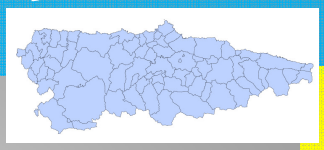
# Systemic sclerosis in Asturias (Spain) in 1996-2012 period



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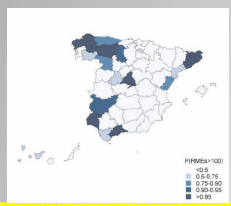



**Incidence of** Diffuse Diseases of Conective Tissue (among them, ISystemic Sclerosis). Spain. Extracted from *Atlas Nacional de Enfermedades Raras*, RepiER-2006

## BACKGROUND AND OBJECTIVES

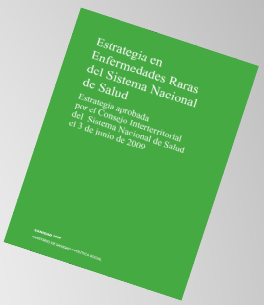
To improve the available information on RD and the existing resources for their care and to analyse existing RD registries at regional level are two of the *Rare Diseases Strategy of the Spanish National Health System* objectives.

We aim to further our knowledge about systemic sclerosis (SSc) in Asturias (a Region in the North of Spain) in order to answer to the needs of patients, health professionals, researchers an the people in charge of health departments.

Systemic sclerosis (SSc) is a chronic immunological disease that affects connective tissue.
Women of 40s are predominantely affected.
CREST syndrome is the typical clinical manifestation. Systemic manifestations include esophageal dysmotility, pulmonary disfunction, pulmonary fibrosis, cardiac and renal involvement.

SSc is generally subdivided into **limited cutaneous SSc** (lcSSc) and **diffuse cutaneous SSc** (dcSSc) depending on the extent of skin sclerosis and by the forms of organ involvement. Thera are other subsets of SSc as **SSc sine scleroderma** (typical vascular features and visceral fibrosis without skin sclerosis), **environmentally-induced scleroderma** (diffuse distribution of skin sclerosis in combination with a history of exposure to agents that precipitate scleroderma as vinyl chloride, epoxy resins, etc.) and **Overlap syndromes** (features of SSc in combination with manifestations of other rheumatic diseases).

Diagnosis and treatment are based on typical clinical manifestations (Table 1).




## Methodology

**Cross-sectional survey** of a 17 year period (1996-2012)

Description of the epidemiology of SSc and estimation of its prevalence in our community (total population is roughly 1,000,000 inhabitants), sex, age distribution and evolution.

Data forms with more relevant characteristics of disease and patients' information were filled for each patient diagnosed with SSc (IDC9-MC 710.1) in our Region from 1996 to 2012. Information were get from hospital discharge Minimun Basic Data Set (MBDS) registries and patients' medical records. All these cases are registered in the Registry of Rare Diseases of Asturias, partially integrated in the National Spanish Registry (SpainRDR).

Finally, information was analysed and a leaflet with summarized results was designed and distributed in clinics and medical centers.

**Table 1. The ACR/EULAR criteria for the classification of Systemic Sclerosis**

| Item | Weight/score* |
|---|---|
| *Skin thickeninf of the fingers of both hands extending proximal to the metacarpophalangeal joints (sufficient criterion)* | 9 |
| Skin thickening of the fingers (only count the higher score)<br>• Puffy fingers<br>• Sclerodactyly of the fingers (distal to the metacarpophalangeal joints but proximal to the proximal interphalangeal joints) | 2<br>4 |
| Fingertip lesions fingers (only count the higher score)<br>• Digital tip ulcers<br>• Fingertip pitting scars | 2<br>3 |
| Telangiectasia | 2 |
| Abnormal nailfold capillaries | 2 |
| Pulmonary arterial hypertension and/or interstitial lung disease (maximun score is 2)<br>• Pulmonary arterial hypertension<br>• Interstitial lung disease | 2<br>2 |
| Raynaud's phenomenon | 3 |
| SSc-related autoantibodies (anticentromere, anti-topoisomerase I [anti-Scl-70], anti-RNA polymerase III) (maximun score is 3) | 3 |

