Prevalence of Sjögren's syndrome according to 2016 ACR-EULAR classification criteria in patients with systemic lupus erythematosus

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Abstract

Background Diagnosis of SS is a complex task, as no symptom or test is unique to this syndrome. The American-European Consensus Group (AECG 2002) and the American-European classification criteria of 2016 (ACR/EULAR 2016) emerged through a search for consensus. This study aims to assess the prevalence of Sjögren's Syndrome (SS) in patients with Systemic Lupus Erythematosus (SLE), according to AECG 2002 and ACR-EULAR 2016 classifications, as well as clinical and histopathological features in this overlap. To date, there is no study that has evaluated SS in SLE, using the two current criteria.

Methods This cross-sectional study evaluated 237 SLE patients at the outpatient rheumatology clinic between 2016 and 2018. Patients were submitted to a dryness questionnaire, whole unstimulated salivary flow (WUSF), "Ocular Staining Score" (OSS), Schirmer's test I (ST-I), and labial salivary gland biopsy (LSGB).

Results After verifying inclusion and exclusion criteria, a total of 117 patients were evaluated, with predominance of females (94%) and mixed ethnicity (49.6%). The prevalence of SS was 23% according to AECG 2002 and 35% to ACR-EULAR 2016. Kappa agreement between AECG 2002 and ACR-EULAR 2016 were 0.7 ($p < 0.0001$). After logistic regression, predictors for SS were: anti/Ro (OR $=$ 17.86, $p < 0.05$), focal lymphocytic sialadenitis (OR $=$ 3.69, $p < 0.05$), OSS $\geq$ 5 (OR $=$ 7.50, $p < 0.05$), ST I positive (OR $=$ 2.67, $p < 0.05$), and WUSF $\leq$ 0.1 mL/min (OR $=$ 4.13, $p < 0.05$).

Conclusion The prevalence of SS in SLE was 23% (AECG 2002) and 35% (ACR-EULAR 2016). The presence of glandular dysfunction, focal lymphocytic sialadenitis, and anti/Ro were predictors of SS in SLE. The greatest advantage of the new ACR-EULAR 2016 criteria is to enable an early diagnosis and identify the overlapping of these two diseases. ACR-EULAR 2016 criteria is not yet validated for secondary SS and this study is a pioneer in investigating prevalence based on the new criteria.

Keywords Systemic lupus erythematosus, Sjögren's syndrome, Classification criteria, ACR-EULAR 2016, Prevalence, Labial salivary gland biopsy

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Gianordoli *et al. Advances in Rheumatology*   (2023) 63:11

Page 2 of 8

Introduction

Systemic Lupus Erythematosus (SLE) and Sjögren's Syndrome (SS) are similar diseases, in clinical, laboratory, genetic, and pathophysiological aspects [1]. Furthermore, they can overlap, occurring more frequently in early stage of the disease [2]. Patients who present an overlap of the two diseases are, in fact, a subgroup with clinical characteristics and prognosis different from those with isolated SS. This characterization can determine early intervention, with individualized treatment, preventing possible complications.

SLE is a chronic autoimmune inflammatory disease, with a wide spectrum of clinical manifestations, without periods of remission and activity, with lower overall survival when compared to general population [3]. The distribution of the disease is universal, in USA, the prevalence varies from 14.5 to 50.8 cases/100,000 inhabitants [4]. In Brazil, comparing northern and southernmost regions, they estimated the incidence of 8.7/100,000 inhabitants in north of the country (tropical region), while in south (lower latitude), the incidence of SLE was 4.8/100,000 inhabitants/year [5], similar to Sweden [6] and United Kingdom [7].

SS is a chronic, autoimmune syndrome characterized morphologically by lymphocyte infiltration in salivary and lacrimal glands, leading to reduction in tears and saliva [8]. The clinical scenario is based on the classic triad: dryness, pain, and fatigue, but around 50% of cases can present systemic manifestations [8]. Data from a Brazilian population study showed that the prevalence of primary SS (SSp) was 0.17% [9].

