Prevalence of sicca syndrome in the Peruvian population

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ABSTRACT

Objective. *Sjögren's syndrome is a complex and heterogeneous autoimmune disease characterised by ocular and oral dryness, which mainly affects the exocrine glands. The objective of this study was to determine the prevalence of sicca syndrome (SS) in the Peruvian population. The age and gender of patients with SS and their national prevalence and in each of the departments were defined.*

Methods. *This was a cross-sectional prevalence study. All the people for whom the Ministry of Health (MINSA) in Peru covered health treatments from January to December 2016 were taken into account. The patients with SS were either newly or previously diagnosed with sicca syndrome (Sjögren's) according to the international classification of diseases version 10 (ICD-10) of the World Health Organisation (WHO). The prevalence was determined considering the number of cases of SS in the total population registered by the Ministry of Health (MINSA).*

Results. *1,301 cases of SS were observed in a total population of 15,417,345 people served in 25 territories. The prevalence of SS in this population was 0.0084%, the prevalence rate was 8.4 cases per 100,000 persons (95% CI: 7.99–8.91). The prevalence of SS was higher in the territories of Tacna, Lima, La Libertad, Arequipa, Callao, and Apurímac.*

Conclusion. *The results of this study show the prevalence of SS in the Peruvian population and serve to strengthen the health strategies of rheumatology, ophthalmology, and oral health to improve the diagnosis, treatment, follow-up of the disease, and the quality of life of patients with SS.*

Introduction

Sjögren's syndrome is a chronic autoimmune rheumatological disease that presents with oral and ocular dryness that diminishes the quality of life of patients. The symptomatology of the disease is complex and heterogeneous (1), which hinders its correct diagnosis and treatment. The disease is classified into two types; the primary Sjögren's syndrome (pSS) that is characterised by dry mouth and eyes without accompanying rheumatic disease and the secondary Sjögren's syndrome (sSS) that is associated with other connective tissue diseases (2-4). In some cases, SS is accompanied by sensory and motor neuropathies, fibromyalgia, risk of cardiovascular diseases, and interstitial lung disease (5-9). pSS is a disease of universal distribution and is one of the most frequent autoimmune diseases, with an estimated prevalence in the general population of 60.82 cases (95% CI 43.69–77.94) per 100,000 persons (10). Their symptomatic poverty, especially in early stages, signals a significant delay in the diagnosis. It affects predominantly the female sex and is more frequent between the fourth and sixth decades of life, although it can appear at any age (11). SS is rare in children (2) and adolescents (12-14) compared to women between the ages of 40-59, who are mostly affected (2, 11).

At the oral level, patients with SS have sparse saliva that makes it difficult to speak, chew, and swallow food properly. The oral mucosa is dry, sticky, and sometimes ulcerated. The tongue is usually red, dry, and fissured. Patients may also present atrophy of the filiform papillae, loss of taste, intolerance to acid and spicy foods, halitosis, and a high risk of recurrent infections such as candidiasis. In addition, the risk of dental caries increases, and there are studies that show a higher risk of periodontal disease and lesions of autoimmune aetiology such as lichen planus. Many of these injuries are due to the decrease of saliva and the buffer capacity of the saliva affected patients (14-16). Parotid or submaxillary tumours

can be observed, in which these glands are slightly enlarged, firm, and painful on palpation. In addition, there is an increased risk of developing non-Hodgkin's lymphoma (17, 18).

At the ocular level, the disease manifests as a grit, absence of tearing, excessive blinking, fatigue and reduction of visual acuity, photosensitivity, and dry keratoconjunctivitis, which can in some cases destroy the cornea.

Not all studies use the same criteria to diagnose SS. The most frequently used are the criteria of the European-American Consensus of 2002 (19) and the classification criteria of the SICCA group of 2012 (Sjögren Internacional Collaborative Clinical Alliance) (20). In 2016, new joint criteria between the ACR (American College of Rheumatology) and the EULAR (European League against rheumatism) was suggested which will probably be the most used in the future (21).

To date, there is no definitive cure for SS and more treatment options are needed (22). Currently the treatment is aimed at symptoms associated with xerostomia and xerophthalmia. Treatments recommended for these patients include: salivary and tear moisturising substitutes, balanced diet, periodic fluoridation, and control reviews to prevent the appearance of a possible lymphoma (23). In cases of intolerance to standard of care, therapies directed to B cells may be considered in patients with severe and refractory systemic disease, although there are several controversies (24). Pilocarpine may also be recommended as long as the residual salivary gland is functioning (16).

