

Raynaud's Phenomenon: Its Prevalence in Systemic Sclerosis and Its Relationship with the Onset and with the Subsets of Systemic Sclerosis – An Experience from the Kashmir Valley, India

T Arif, I Hassan

ABSTRACT

Background: Raynaud's phenomenon (RP) is a very common clinical sign in patients with systemic sclerosis (SSc). Within the same country, its prevalence may vary depending on climatic changes. Usually, it predates the onset of cutaneous involvement in SSc, but in rare cases, it can follow the skin changes in these patients. Its evolution differs in the two subsets of SSc (limited and diffuse) and can serve as a clinical pointer to differentiate between the two disease subsets.

Objective: To study the prevalence of RP in SSc and report its relationship with the onset and with the subsets of SSc.

Methods: A prospective observational study of 56 patients with SSc was carried out at the Postgraduate Department of Dermatology, STDs and Leprosy of Shri Maharaja Hari Singh Hospital, Kashmir, India.

Results: Of the 56 patients, 40 (71.4%) had limited SSc (lSSc) and 16 (28.6%) had diffuse SSc (dSSc). Raynaud's phenomenon was seen in 54 (96.4%) of the 56 patients, comprising 39 (97.5%) of the 40 patients with lSSc and 15 (93.8%) of the 16 patients with dSSc. Thirteen (81.3%) patients with dSSc and two (5%) patients with lSSc had a short history (less than one year) of RP preceding the skin changes. Twenty-six (65%) patients with lSSc and only two (12.5%) patients with dSSc had a long history (more than one year) of RP preceding the cutaneous manifestations. Six (15%) of the 40 patients with lSSc had a simultaneous onset of RP and skin changes. In five (12.5%) of the 40 patients with lSSc, RP followed the skin changes.

Conclusion: Raynaud's phenomenon was very common in these patients with SSc. Patients with lSSc had a longer history of RP compared with those with dSSc. It could occur simultaneously with skin changes or even postdate the onset of skin changes.

Keywords: Observational study, Raynaud's phenomenon, skin changes, systemic sclerosis

Fenómeno de Raynaud: su prevalencia en la esclerosis sistémica y sus relación con el inicio y los subconjuntos de la esclerosis sistémica – una experiencia del Valle de Kashmir, India

T Arif, I Hassan

RESUMEN

Antecedentes: El fenómeno de Raynaud (FR) es una manifestación clínica muy común en pacientes con esclerosis sistémica (ES). Dentro del mismo país, su prevalencia puede variar en función de los cambios climáticos. Generalmente, precede al inicio de la afección cutánea en la ES, pero en raros casos puede seguir a los cambios de piel en estos pacientes. Su evolución difiere en los dos subconjuntos de ES (limitada y difusa), y puede servir como indicador clínico para poder diferenciar entre estos dos subconjuntos.

Objetivo: Estudiar la prevalencia de FR en la ES y reportar sus relación con el inicio y los subconjuntos de ES.

Métodos: Se realizó un estudio observacional prospectivo de 56 pacientes con ES en el Departamento de Posgrado de Dermatología, Enfermedades de Transmisión Sexual y Lepra del Hospital Shri Maharaja Hari Singh, India.

Resultados: De los 56 pacientes, 40 (71.4%) tenían ES limitada (ESL) y 16 (28.6%) tenían ES difusa (ESD). El fenómeno de Raynaud se observó en 54 (96.4%) de los 56 pacientes, abarcando 39 (97.5%) de los 40 pacientes con la variante ESL y 15 (93.8%) de los 16 pacientes con la variante ESD. Trece (81.3%) pacientes con ESD y dos (5%) pacientes con ESL tenían una historia corta (menos de un año) de FR, que precedía a los cambios cutáneos. Veintiséis pacientes (65%) con ESL y solamente dos (12.5%) pacientes con ESD tenían una historia larga (más de un año) de FR, que precedía a las manifestaciones cutáneas. Seis (15%) de los 40 pacientes con ESL tuvieron un inicio simultáneo de FR y cambios de piel. En cinco (12.5%) de los 40 pacientes con ESL, FR siguió a los cambios de la piel.

Conclusión: El fenómeno de Raynaud fue muy común en estos pacientes con ES. Los pacientes con ESL tuvieron una historia más larga de FR, a diferencia de aquellos con ESD. El fenómeno de Raynaud podía ocurrir simultáneamente con cambios cutáneos o incluso presentarse tras el comienzo de los cambios cutáneos.

