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## Prevalence of Sjögren's syndrome in autoimmune diseases

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**SUMMARY** Investigations were carried out in 122 patients in order to identify features of Sjögren's syndrome (keratoconjunctivitis sicca and xerostomia). There were 78 patients with autoimmune diseases (rheumatoid arthritis 21, scleroderma 16, sicca syndrome 16, primary biliary cirrhosis 14, and other autoimmune disorders 11), 11 patients with chronic liver disease other than primary biliary cirrhosis, and 33 patients with a variety of non-autoimmune conditions or no obvious disease. Keratoconjunctivitis sicca was diagnosed by Schirmer's test and rose bengal staining. The oral component was diagnosed by labial biopsy and salivary scintigraphy. Forty nine patients had a definite Sjögren's syndrome, and 77 patients had the syndrome definitely or probably. Definite Sjögren's syndrome occurred in 62% of patients with rheumatoid arthritis, in 69% of patients with scleroderma, and in 71% of patients with primary biliary cirrhosis. Sjögren's syndrome was not present in any of the patients with non-autoimmune conditions. These results show that in an unselected group of patients with Sjögren's syndrome the prevalence of rheumatoid arthritis (26%), scleroderma (22%), sicca syndrome (22%), and primary biliary cirrhosis (20%) is similar. Also the occurrence of Sjögren's syndrome in primary biliary cirrhosis is even higher than that in rheumatoid arthritis.

**Key words:** rheumatoid arthritis, scleroderma, primary biliary cirrhosis, xerostomia, sicca syndrome, keratoconjunctivitis sicca.

The prevalence of definite Sjögren's syndrome in diseases such as rheumatoid arthritis, scleroderma, primary biliary cirrhosis, and other autoimmune disorders is not well established.<sup>1,2</sup> This paper describes an investigation into the prevalence of Sjögren's syndrome in a group of patients with a variety of autoimmune diseases and in patients with non-autoimmune conditions.

### Patients and methods

A total of 122 patients was considered for inclusion in this study. There were 78 patients with autoimmune diseases (rheumatoid arthritis 21, scleroderma 16, sicca syndrome 16, primary biliary cirrhosis 14, and other autoimmune diseases 11), 28 patients with

non-autoimmune disorders (chronic liver disease other than primary biliary cirrhosis 11, non-hepatic diseases 17), and 16 healthy subjects. Of the 122 patients, 108 were women and 14 were men. The average age was 52 years with a range of 17 to 83 years.

### DIAGNOSIS OF KERATOCONJUNCTIVITIS SICCA

The diagnosis of keratoconjunctivitis sicca was based on the results of (a) a clinical questionnaire, (b) type I Schirmer's test, and (c) rose bengal staining. The clinical questionnaire was designed to assess symptoms of burning, itching, and blurring of vision. The questions were addressed also to a group of 125 outpatients; positive results were achieved in 8% of the cases. For the Schirmer's test a piece of 5×35 mm Whatman 41 filter paper was inserted into the conjunctival sac over the lower eyelid; moistening of less than 5 mm in both eyes was regarded as abnormal. The test was negative in 20 control

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subjects. One drop of 1% rose bengal solution was instilled into each eye and staining of the conjunctiva and cornea was assessed by direct vision and by slit lamp examination. Holm's grades A and B were considered as evidence of disease.<sup>3</sup> Rose bengal staining was negative in 20 control subjects.

#### DIAGNOSIS OF THE ORAL COMPONENT

The diagnosis of the oral component was based on the results of (a) a clinical questionnaire, (b) physical examination of the mouth and salivary glands, (c) gammascan of the salivary glands, and (d) labial biopsy. The clinical questionnaire was designed to assess symptoms of dryness of the mouth from lack of the normal secretion. This questionnaire was addressed also to 125 outpatients; positive results were obtained in 8% of the cases. Physical examination evaluated the presence of salivary gland enlargement, cheilosis, cracks at the corners of the mouth, dry mouth, atrophy of the lingual papillae, and fissures on the tongue. A Picker Dyna 4 gammacamera was used for salivary scintigraphy. Gammascans were taken after 5, 10, 15, 30, 45, and 60 min of an intravenous injection of 4 mCi (148 MBq) of <sup>99</sup>Tc. Schall's grades III and IV were regarded as abnormal.<sup>4</sup> No abnormalities were found in 20 control subjects. Ten millimetre punch biopsy specimens were taken from the lower lip. Chisholm's histological grades III and IV were regarded as abnormal.<sup>5</sup> No abnormalities were found in 20 consecutive postmortem biopsy specimens from patients who died of diseases other than autoimmune disorders or chronic liver dysfunction.