The most relevant and good quality epidemiological studies on the disease have been carried out in more advanced countries such as Greece with a prevalence rate of 86.40 (95% CI: 78.16–94.64) (25), France 11.34 (95% CI: 9.42–13.27) (26), Italy 30.91 (95% CI: 9.49–52.32) (27), Norway 49.75 (95% CI: 45.01–54.48) (28), Denmark 47.79 (95% CI: 45.96–49.62) (29), and Taiwan 58.30 (95% CI: 53.57–63.03) (30) for each 100,000 people respectively. In Brazil, a prevalence rate of 60.82 (95% CI: 43.69–77.94) was reported (31), but in other countries of South and Central America there are no studies on the subject. Therefore, the objective of our work was to estimate the prevalence of SS in the Peruvian population and in its different territories. In the same way, the distribution of the disease by sex and age was also studied.

Table I. Prevalence and prevalence rate of sicca syndrome in the MINSA Service in Peru, year 2016.

Territorial Department	Cases of SS	Population	Prevalence	Prevalence rate (x100,000 people IC: 95%)	
AMAZONAS	2	203835	0.0010%	1.0	(0.27- 3.58)
ANCASH	9	639192	0.0014%	1.4	(0.74- 2.68)
APURIMAC	24	353448	0.0068%	6.8	(4.56- 10.10)
AREQUIPA	112	818843	0.0137%	13.7	(11.37-16.46)
AYACUCHO	8	486499	0.0016%	1.6	(0.83- 3.25)
CAJAMARCA	21	1022043	0.0021%	2.1	(1.34- 3.14)
CALLAO	54	541688	0.0100%	10.0	(7.64-13.01)
CUSCO	14	815910	0.0017%	1.7	(1.02- 2.88)
HUANCAVELICA	9	306601	0.0029%	2.9	(1.54-5.58)
HUANUCO	4	482872	0.0008%	0.8	(0.32-2.13)
ICA	10	449056	0.0022%	2.2	(1.21-4.10)
JUNIN	14	797272	0.0018%	1.8	(1.05-2.95)
LA LIBERTAD	137	921241	0.0149%	14.9	(12.58-17.58)
LAMBAYEQUE	12	590697	0.0020%	2.0	(1.16-3.55)
LIMA	690	3428645	0.0201%	20.1	(18.68-21.68)
LORETO	11	485551	0.0023%	2.3	(1.27-4.06)
MADRE DE DIOS	3	160205	0.0019%	1.9	(0.64-5.51)
MOQUEGUA	5	117311	0.0043%	4.3	(1.82-9.98)
PASCO	4	113769	0.0035%	3.5	(1.37-9.04)
PIURA	2	796519	0.0003%	0.3	(0.07-0.92)
PUNO	16	713418	0.0022%	2.2	(1.38-3.64)
SAN MARTIN	8	468041	0.0017%	1.7	(0.87-3.37)
TACNA	128	237250	0.0540%	54.0	(45.38-64.14)
TUMBES	3	141719	0.0021%	2.1	(0.72-6.22)
UCAYALI	1	325720	0.0003%	0.3	(0.05-1.74)
Overall	**1.301**	**15.417.345**	**0.0084%**	**8.4**	**(7.99-8.91)**

IC: interval of confidence; SS: sicca syndrome.

Material and methods

This is a cross-sectional prevalence study. To this end, the population that received health coverage during 2016 in the MINSA service in Peru was taken as a reference. To calculate the prevalence, patients with a diagnosis of SS were classified according to the M35.0 nomenclature of the Sicca Syndrome (Sjögren) of the ICD-10 of the WHO using the MINSA. In order to obtain the data, the external consultation records of the MINSA health establishments of the 25 departments nationwide were used. Newly or previously diagnosed patients were included. Prevalence was defined as the proportion of individuals with SS in the total of the Peruvian population treated at the national level by the Ministry of Health during the year 2016.

The collection of the information was authorised through documents no. 17-008380 and no. 18-002028. Patient data was treated according to the Helsinki Declaration of 1975/83 and its subsequent revisions, and according to Legislative Decree no. 1353 of the National Authority on Transparency and Access to Public Information, which strengthens the protection regime of personal data applicable in Peru based on the characteristics of this study.