Diagnosis of SS is a complex task, as no symptom or test is unique to this syndrome. The American-European Consensus Group (AECG 2002) and the American-European classification criteria of 2016 (ACR/EULAR 2016) emerged through a search for consensus, which performs a broader screening of patients to be submitted to this classification, based on objective tests.

In a prospective cohort study, it was found that approximately half of the patients with SLE had manifestations of dryness and fatigue and 11% had diagnosis of associated SS [10]. The prevalence of SS is possibly underestimated and could be diagnosed if patients with dryness and common systemic manifestations were evaluated with objective tests and, when necessary, labial salivary biopsy.

Few studies have assessed prevalence of SS in SLE, among which it is noted that the prevalence is quite variable, according to the classification criteria used and sample studied, ranging from 6.5% to 32.4% [1, 11–17]. In a meta-analysis, Alani et al. (2017) demonstrated a prevalence of SS between 5 and 22%, recommending investigation of SS in SLE with dryness. However, a biopsy was not performed in all patients, which makes the differential diagnosis difficult, strengthening the need for a consensus regarding the diagnostic and classification criteria for SS in the context of other autoimmune diseases. It is noteworthy that there is no study that has evaluated SS in SLE, using the two current criteria, including salivary gland biopsy, and considering systemic manifestations as criteria for screening for SS.

The present study aims to assess the frequency of Sjögren's Syndrome in patients with Systemic Lupus Erythematosus using the new ACR-EULAR 2016 criteria compared to the 2002 American-European Consensus Group criteria.

Materials and methods

This is a cross-sectional and uncontrolled study of patients diagnosed with SLE included from August 2016 to August 2018. Patients were sequentially (convenience sample) recruited from the rheumatology outpatient clinic of the University Hospital of Federal University of Espírito Santo (HUCAM-UFES/EBSERH).

The inclusion criteria were: patients with SLE classified according to the SLICC (Systemic Lupus International Collaborating Clinics) 2012 and/or ACR (American College of Rheumatology Classification) 1982 criteria. The exclusion criteria were age under 18 years old, C hepatitis, AIDS, lymphoma, graft-host disease, sarcoidosis, HyperIgG4 syndrome, overlap with connective tissue diseases, pregnancy, head and neck radiotherapy in the past, and patients on cyclophosphamide or methylprednisolone pulse therapy.

All patients were submitted to dryness questionnaire. Those who had symptoms of dryness or anti/Ro were submitted to glandular function evaluation by whole unstimulated salivary flow (WUSF) measurement, Schirmer's test I (ST I), lissamine green, and fluorescein test. Criteria for performing labial salivary gland biopsy (LSGB) were: salivary and/or lacrimal dysfunction or positive anti/Ro or systemic manifestation according to ESSDAI.

Classification criteria were based on the 2002 American-European Consensus Group (AECG) consensus, which assesses ocular and oral symptoms, ocular and oral objective tests, minor salivary gland histopathology, and the presence of autoantibodies. In addition, the new criteria of the American College of Rheumatology and the European League Against Rheumatism (ACR-EULAR) 2016 were used to classify SS, including the following items: the presence of focal lymphocytic sialadenitis with a focal score ≥ 1 (3 points), presence of anti/Ro (3 points), Schirmer test I (ST-I) ≤ 5 mm/5 min (1 point), ocular surface staining score (or van Bijsterveld score) ≥ 5 (1 point) and unstimulated salivary flow ≤ 0.1 ml/min (1

Gianordoli *et al. Advances in Rheumatology*   (2023) 63:11

Page 3 of 8

point), being positive when result is ≥ 4 points. In SS/SLE patients, the ESSDAI instrument was applied to assess disease activity.

The WUSF measurement procedure was performed using the passive flow technique, for 15 min. All collected saliva was weighed on a calibrated precision scale equipment, brand BEL Engineering®, mark 160, class II. A value ≤ 0.1 ml/min was considered positive.