Palabras clave: Estudio observacional, fenómeno de Raynaud, cambios cutáneos, esclerosis sistémica

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INTRODUCTION

Maurice Raynaud described a phenomenon characterized by sequential colour changes of the fingers and toes upon exposure to cold or to emotional stimuli. It can also involve other parts of the body, such as the nose, lips and ears. The colour changes occur episodically and in a triphasic manner with white, blue and red discolouration in that order (1). Raynaud's phenomenon (RP) can be primary (idiopathic) or secondary (associated with an underlying disease). Primary RP is caused by functional changes in blood vessels and/or their innervations and is a benign condition. On

the other hand, patients with secondary RP may have digital ulceration, gangrene and scarring. Various disorders, such as systemic sclerosis (SSc), vasculitis, atherosclerosis and systemic lupus erythematosus, can be associated with secondary RP (2). Raynaud's phenomenon has a prevalence of 5–20% in the general population (3–5). It affects women more than men. Through a postal survey, Silman *et al* estimated a prevalence of 19% in women and 11% in men. However, a prevalence of 21% in women and 16% in men was seen at a physician's office (3). The prevalence of RP is affected by climactic changes. Cool geographic

areas have a higher prevalence (16.8% in Tarentaise, Savoie, France), while warm climactic regions have a lower prevalence [5% in Charleston, South Carolina, United States of America] (5). The prevalence of RP in SSc has been reported to be 90–98% (6). Raynaud's phenomenon usually precedes skin changes in SSc, but the time duration between the onset of RP and the development of skin disease varies between the two subsets of SSc (limited and diffuse) and has diagnostic importance. While patients with the diffuse variant of SSc (dSSc) have a short history (less than one year) between the onset of RP and the development of skin changes, patients with limited SSc (lSSc) may have a long history of many years of RP preceding the cutaneous disease (7). However, RP and cutaneous changes can occur simultaneously or even postdate cutaneous sclerosis in such patients (8). The present study was carried out to estimate the prevalence of RP in patients with SSc in Kashmir Valley, India, and to address the relationship in its evolution with the skin changes in SSc with respect to its subsets.

SUBJECTS AND METHODS

This was a prospective observational study of 56 patients with SSc carried out at the Postgraduate Department of Dermatology, STDs and Leprosy of Shri Maharaja Hari Singh Hospital, India. The diagnosis of SSc was made as per the criteria of the American College of Rheumatology (9). Patients with SSc were classified into the lSSc and dSSc variants according to the classification of Le Roy *et al* (7). Diagnosis of RP was based on the history of sequential colour changes in the fingers. However, where the typical triphasic colour changes of pallor, cyanosis and redness were not present, digital pallor was taken as diagnostic of RP. Data collected included age, gender, occupation, clinical

characteristics of the disease (age at onset, duration, extent of skin involvement), type of SSc (diffuse or limited) and evolution of skin changes in relation to RP.

The inclusion criteria were: (a) all newly and already diagnosed patients with SSc; and (b) both genders.

The exclusion criteria were: (a) presence of pregnancy or a history of pregnancy in the previous six months; (b) other connective tissue diseases or mixed connective tissue diseases; (c) diabetes mellitus; and (d) patients on drug treatment (such as beta-blockers) or with an occupational history (such as the use of a vibratory tool).

RESULTS

Of the 56 patients with SSc, 50 (89.3%) were female and 6 (10.7%) were male, with a female to male ratio of 8.3:1. The average age of the patients was 44.96 ± 13.80 years [range: 21–80] (Table 1). Most of the patients (17, 30.4%) were in the age group of 50–59 years, followed by 40–49 years (12, 21.4%).

The average age of the onset of disease in SSc in females (35.2 ± 13.3 years) was earlier than that in males (42.3 ± 13.5 years), but it was statistically insignificant, with a *p*-value of 0.219 (Table 2). However, the average duration of disease in females (9 ± 7 years) was lower than that in males (9.3 ± 11.98 years); it was

Table 1: Demographic profile of the patients with SSc (n = 56)

Age group (years)	Number	%
20–29	7	12.5%
30–39	10	17.9%
40–49	12	21.4%
50–59	17	30.4%
≥ 60	10	17.9%

Mean \pm standard deviation = 44.96 ± 13.80 years
Range = 21–80 years

Table 2: Clinical parameters of the patients with SSc (n = 56)

	Gender	Number	Mean	Standard deviation	<i>p</i>	Remarks
Age at onset	Male	6	42.3 years	13.5 years	0.219	Not significant
	Female	50	35.2 years	13.3 years		
Duration	Male	6	9.3 years	11.9 years	0.927	Not significant
	Female	50	9.0 years	7.00 years		
Gender	Type of SSc				<i>p</i>	Remarks
	Limited (n = 40)		Diffuse (n = 16)			
	Number	%	Number	%		
Male	6	15	0	0	0.168	Not significant
Female	34	85	16	100		
Total	40	100	16	100		

also statistically insignificant ($p = 0.927$). According to the classification of Le Roy *et al*, 40 (71.4%) patients had ISSc while the remaining 16 (28.6%) patients had dSSc.