#### DIAGNOSTIC CRITERIA

A definite diagnosis of keratoconjunctivitis sicca was established when a positive Schirmer's test and grades A or B rose bengal staining were observed. A probable diagnosis of keratoconjunctivitis sicca was made in the presence of suggestive clinical symptoms and a positive Schirmer's test, or in the presence of grade B rose bengal staining. A definite diagnosis of xerostomia was accepted when there was either a grade IV labial biopsy or a grade III labial biopsy with a grade III or IV gammascan. A probable diagnosis of xerostomia was established when there was a grade III labial biopsy alone or a grade III or grade IV gammascan alone.

A definite diagnosis of Sjögren's syndrome was made when two of the three following components were present: keratoconjunctivitis sicca, xerostomia, and autoimmune disease. A probable diagnosis of Sjögren's syndrome was made when there was a definite diagnosis of one of the three aforementioned components together with a probable diagnosis of the other two, or when there was one definite

diagnosis with one probable, or two probable diagnoses.<sup>6</sup>

#### Results

##### KERATOCONJUNCTIVITIS SICCA

Definite keratoconjunctivitis sicca occurred in 24% of patients with rheumatoid arthritis, in 19% of patients with scleroderma, in 50% of patients with primary biliary cirrhosis, in 10% of patients with other autoimmune diseases, in 10% of patients with chronic liver disease other than primary biliary cirrhosis, and in 6% of patients with non-hepatic diseases and healthy subjects. Definite keratoconjunctivitis sicca was found in 35% of patients with autoimmune diseases and in 5% of those with other disorders.

##### ORAL COMPONENT

Definite xerostomia occurred in 52% of patients with rheumatoid arthritis, in 69% of patients with scleroderma, in 58% of patients with primary biliary cirrhosis, in 36% of patients with other autoimmune diseases, in 9% of patients with chronic liver disease other than primary biliary cirrhosis, and in 3% of patients with non-hepatic diseases and healthy subjects. Definite xerostomia was present in 67% of patients with autoimmune diseases and in 4% of those with other disorders.

##### SJÖGREN'S SYNDROME

Fig. 1 shows the prevalence of definite Sjögren's syndrome in association with a variety of pathological conditions; it occurred in 62% of patients with rheumatoid arthritis, in 69% of patients with scleroderma, in 71% of patients with primary biliary cirrhosis, and in 36% of patients with other autoimmune diseases. Sjögren's syndrome was not present in any of the patients with chronic liver disease other than primary biliary cirrhosis, in any of the patients with non-hepatic disorders, or in any of the healthy subjects. Definite Sjögren's syndrome was found in 61% of patients with autoimmune diseases and in none of the patients with non-autoimmune conditions.

Definite or probable Sjögren's syndrome occurred in 86% of patients with rheumatoid arthritis, in 88% of patients with scleroderma, in all patients with primary biliary cirrhosis, and in 82% of patients with other autoimmune diseases. Nine per cent of patients with chronic liver disease other than primary biliary cirrhosis and 6% of patients with non-hepatic diseases and healthy subjects had probable Sjögren's syndrome, but in none of them was a definite diagnosis made. Definite or probable Sjögren's syndrome was present in 88% of patients with

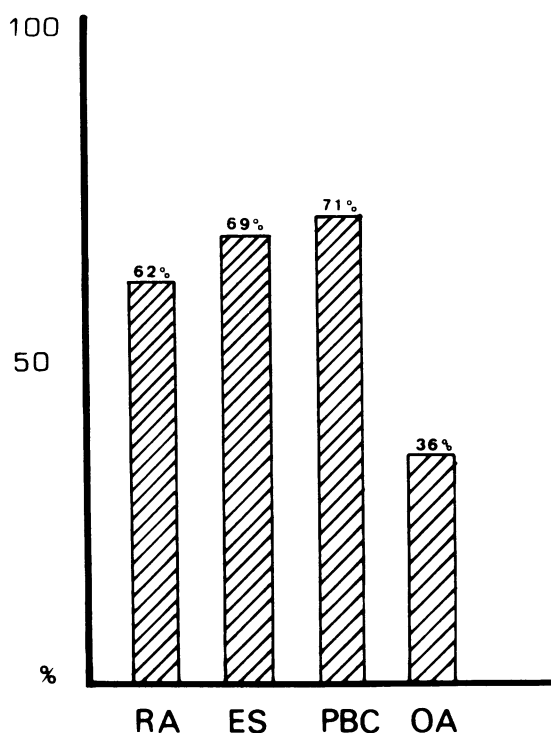


Fig. 1 Prevalence of definite Sjögren's syndrome in association with various diseases. RA=rheumatoid arthritis; ES=scleroderma; PBC=primary biliary cirrhosis; OA=other autoimmune diseases.

autoimmune diseases and in only 6% of patients with other diseases.