The ST-I was performed after unstimulated salivary flow in conjunctival sac in both eyes, for 5 min, using standardized paper filters (Whatman no. 41). This method quantifies the tear and is considered normal when the moisture is > 15 mm. Values ≤ 5 mm in at least one eye were considered positive [18].

The ocular surface staining tests, lissamine green, and fluorescein were performed without anesthetic eye drops, on a different day and after the ST-I (Fig. 1). The pattern of ocular surface impregnation (conjunctiva and cornea) was evaluated and scored according to the "Ocular Staining Score" (OSS) scale. The OSS ≥ 5 was considered positive [19].

The LSGBs were performed by a trained rheumatologist using the 0.5–1.5 cm linear incision technique, with a mental nerve block (EVS) [20].

The autoantibodies for investigation of SLE/SS were anti/Ro, anti/LA, Rheumatoid Factor (RF), and Antinuclear Autoantibody (ANA). Tests for anti/Ro and anti/LA antibodies were performed using the ELISA method (enzyme immunoassay). ANA was performed using the indirect immunofluorescence method in human epithelial cells (Hep-2) and interpreted by an experienced examiner (MFB). The RF was performed by nephelometry.

The specimen obtained from the LSGB was fixed in 10% formalin and processed in paraffin. Histological sections were stained using hematoxylin and eosin (H&E) and evaluated under optical microscopy (OM) by an experienced pathologist (MCLFSS) (Fig. 2).

The characteristics of the population were described and compared. To verify the association between some qualitative variables in the study, the chi-square test or Fisher's exact test were applied.

The Kolmogorov-Smirnoff test, Student's t-test, and the non-parametric Mann–Whitney test were used for continuous variables. In all analysis carried out, a significance level of 5% was considered. Kappa Index was used to evaluate agreement between AECG 2002 and ACR-EULAR 2016 classification criteria. All analyzes performed in the present study were obtained using the IBM SPSS 20.0 (IBM Corp.2011) statistical software.

The protocol was approved by Research Ethics Committee of the University Hospital of the Federal University of Espírito Santo, on July 31, 2016 (approval number 1.655.292).
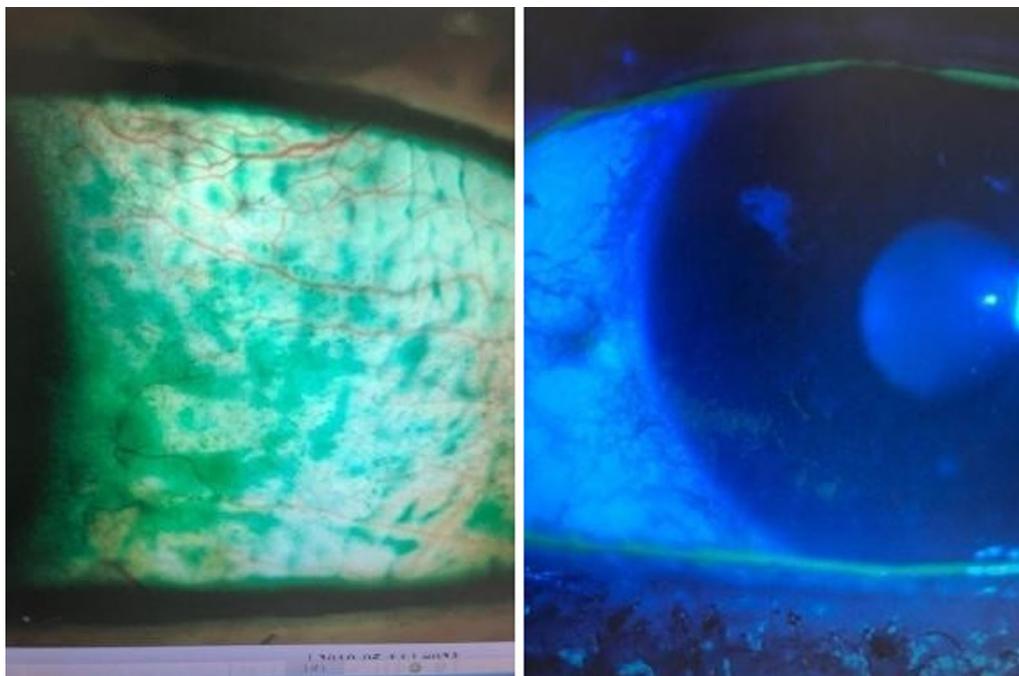
Fig. 1 Ocular surface staining tests using Lissamine (**a**) and Fluorescein (**b**). Findings from a patient enrolled in the study (Courtesy of Dr. Fabiano Cade Jorge)