Raynaud’s phenomenon was seen in 54 (96.4%) of the 56 patients, comprising 39 (97.5%) of the 40 patients with ISSc and 15 (93.8%) of the 16 patients with dSSc, as shown in Table 3. However, its prevalence in females (98%) was higher than that in males (83.3%). Among the patients with ISSc, females (100%) had a greater prevalence of RP than men (83.3%). None of the men had dSSc.

Table 4 shows the onset of RP and skin changes in relation to the two subsets of SSc. Among the patients with dSSc, 81.3% had a short history (less than one year) of RP preceding the skin changes, and only 5% of those with ISSc had a short history of it. This was statistically highly significant ($p < 0.001$). Conversely, 65% of the patients who had ISSc had a long history (more than one year) of RP preceding skin disease, and only 12.5% of those who had dSSc had a long history of it. This was also statistically highly significant ($p = 0.0008$). It should be noted that 15% of the patients with ISSc had a simultaneous onset of RP and skin changes while in 12.5% of the patients with ISSc, RP followed skin changes.

DISCUSSION

In this study, females comprised 89.3% of the patients with SSc which is in accordance with various studies. Lahcene *et al* studied 194 patients with SSc for oesophageal involvement. In their study group, 87.6% of the patients were female which is consistent with our study (10). In our study, the average age of onset of disease in patients with SSc was earlier in females (fourth decade, 35.2 years) than that in males (fifth decade, 42.3 years). Similar observations were made by Medsger and Masi who studied the epidemiology of SSc and found the peak onset of disease in females to be in the fourth decade and later in males (11). The ISSc subset predominated

in our study which is consistent with previous studies (10, 12).

Tuffanelli and Winkelman studied 727 cases of SSc and found the prevalence of RP to be 90–98% (6). Sharma *et al* from northern India reported a prevalence of 92.9% in their 100 patients with SSc (13). In our study of 56 cases of SSc, the prevalence of RP was found to be 96.4% and is consistent with the above-mentioned studies. However, from South India, the reported frequency was lower (46.9%) which is explained by the hotter climate compared to the North (14).

According to LeRoy *et al*, dSSc has a short history (less than one year) between the onset of RP and the development of skin changes while RP may precede skin changes by many years in ISSc (7). This was observed in our study as well: 81.3% of the patients with dSSc had a short history (less than one year) of RP preceding the skin changes while, conversely, 65% of the patients with ISSc had a long history (more than one year) of RP preceding skin disease. In some cases, RP may follow the onset of cutaneous or other extra-cutaneous manifestations in SSc (15). Similar findings were observed in our study as well. In five (12.5%) of the 40 patients with ISSc, RP followed the cutaneous changes while in six (15%) of the 40 patients with ISSc, RP and cutaneous changes occurred simultaneously (Table 4). This finding has been rarely reported in the literature. It should be noted that no patients with dSSc had RP which occurred concurrently with the skin sclerosis or followed it. Hence, RP was a very common clinical sign in patients with SSc, and its evolution had a definite relationship with the onset of skin changes. Most of the times, it

Table 3: Prevalence of Raynaud’s phenomenon in the patients with SSc (n = 56)

Variable	Overall	Female	Male
SSc (n = 56)	54 (96.4%)	49 (98%)	5 (83.3%)
Limited SSc (n = 40)	39 (97.5%)	34 (100%)	5 (83.3%)
Diffuse SSc (n = 16)	15 (93.8%)	15 (93.8%)	0

Table 4: Raynaud’s phenomenon in relation to skin changes in patients with SSc

	Onset of Raynaud’s phenomenon			
	Preceded (< 1 year of onset of skin disease)	Preceded (> 1 year of onset of skin disease)	Simultaneous with skin changes	Followed skin changes
Diffuse (n = 16)	13 (81.3%)	2 (12.5%)	–	–
Limited (n = 40)	2 (5%)	26 (65%)	6 (15%)	5 (12.5%)
<i>p</i>	< 0.001	0.0008	0.168	0.309

predated the skin changes, but rarely it could postdate them as well.

CONCLUSION

There was a high prevalence of RP in patients with SSc. Though RP was usually the initial sign in patients with SSc preceding the skin changes, it could occur concurrently or follow cutaneous changes. The two subsets of SSc showed a different historical relationship with the development of RP which could help to differentiate between the two disease subsets.

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