Forty nine of the 122 patients included in the study had a definite Sjögren's syndrome, and 77 had the syndrome definitely or probably. Of these 49 patients, 13 (26%) had rheumatoid arthritis, 11 (22%) had scleroderma, 11 (22%) had sicca syndrome alone, 10 (20%) had primary biliary cirrhosis, one had systemic lupus erythematosus, one had dermatomyositis, one had idiopathic pulmonary fibrosis, and one had Hashimoto's thyroiditis. All these 49 patients were women except for one man who had rheumatoid arthritis. Of the 77 patients with definite or probable Sjögren's syndrome, 18 (23%) had rheumatoid arthritis, 17 (22%) had sicca syndrome, 14 (18%) had scleroderma, 14 (18%) had primary biliary cirrhosis, three had idiopathic pulmonary fibrosis, three had systemic lupus erythematosus, one dermatomyositis, one polyarteritis nodosa, one Hashimoto's thyroiditis, one idiopathic cirrhosis, one sarcoidosis, and one a thyroid adenoma. Of these 77 patients, 70 were women and seven men.

## Discussion

The prevalence of Sjögren's syndrome in association with autoimmune disease is not well established. This results from the lack of uniform criteria for diagnosis of the syndrome, differences in diagnostic techniques for evaluating keratoconjunctivitis sicca and xerostomia, and absence of prospective studies on the true prevalence of the syndrome in association with other diseases.

In 1933 Sjögren described keratoconjunctivitis sicca usually in association with rheumatoid arthritis.<sup>7</sup> Subsequently the same ocular and oral lesions originally reported by Sjögren<sup>7</sup> were found in patients with collagen diseases, chronic liver dysfunction (persistent and active hepatitis, primary biliary cirrhosis), Hashimoto's disease, idiopathic pulmonary fibrosis, mixed cryoglobulinaemia, and hyperglobulinaemic purpura.

Sjögren's syndrome can be diagnosed when any two of the following three clinical features are present: dry eyes, dry mouth, arthritis. Typical lesions in the eyes and mouth, however, are not always present at the same time nor at the same stage of development; also, spontaneous clinical remission may occur. Rheumatoid arthritis is present in one to two thirds of the patients with Sjögren's syndrome.<sup>1 8-10</sup> In the present study 26% of patients with Sjögren's syndrome had rheumatoid arthritis, though Sjögren's syndrome occurred in 62% of patients with rheumatoid arthritis and in 71% of patients with primary biliary cirrhosis. Our results suggest that if similar groups of patients with rheumatoid arthritis and primary biliary cirrhosis were screened for Sjögren's syndrome, the prevalence would be the same.

Involvement of the salivary glands in patients with rheumatoid arthritis has been investigated by means of gammascans of the major salivary glands and histopathological study of the minor glands. Whaley *et al* observed abnormal changes of the minor salivary glands in 65% of patients with rheumatoid arthritis and Sjögren's syndrome, and in 27% of patients with rheumatoid arthritis alone.<sup>11</sup> Simon *et al* demonstrated abnormal gammascans in 24% of patients with rheumatoid arthritis and identified salivary gland involvement in two of every three patients with rheumatoid arthritis.<sup>12</sup> The oral component of Sjögren's syndrome was present in 11 of our 21 patients with rheumatoid arthritis, but only three patients had both keratoconjunctivitis sicca and xerostomia. It is reasonable to assume that patients with rheumatoid arthritis with involvement of the salivary glands have Sjögren's syndrome, whether or not keratoconjunctivitis sicca is also present.

In the present study definite Sjögren's syndrome occurred in 69% of patients with scleroderma, whereas in the study of Alarcón-Segovia *et al* Sjögren's syndrome was diagnosed in all their patients with scleroderma.<sup>13</sup> On the basis of labial biopsies Cipoletti *et al* did not find a frequent association of the two disorders.<sup>14</sup>

The high prevalence of Sjögren's syndrome in association with primary biliary cirrhosis is in agreement with the results of Alarcón-Segovia *et al*.<sup>2</sup> Obviously the association is not coincidental and there may be some unknown common factors in the pathogenesis of both conditions. The immunological nature of primary biliary cirrhosis may correlate the lymphocytic infiltration in the minor salivary glands with changes in the liver. McFarlane *et al* described certain antigenic substances extracted from the bile of a patient with primary biliary cirrhosis which were able to react with the salivary ducts.<sup>15</sup> In the series of Golding *et al* Sjögren's syndrome occurred in 52% of patients with primary biliary cirrhosis,<sup>16</sup> which is a lower prevalence than the 71% found in the present study. The systematic investigations carried out in our patients may be the reason for the difference. There was no evidence of definite Sjögren's syndrome in any of our patients with chronic liver disease other than primary biliary cirrhosis, which may support the view that these disorders have different aetiologies.