Gianordoli *et al. Advances in Rheumatology*   (2023) 63:11

Page 4 of 8
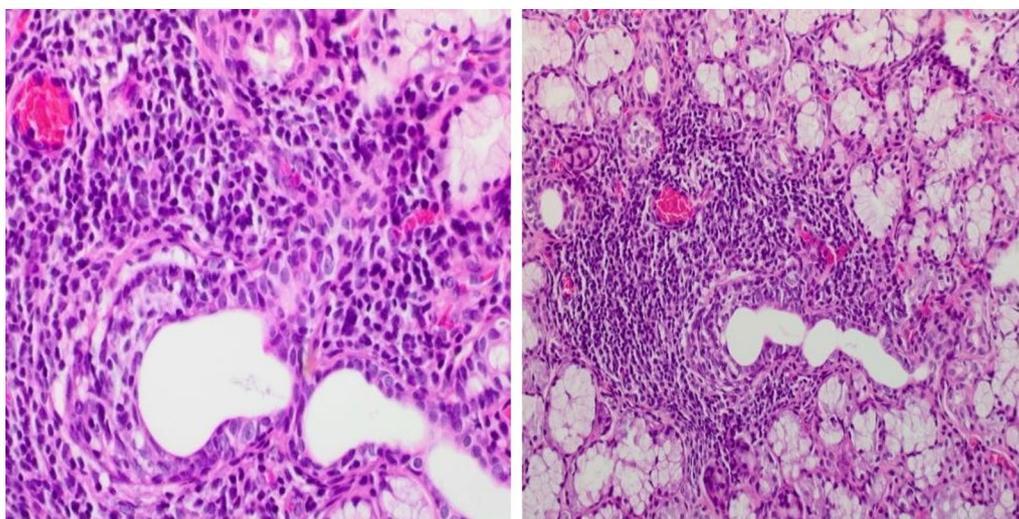
Fig. 2 **a** H&E 400 × lymphoepithelial lesion; **b** inflammatory focus H&E ×200. Findings from a patient enrolled in the study (photos provided by Dr. Maria Carmen L. F. Silva Santos)

Table 1 Comparison of demographic variables in patients with systemic lupus erythematosus without (SS−) and with (SS+) Sjögren's syndrome

Variable	Category	SS− n (%)	SS+ n (%)	Total	P
Race (n = 117)	Brown	36 (47)	22 (54)	58	0.331
	White	21 (28)	9 (22)	30	
	Black	19 (25)	8 (20)	27	
	Indigenous	0 (0)	1 (2)	1	
	Yellow	0 (0)	1 (2)	1	
Gender (n = 117)	Feminine	69 (91)	41 (100)	110	0.094
	Masculine	7 (9)	0 (0)	7	
Age Group (n = 117)	17–41	40 (53)	15 (37)	55	0.169
	42–65	33 (43)	22 (54)	55	
	>66	3 (4)	4 (10)	7	

Results

A total of 237 were approached to participate, according to their medical visiting (convenience sample). Out of them, 120 patients were excluded due to non-attendance for examinations, refusal to participate, incomplete data, or death. In the end, 117 patients were included in the analyses.

