–98.17)		18.09 ± 10.83 (5.10–51.83)	
Head of the 5th Metatarsal	Case Group	20.08 ± 9.86 (4.23–53.83)	0.524¥	20.50 ± 10.84 (4.10–55.23)	0.180¥
	Control Group	19.06 ± 10.36 (2.57–44.93		17.94 ± 9.45 (3.70–46.30)	
Foot Arch	Case Group	15.48 ± 9.56 (0–41.77)	0.006¥	17.58 ± 12.37 (0–62.33)	0.184¥
	Control Group	22.83 ± 13.99 (3.57–87)		19.81 ± 8.87 (3.63–43.37)	
Medial Heel Area	Case Group	11.98 ± 6.00 (3.47–29.10)	0.342¥	13.70 ± 8.62 (2.93–40.57)	0.947¥
	Control Group	15.27 ± 14.46 (3.63–98.23)		14.14 ± 11.22 (2.83–76.14)	
Lateral Heel Area	Case Group	15.59 ± 8.75 (2.90–41.57)	0.604¥	14.82 ± 8.13 (3.97–37.53)	0.758¥
	Control Group	18.09 ± 13.81 (2.53–81.87)		16.15 ± 11.10 (3.70–69.50)	
Dorsal Foot	Case Group	33.50 ± 12.99 (8.33–66.43)	0.773	33.49 ± 11.02 (14.07–58.47)	0.209
	Control Group	32.88 ± 7.73 (15.43–52.53)		30.88 ± 9.26 (11.23–49.93)	
Total Mean Foot Hydration	Case Group	26.37 ± 7.23 (11.59–42.51)	0.254	26.09 ± 7.74 (14.05–45.59)	0.835
	Control Group	28.33 ± 9.65 (10.37–61.10)		26.20 ± 8.77 (10.86–50.31)	

Student's t-test and ¥Mann-Whitney test.
$p < 0.05$ statistically significant.

tests such as the Chi-square test or Fisher's exact test for qualitative variables, and the Student's t-test or Mann-Whitney *U* test for quantitative variables, depending on data distribution. The correlation between continuous variables, such as age and hydration levels, was evaluated using Pearson's or Spearman's correlation coefficient, depending on data normality. A statistical significance level of $p < 0.05$ was established.

Age matching was performed manually by sorting the dataset by age and identifying subjects with similar ages for pairing.

3. Resultados

A total of 99 participants were recruited, of whom 47 (47.5 %) were patients diagnosed with systemic sclerosis (SSc) (case group), and 52 (52.5 %) comprised the control group. The mean age was 58.6 ± 8.66 years, and 86.9 % of the sample were women. In terms of nationality, 92.9 % were Spanish, followed by 2 % Argentine and Venezuelan, and 1 % Peruvian, Romanian, and Paraguayan. The sample characteristics (case and control groups) are detailed in Table 1.

The assessments were performed in a controlled environment, with an average room temperature of 23.82 ± 1.62 °C and an average humidity of 46 ± 6.11 %.

The mean total foot hydration in the SSc group was 26.37 ± 7.23 in the right foot and 26.09 ± 7.74 in the left foot, while in the control group, it was 28.33 ± 9.65 and 26.20 ± 8.77, respectively. No statistically significant differences were found in overall foot hydration between groups ($p = 0.254$ for the right foot, $p = 0.835$ for the left foot), although a trend toward lower hydration was observed in the feet of SSc patients (Table 2).

The hydration assessment of specific foot regions revealed that, in both groups, the least hydrated areas were the arch, medial heel, and lateral heel (Table 2). Moreover, a more pronounced hydration reduction was observed in these same areas in the SSc group compared to the control group, with a statistically significant difference in the medial arch of the right foot ($p = 0.006$) (Table 3).

The association between sociodemographic and clinical factors and foot hydration was explored. No significant differences were found in total foot hydration between men and women in either group (control group $p = 0.489$). Likewise, no significant correlations were observed with age (case group $p = 0.517$; control group $p = 0.918$), BMI (case group $p = 0.450$; control group $p = 0.547$), physical activity (case group $p = 0.243$; control group $p = 0.473$), or water intake (case group $p = 0.395$; control group $p = 0.487$). Additionally, no clear relationship was found between disease duration in SSc and foot hydration ($p = 0.927$).

However, an association with smoking habits was observed in the SSc group, where patients who had never smoked had higher foot hydration levels compared to former and active smokers ($p = 0.06$) (Table 4).

Table 4
Associations between different sociodemographic and clinical factors and foot hydration.