The variables collected for this study, in addition to the diagnosis of SS, were the age and sex of the patients. The age variable was categorised by groups: 0–11 years, 12–17 years, 18–29 years, 30–59 years and >60 years, respectively, due to the organisation of data per life cycle of the Peruvian Public Health System.

Statistic analysis

The prevalence was calculated as a percentage. We also estimated the prevalence rate in cases per every 100,000 people and the 95% confidence interval (CI).

Table II. Prevalence rates of sicca syndrome by age and gender groups of the study.

Age range	Peruvian population 2016	General population MINSA	Cases of SS (Total)	Women			Men		
				Cases of SS	Population MINSA	Rate of prevalence x 100.000 people CI:95%	Cases of SS	Population MINSA	Rate of prevalence x 100.000 people CI:95%
00a - 11a	6922109	4760048	48	22	2331302	1 (0.62-1.43)	26	2428746	1 (0.73-1.57)
12a - 17a	3482162	1478763	20	12	838763	1 (0.82-2.50)	8	640000	1 (0.63-2.47)
18a - 29a	6676249	3212614	101	73	2356200	3 (2.46-3.90)	28	856414	3 (2.26-4.73)
30a - 59a	11289493	4420333	676	581	3049596	19 (17.56-20.66)	95	1370737	7 (5.67-8.47)
60a >	3118612	1545587	456	373	873634	43 (38.58-47.25)	83	671953	12 (9.97-15.31)
Overall	**31488625**	**15417345**	**1301**	**1061**	**9449495**	**11 (10.57-11.92)**	**240**	**5967850**	**4 (3.54-4.56)**

IC: interval of confidence; SS: sicca syndrome.

Results

The total Peruvian population in 2016 was 31.488.625 and 15.417.345 people were registered in the MINSA service in that same year. This was the population selected for this study. Of the total sample, 61% were women and 39% were men. The study identified 1.301 people newly or previously diagnosed with SS during the study period, of whom 82% were women and 18% were men. Therefore, the prevalence of SS was 0.0084% with a rate of 8.4 cases (95% CI: 7.99–8.91) per 100,000 people (Table I). The prevalence rate for women was 11.23 cases (95% CI: 10.57–11.92) and for men 4.02 cases (95% CI: 3.54–4.56) per 100,000 people respectively (Table II). The female/male ratio in the national prevalence rate was 2.79 (95% CI: 2.43–3.21).

Regarding the age of patients with SS, 48 cases (4%) were observed in an age range of 0–11 years, 20 cases (2%) in ages between 12–17 years, 101 cases (8%) in 18–29 years, 676 cases (52%) with ages between 30–59 years, and 456 cases (35%) older than 60 years (Table II).

The territories with the highest prevalence rate of SS were Tacna with 54 cases (95% CI: 45.38–64.14), Lima with 20.1 cases (95% CI:18.68–21.68), La Libertad with 14.9 cases (95% CI: 12.58–17.58), Arequipa with 13.7 cases (95% CI: 11.37–16.46), Callao with 10 cases (95% CI: 7.64–13.01), and Apurimac with 6.8 cases (95% CI: 4.56–10.10) per 100.000 people (Table I).

Discussion

This study is the first work that shows the prevalence of SS in Peru where a prevalence of 0.0084% or a prevalence rate of 8.4 cases per every 100,000 persons were observed. These results differ from other studies that show a much higher prevalence. For example, there are studies conducted in advanced countries such as Norway and Italy, reported by Goransson *et al*. and Sardu *et al*., which showed a prevalence rate of 49.75 (95% CI: 45.01–54.48) and 30.91 (95% CI: 9.49–52.32) per 100,000 persons-year respectively (27, 28). Similarly, Eaton *et al*. reported a prevalence rate for SS of 47.79 (95% CI: 45.96–49.62) in Denmark and See *et al*. reported a prevalence rate of 58.30 (95% CI: 53.57–63.03) in Taiwan per 100.000 persons, respectively. These two studies used the WHO ICD registry (29, 30). However, the results of our study are closer to the study by Maldini *et al*. in France where they obtained a prevalence rate of 11.34 (95% CI: 9.42–13.27) per 100,000 persons (26). There is no data on the SS prevalence rate in non-advanced countries, except the study of Valim *et al*. that reported a prevalence rate of 60.82 cases per 100,000 persons-year in Brazil using the 2002 SS criteria (31). The low prevalence rate of SS observed in Peru in comparison with advanced countries could be due to the greater number of aging population and especially women who live in advanced countries (32).