There was a predominance of females (94%) and mixed ethnicity (49.6%). The sociodemographic variables of the 117 (41 SS+ and 76 SS−) patients studied are shown in Table 1.

The prevalence of SS was 23% (27/117) based on the 2002 AECG criteria and 35% (41/117) using the ACR-EULAR 2016 criteria. Kappa Agreement between

AECG 2002 and ACR-EULAR 2016 were 0.7 ($p < 0.001$). There was no comparative statistical significance difference between demographic characteristics and clinical manifestations of SLE patients who met the 2016 criteria but not the 2002 criteria vs SLE patients who only met the 2002 criteria.

The patients were asked about symptoms of eye and oral dryness and others such as difficulty in swallowing dry food, crying without tears, photophobia, visual blurring, frequent caries, dry skin, vaginal dryness, itchy skin, and dryness of the nasal mucosa. The frequency of dryness symptoms was similar between patients with and without SS. The sensation of sand in eyes, vaginal dryness, and dry skin were more frequent in patients with SS ($p < 0.05$) (Table 2).

The results of objective tests of ocular and oral gland function and biopsy analysis in patients with lupus are detailed in Table 3, comparing SS− and SS+ groups.

Patients with SLE/SS+ showed moderate disease activity as measured by EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI) 8.9 ± 7.6.

After logistic regression, the predictors for SS were: presence of anti/Ro, with OR = 17.86 (6.7–47.6) $p < 0.001$; the compatible LSGB, OR = 3.69 (1.8–7.3), $p < 0.001$; OSS ≥ 5 OR = 7.50 (2.6–21.7), $p < 0.001$; ST I OR = 2.67 (1.028–6.8) and UWSF ≤ 0.1 ml/min, OR = 4.13 (1.7–10.2), $p = 0.002$. Symptoms of oral and ocular dryness were not predictors for diagnosis of SS.

Of the 117 patients included in the sample, 105 individuals participated in the histological study. The samples sizes were satisfactory, with a mean and median area ≥ 8mm². Considering the degree of inflammation observed in labial minor salivary glands, 29 (24.8%) patients presented grade

Gianordoli *et al. Advances in Rheumatology*   (2023) 63:11

Page 5 of 8

Table 2 Comparison of dryness symptoms in patients with systemic lupus erythematosus with (SS+) and without (SS−) Sjögren's syndrome

Variable	Total n (%)	SS− n (%)	SS+ n (%)	*p* value
Eye AECG				
Dry eyes for > 3 months	54 (46.2)	32 (42)	22 (54)	0.232
Persistent feeling of sand in the eyes	67 (57.3)	38 (50)	29 (71)	0.031
Use of lubricant eye drops > 3 times/day	28 (23.9)	15 (20)	13 (32)	0.148
Oral AECG				
Dry mouth feeling for > 3 months	72 (61.5)	48 (63)	24 (59)	0.624
Recurrent and persistent swelling of the parotids	30 (25.6)	18 (24)	12 (29)	0.509
Often drink liquids to help swallow dry food	52 (44.4)	33 (43)	19 (46)	0.762
Others out AECG				
Cry without tears	28 (24.1)	15 (20)	13 (32)	0.159
Photophobia	77 (65.8)	46 (61)	31 (76)	0.101
Visual blurring	82 (70.1)	54 (71)	28 (68)	0.756
Frequent caries	47 (40.2)	31 (41)	16 (39)	0.853
Dryness or vaginal itching	46 (39.3)	24 (32)	22 (54)	0.020
Dry skin	78 (66.7)	45 (59)	33 (80)	0.020
Itchy skin	60 (51.3)	40 (53)	20 (49)	0.691
Nasal mucosa dryness	45 (38.5)	29 (38)	16 (39)	0.927

Table 3 Criteria item comparison between systemic lupus erythematosus with (SS+) and without (SS−) Sjögren's syndrome