## RESULTS

**Figure 1. SSc by Sex. Asturias, 1996-2012**

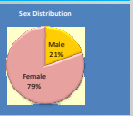



**Figure 2. SSc by Age at Diagnose. Asturias, 1996-2012**

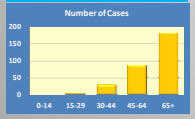
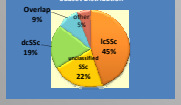



**Figure 4. SSc Subtypes Asturias, 1996-2012**




A total of **308** cases were registered from 1996 to 2012.
Cumulative Incidence in the period is 29 cases per 100,000 inhabitants and estimated period **incidence** is 17 cases per 1,000,000 person-year.
SSc is more common among women (79%) with an estimated incidence rate of 26 cases per 1,000,000 women-year.
Less frequent in men with 7 cases per 1,000,000 men-year. **(FIGURE 1)**
Incidence also differs among aged-diagnosed groups. More older, the patient, more frequent the disease **(FIGURE 2)**.
Evolution of new diagnosed cases is relatively constant , about 20 cases per year **(FIGURE 3)**

Raynaud's phenomenon is the first (manifested years before of disease diagnosed) and most common sign of SSc **(TABLE 2)** followed by cutaneous (oedema and skin thickening) and articular symptons (stiffness and joint pain). Main extracutaneous systemic manifestations were dysphagia, pulmonary fibrosis (mainly life-threatening complication) and musculoeskeletal involvement, **(TABLE 3)**.

More frequent subtype of SSc was its limited form and less frequents others as SSc sine escleroderma. A nine percent of patients presented overlap syndromes **(FIGURE 4)**.

Progression of disease is unpredictable. It highly varies among patients, although dcSSc has worse prognosis. A few number of cases were even asymptomatically for many years after diagnoses.

Aproximately, half of the SSc patients still live. In Asturias, survival rate is 72% at 5 years. First cause of death was pulmonary complication (intersticial neumonitis and pulmonary fibrosis in lcSSc and pulmonary hypertension in dcSSc). Mortality was proportionally higher in males (61% men versus 43% women).

Diagnostic strategies more frequently used were serological tests (antinuclear antibodies, **FIGURE 5**), serum and urine electrophoresis (high ESR, hematuria) and capillaroscopy.

Drugs more used were NSAID (79%), corticosteoroids (67%, mainly in women), immunosuppresive agents (26%), PPIs (26%), protaglandins (23%) and ciclofosfamid (12%).

25 patients (mainly with dcSSc) were treated with orphan drugs: TRACLEER (Bosentan), antagonist of human endothelin receptors, for treatment of pulmonary arterial hypertension (PAH) or to reduce the number of new digital ulcers in patients with systemic sclerosis and ongoing digital ulcer diseaseand and REVATIO (sildenafil), an specific inhibitor of phosphodiesterase type 5, for reduce PAH.

In cases of severe afectation other treatments as surgery (digit amputation) and oxigenoterapy were used.

**Table 2. Systemic Sclerosis. Porportion of CREST Symptoms. Asturias, 1996-2012**

| CREST | Male % | Female % | Total % |
|---|---|---|---|
| Calcinosis | 18,9 | 41,0 | 39,5 |
| Raynaud | 68,6 | 85,9 | 81,5 |
| Esophageal dysmotility | 40,6 | 44,2 | 44,8 |
| Sclerodactyly | 52,8 | 58,2 | 56,9 |
| Telangiectasia | 47,2 | 51,7 | 50,4 |