These important variations may be also due to the diagnostic criteria of the SS used. In this case, it is known that the registration was made following the WHO ICD-10, but the criteria followed for the diagnosis of SS in each of the centres or patients is not known. Although the purpose of this study has been to provide epidemiological information about SS in Peru, it is important to achieve a registry of the diagnostic criteria used in the future in order to know if patients have been diagnosed correctly. Therefore, it would be necessary to make an effort for the specialists in rheumatology and the Peruvian Health System to register patients correctly following the current SS criteria. At the institutional level, the Peruvian Health System is made up of health services provided by the Ministry of Health and regional governments, the Ministry of Defense, the Ministry of the Interior and private health companies. In our study, the population of the Ministry of Health and regional governments were only studied. It was not possible to collect information from the other institutions.

The WHO ICD-10 disease registry whose nomenclature is "M35.0 syndrome sicca (Sjögren)" does not separate between pSS and sSS. As we saw, pSS and sSS are two distinct entities and the new classification criteria for the disease take in account these SS types (19-21). MINSA data does not show the SS type. We suggest diagnosing SS patients correctly defining and recording SS type. These modifications could contribute to the standardisation of registration methods at a national and global level in accordance with the corresponding scientific advances for the SS (19, 20).

In our study, a female/male ratio (M/H) in the prevalence rate of 2.79 (95% CI: 2.43–3.21) was observed. This number is close to the reports by Sardu *et al*. and Valim *et al*. in Italy and Brazil that showed a female/male rate of

2.48 (95% CI: 0.50–12.29) and 4.81 (95% CI: 0.23–100.25), respectively (27, 31). However, the majority of SS prevalence studies showed a greater female/male ratio that varies between 8.7 to 17.27 (26, 30).

There are studies that observed how the prevalence of SS increases with age (33). Similarly, Goransson *et al*. showed that the average age of patients with pSS was 61.6±13.2 years (28). Maciel *et al*. also observed in his study that 86% of pSS cases corresponded with a mean age of 64.6±15.2 years (34). Regarding the age, the greater part of our patients was between 30–59 years old (52%) and older than 60 years old (35%). In this case, the average age of the patients could not be obtained, since the Peruvian Health System registered age in categories. It would be more convenient to record age in years, since the age ranges shown in the MINSA registry are very broad, to give a clear view of the average age of patients with SS in Peru.

The Peruvian departments with the highest prevalence of SS were Tacna, Lima, La Libertad, Callao, Arequipa, and Apurimac. This may respond to the population density and the high number of doctors that these territories have, unlike the others. Nine of these departments' total population is over 60 years old and 1–9% of total sanitary infrastructure is hospitals owned by these departments. In addition, during 2016, the national government transferred authorised financial resources to these departments from 2–11%. This specialised sanitary attendance could be one of the reasons for the highest prevalence in these departments. The SS prevalence results in each department provide scientific evidence for the teaching-learning of the disease. We think that these departments should improve health strategies to diagnose and treat these patients correctly. These health strategies will help to identify early symptoms and signs suggestive of SS, useful in the early diagnosis of the disease.

The purpose of this study was to provide scientific evidence that contributes to the education of the Peruvian population about SS, and to improve health policies at the national level about autoimmune diseases such as SS. However, due to logistical and technical issues, the study has limitations, since it has been impossible to know the signs and symptoms of the disease, how the diagnosis of the patients was reached, the professionals involved in the diagnosis (rheumatologists, ophthalmologists and/or dentists) and also the information regarding their socioeconomic status, educational level, quality of life, perception of the service received by patients, and the level of severity of the disease. We believe that these records should be improved in order to carry out future research.

In conclusion, this study shows the prevalence of SS in the Peruvian population attended by MINSA. The prevalence was 0.0084% with a prevalence rate of 8.4 cases per 100,000 people. Regarding the distribution by departments, the prevalence of SS was greater in the departments of Lima, Tacna, La Libertad, Apurímac and Callao. Knowledge of this disease must be promoted in the Peruvian health system, and it is essential that patients with SS potential receive the necessary diagnostic techniques to be able to make an early diagnosis of the disease following the current criteria. It is necessary to promote health policies and resources aimed at improving the diagnosis and treatment of the disease to improve the quality of life of these patients.

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