Sociodemographic and Clinical Characteristics	Total Foot Hydration Case Group (n = 47)	p-value	Total Foot Hydration Control Group (n = 52)	p-value
Sex				
Male	17.57	–	25.61 ± 12.39	0.489
Female	26.42 ± 7.20		27.79 ± 7.98	
Age				
< 55 years	27.51 ± 7.34	0.517 χ	27.36 ± 7.10	0.918 χ
55–65 years	26.62 ± 7.24		26.88 ± 9.63	
> 65 years	24.33 ± 7.32		28.44 ± 11.80	
Body Fat Percentage	r = −0.174	0.243[a]	r = −0.046	0.756[a]
Body Water Percentage	r = 0.189	0.204[a]	r = 0.020	0.891[a]
BMI	r = −0.92	0.450[a]	r = − 0.088	0.547[a]
Daily Water Intake (liters)	r = −0.127	0.395[a]	r = − 0.102	0.487[a]
Disease duration (years)				
< 10 years	26.35 ± 8.24	0.927¥	–	–
10–20 years	25.50 ± 7.31			
> 20 years	26.62 ± 5.81			
Smoking habit				
Current smoker	22.06 ± 4.48	0.06 χ	32.73 ± 13.61	0.364 χ
Ex-smoker	23.87 ± 6.91		27.03 ± 9.67	
Never smoked	28.23 ± 7.32		26.34 ± 7.08	
Physical activity				
Sedentary lifestyle	27.45 ± 6.81	0.243¥	29.05 ± 9.88	0.473¥
Physically active	24.96 ± 7.60		26.79 ± 8.87	
Foot Surgery				
Yes	23.79 ± 2.97	0.552¥	28.03 ± 3.68	0.869¥
No	26.40 ± 7.43		27.24 ± 9.40	

¥ Student's t-test.
χ ANOVA test.
$p < 0.05$ statistically significant.
[a] Pearson correlation.

4. Discussion

Our results indicate that patients with systemic sclerosis (SSc) generally exhibit lower skin hydration in the foot compared to healthy individuals, although this difference was not statistically significant. This decrease was particularly evident in the arch and heel, where the lowest hydration values were observed in both groups. The reduction was most pronounced in the medial arch of the right foot in SSc patients, with statistically significant differences.

This finding suggests a potential localized dehydration pattern, which could be attributed to biomechanical differences in gait, plantar load distribution, or vascularization in the affected areas. In fact, previous studies have described that patients with SSc exhibit gait abnormalities and altered plantar pressure distribution, which could contribute to decreased hydration in specific foot regions [14,15].

Vascular dysfunction and dermal fibrosis are key characteristics of SSc, and they may impair the skin's barrier function, affecting water retention capacity and increasing susceptibility to dryness and ulceration [24–26]. Some studies provide insight into the impact of the disease on the hands [6,7]. However, there is a significant lack of data regarding its effects on the feet, which are crucial for mobility and quality of life [10], Notably, SSc has been reported to significantly impact foot function, particularly in terms of pain levels [27].

Our results indicate that the most hydrated areas in both groups were the toes, aligning with previous studies on hydration distribution in the general population [20,21], Conversely, the heel region exhibited the lowest hydration levels.

We did not observe a decrease in hydration levels with age in either group, contrasting with the findings of Chicharro et al. [21]. This discrepancy may be due to the fact that our sample consisted of individuals aged 40–75 years, excluding younger participants, which could have reduced the influence of age on hydration levels.

Additionally, no significant associations were found between hydration and other factors such as age, Body Mass Index (BMI), body fat percentage, total body water percentage, daily water intake, or physical activity. These findings suggest that foot skin hydration is not significantly influenced by these variables. However, previous studies have reported that external factors such as environmental exposure, footwear use, and mechanical friction can influence plantar skin hydration, and these variables should continue to be considered in future research [16,23].

Only an association with smoking habits was observed in the case group, showing that patients who had never smoked exhibited higher hydration levels compared to former and current smokers. This suggests that tobacco use may contribute to reduced skin hydration in patients with SSc, possibly due to its vasoconstrictive effects and its negative impact on microcirculation, factors that have already been described in the pathophysiology of the disease.

This study has several strengths. First, the sample size exceeded the initial estimate, providing greater statistical power. This sample size allows the detection of significant differences in skin hydration between the two groups with adequate reliability, reinforcing the robustness of the results. Additionally, this is the first study to compare foot skin hydration in patients with systemic sclerosis and healthy individuals, providing novel data in an understudied area. The use of a validated and widely used instrument such as the Corneometer ensures an objective and reproducible evaluation [22], providing reliable information on skin condition under different clinical conditions [28,29]. Finally, the study design, including an age- and sex-matched control group, allows for stronger conclusions regarding the comparison of skin hydration in patients with and without SSc.

However, some limitations should be acknowledged. Skin hydration can be influenced by multiple external factors, such as temperature, ambient humidity, and the use of moisturizing products, which were not fully controlled. Secondly, the study is based on cross-sectional measurements, making it impossible to determine whether foot hydration in SSc patients changes over time with disease progression or specific interventions.

Given that systemic sclerosis is a disease with high morbidity and significant skin involvement, future research should explore whether foot hydration is related to SSc severity, the progression of cutaneous fibrosis, or the risk of developing podiatric complications such as digital ulcers or pressure-related lesions. Additionally, longitudinal studies could evaluate whether skin hydration changes over time in these patients and whether certain interventions, such as the use of specific emollients or microcirculation-targeted therapies, can improve hydration in vulnerable foot regions.

5. Conclusion

The findings of this study suggest that patients with systemic sclerosis (SSc) exhibit generally lower skin hydration in the foot compared to healthy individuals, particularly in the arch and heel regions, with significant differences observed in the medial arch of the right foot.

The most hydrated areas in both groups were the toes, consistent with previous studies in the general population.

Additionally, patients who had never smoked showed higher

hydration levels compared to former and current smokers, suggesting that smoking may negatively influence skin hydration in SSc patients.

These results open new avenues for research on the relationship between systemic sclerosis, skin hydration, and podiatric complications, particularly in specific anatomical regions.

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Conflict of interest

The authors declare that there are not conflict of Interest.

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