**Figure 3. SSc by Year of Diagnoses Asturias, 1996-2012**


**Table 3. Systemic Sclerosis. Clinical manifestations (General& Cutaneous) Asturias, 1996-2012**

| | Male % | Female % | Total % |
|---|---|---|---|
| **General manifestations** | | | |
| Raynaud phenomenon | 83,3 | 93,5 | 90,7 |
| Skin hardening | 25 | 16,1 | 18,6 |
| Joint Pain | 75 | 77,4 | 76,7 |
| Stiffness | 58,3 | 48,4 | 51,2 |
| Dysnea | 33,3 | 25,8 | 27,9 |
| Weight Loss | 25 | 9,7 | 14 |
| **Skin manifestations** | | | |
| Oedema | 58,3 | 77,4 | 72,1 |
| Skin thickening | 58,3 | 45,2 | 48,8 |
| Disappearance of folds | 16,7 | 6,4 | 9,3 |
| Inexpressive face | 16,7 | 19,3 | 18,6 |
| Microstomy | 33,3 | 38,7 | 37,2 |
| Circumoral Wrinkles | 16,7 | 3,2 | 7 |
| Skin atrophy | 16,7 | 12,9 | 14 |
| Sores | 25 | 38,7 | 34,9 |
| Calcinosis | 16,7 | 41,9 | 34,9 |
| Pigmentary changes | 8,3 | 32,2 | 25,6 |

**Figure 5. Serum Autoantibodies Asturias, 1996-2012**

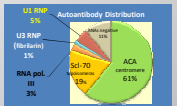



**Table 4. Systemic Sclerosis. Clinical manifestations (systemic). Asturias, 1996-2012**

| | Male % | Female % | Total % |
|---|---|---|---|
| **VISCERAL INVOLVEMENT** | | | |
| Dysphagia | 83,3 | 93,5 | 90,7 |
| Lower esophageal sphincter failure | 25 | 16,1 | 18,6 |
| Reflux Esophagitis | 75 | 77,4 | 76,7 |
| Pneumatosis | 58,3 | 48,4 | 51,2 |
| Primary biliary cirrhosis | 33,3 | 25,8 | 27,9 |
| Lower esophageal sphincter failure | 25 | 9,7 | 14 |
| **CARDIORESPIRATORY INVOLVEMENT** | | | |
| Pulmonar fibrosis | 58,3 | 45,2 | 48,8 |
| Pleuritis | 8,3 | 6,4 | 7 |
| Pericarditis | 0 | 3,2 | 2,3 |
| Pulmonary hypertension (PAH) | 8,3 | 19,3 | 16,3 |
| Arrhythmia | 8,3 | 6,4 | 7 |
| Congestive Heart Failure | 25 | 12,9 | 16,3 |
| **RENAL INVOLVEMENT** | | | |
| Nephropathy | 0 | 9,7 | 7 |
| Malignant Hypertension | 8,3 | 6,4 | 4,7 |
| Renal Failure | 0 | 9,7 | 7 |
| **Barrett's esophagus** | 8,3 | 3,2 | 4,7 |
| **Sjögren Syndrome** | 8,3 | 19,3 | 16,3 |
| **Wheezes** | 16,7 | 6,4 | 9,3 |
| **MUSCULOESKELETAL INVOLVEMENT** | | | |
| Knee friction | 16,7 | 12,9 | 14 |
| Tendon friction rub | 25 | 12,9 | 16,3 |
| Flexion Contractures | 25 | 9,7 | 14 |
| Digital scars | 58,3 | 45,2 | 48,8 |

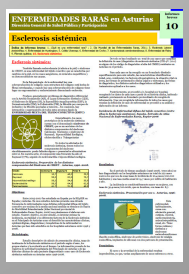
## CONCLUSIONS

Autonomic RD Registry have contributed to the epidemiological surveillance of SSc and to analysed SSc morbimortality pattern in Asturias. Our data could also be compared with ones available from other Spanish regions in order to find differences or similarities and further pur knowdlege of this chronic and rare disease.

Electronic dissemination of this study results (leaflet format) in website www.astursalud.es makes description and characteristics of SSc visible to all health professionals.

There aren't a curative treatment. It's aimed to palliate symptoms. Recent use of orphan drugs appears to improve ulcers and pulmonary disease progression.

Epidemiological patterns of SSc in Asturias are quite similar to other cases series published, with same proportion by sex, incidence rates, subtypes and incidence evolution.




**Sclerosis Systemic Leaflet**

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