There is no doubt that Sjögren's syndrome is associated with diseases caused by immunopathological mechanisms. Nearly all the patients in our series presented with an associated autoimmune disease. Those patients with sicca syndrome alone (primary Sjögren's syndrome) had typical clinical features of the eye and mouth similar to those of patients with Sjögren's syndrome in association with some other disease. Patients with sicca syndrome, however, may be considered as a separate group with different clinical evolution and an increased tendency to develop lymphomas.<sup>17 18</sup>

Investigation of the sicca component in Sjögren's syndrome in various autoimmune diseases shows that in most cases the two disorders are associated. The present results indicate that Sjögren's syndrome is associated with autoimmune diseases, such as primary biliary cirrhosis and connective tissue diseases (scleroderma, lupus erythematosus), to the

same extent as with rheumatoid arthritis, though clinical manifestations are sometimes absent and the presence of features of Sjögren's syndrome can be demonstrated only by salivary scintigraphy, labial biopsy, or careful examination of the eye.

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#### References

- 1 Shearn M A. Sjögren's syndrome. *Semin Arthritis Rheum* 1972; **2**: 165-89.
- 2 Alarcón-Segovia D, Díaz-Jouanen E, Fishbein E. Features of Sjögren's syndrome in primary biliary cirrhosis. *Ann Intern Med* 1973; **79**: 31-6.
- 3 Holm S. Keratoconjunctivitis sicca and the sicca syndrome. *Acta Ophthalmol [Suppl] (Copenh)* 1949; **33**: 1-230.
- 4 Schall G L, Anderson L G, Wolf R O, *et al*. Xerostomia in Sjögren's syndrome. Evaluation by sequential salivary scintigraphy. *JAMA* 1971; **216**: 2109-16.
- 5 Chisholm D M, Mason D K. Labial salivary gland biopsy in Sjögren's disease. *J Clin Pathol* 1968; **21**: 656-60.
- 6 Coll J. Síndrome de Sjögren: métodos diagnósticos y su incidencia en distintas enfermedades autoinmunes. Barcelona: Universidad de Barcelona, 1978. (Tesis Doctoral.)
- 7 Sjögren H. Zur Kenntnis der Keratoconjunctivitis sicca (Keratitis filiformis bei Hypofunktion der Tränenrüsen). *Acta Ophthalmol (Copenh)* 1933; suppl 2: 1-151.
- 8 Bloch K J, Buchanan W W, Wohl M J, Bunim J J. Sjögren's syndrome: a clinical, pathological and serological study of sixty-two cases. *Medicine (Baltimore)* 1965; **44**: 187-231.
- 9 Sjögren H. Keratoconjunctivitis sicca and chronic polyarthritis. *Acta Med Scand* 1948; **130**: 484-8.
- 10 Vanselow N A, Dodson U N, Angeli D C. A clinical study of Sjögren's syndrome. *Ann Intern Med* 1963; **58**: 124-35.
- 11 Whaley K, Williamson J, Dick W C. Liver disease in Sjögren's syndrome and rheumatoid arthritis. *Lancet* 1970; **i**: 861-3.
- 12 Simon L, Souyris F, Suquet P, *et al*. Les glandes salivaires au cours de la polyarthrite rhumatoïde. *Rev Rhum Mal Osteoartic* 1976; **43**: 185-92.
- 13 Alarcón-Segovia D, Ibáñez G, Hernández-Ortiz J, Velázquez-Forero F, González-Jiménez Y. Sjögren's syndrome in systemic progressive sclerosis (scleroderma). *Am J Med* 1974; **57**: 78-85.
- 14 Cipoletti J, Buckingham R, Barnes E. Sjögren's syndrome in progressive systemic sclerosis. *Ann Intern Med* 1977; **87**: 535-41.
- 15 McFarlane I G, Tsantoulas D C, Wojcicka B M. Cellular immunity to salivary antigens in autoimmune diseases with sicca syndrome. *Digestion* 1974; **10**: 305.
- 16 Golding P L, Bown R, Mason A M, Taylor E. 'Sicca complex' in liver disease. *Br Med J* 1970; **ii**: 340-2.
- 17 Kassan S S, Thomas T L, Moutsopoulos H M, *et al*. Increased risk of lymphoma in sicca syndrome. *Ann Intern Med* 1978; **89**: 888-92.
- 18 Moutsopoulos H M, Chused T M, Mann D L, *et al*. Sjögren's syndrome (sicca syndrome): current issues. *Ann Intern Med* 1980; **92**: 212-26.



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