Variable	Category	SS− n (%)	SS+ n (%)	Total	*P*
Biopsy	No	65 (98)	22 (56)	87	< 0.001
	Yes	1 (2)	17 (44)	18	
Anti/Ro	No	51 (71)	6 (15)	57	< 0.001
	Yes	21 (29)	35 (85)	56	
OSS	No	45 (88)	19 (50)	64	< 0.001
	Yes	6 (12)	19 (50)	25	
Schirmer's Test I (mm)	No	41 (77)	18 (56)	59	0.041
	Yes	12 (23)	14 (44)	26	
WUSF (ml/15 min)	No	36 (65)	11 (31)	47	0.002
	Yes	19 (35)	24 (69)	43	

OSS Ocular Staining Score, *WUSF* Whole Unstimulated Salivary Flow

0, without any sign of inflammation; 58 (49.6%) patients the grade 1 and 2, nonspecific; 4 (3.4%) patients the grade 3, 14 (12%) patients the grade 4. In other words, 18 (17.2%) of the biopsies performed were characteristic of SS. Patients with SS had a higher degree of inflammation and a tendency towards more adipose infiltration and ductal dilatation than patients without SS (Table 4). Of the 18 patients with biopsy with a focal score ≥ 1, only 1 had a germinal center and 4 (22%) had lymphoepithelial lesions.

Discussion

This study evaluated the frequency of SS in 117 patients with SLE from a tertiary hospital, using the 2002 AECG criteria and the new ACR-EULAR 2016 criteria. The prevalence based on AECG criteria was similar to other studies that used the same criteria [11–13]. However, when applying ACR-EULAR 2016 criteria, the prevalence was higher, once ACR/EULAR criteria is slightly more sensitive, encompassing some patients with systemic disease but mild or no sicca symptoms as having pSS [21].

In the literature, it is noted that the prevalence of SS in patients with SLE is quite variable and studies suggest that patients with overlapping LES-SS are, in fact, a subgroup with clinical and laboratory characteristics and with a different prognosis from those with SLE or isolated SS [22–26].

Our study found that the frequency of anti/Ro in patients with SLE/SS+ was 85%, while in patients with SLE/SS− it was 29%, with anti/Ro being an important tool for investigating SS in SLE. The results shown in our study are in agreement with those found in the literature, in which anti/Ro was significantly present in LES/SS+ (82%) versus LES/SS− (43.4%), which indicates the possibility of anti/Ro being a predictor of SS [27]. In SS, the presence of anti/Ro 60 and anti/Ro 52 is observed. Anti/Ro 52 was related to pulmonary manifestations in SS [28], while in SLE only anti/Ro 60 was observed [29]. In the present study, the frequency of anti/Ro was similar

Gianordoli *et al. Advances in Rheumatology*   (2023) 63:11

Page 6 of 8

Table 4 Frequency of alterations in salivary gland histology in SLE patients with SS (SS+) and without SS (SS−)

Variable	Category	Total n (%)	SS n (%)	SS+ n (%)	*p* value
Degree of inflammation (n = 105)	0	29 (27.6)	26 (39.4)	3 (7.7)	< 0.001[a]
	1	32 (30.5)	20 (30.3)	12 (30.8)	
	2	26 (24.8)	18 (27.3)	8 (20.5)	
	3	4 (3.8)	2 (3)	2 (5.1)	
	4	14 (13.3)	0 (0)	14 (35.9)	
Acinar atrophy (n = 102)	Absent	44 (43.1)	29 (46)	15 (38.4)	0.129[a]
	Discreet	50 (49)	31 (49.2)	19 (48.7)	
	Focal	1 (1)	0 (0)	1 (2.6)	
	Moderate	7 (6.9)	3 (4.8)	4 (10.3)	
Ductal dilatation (n = 102)	Absent	29 (28.4)	17 (27)	12 (30.8)	0.052
	Discreet	64 (62.7)	43 (68.3)	21 (53.8)	
	Moderate	9 (8.8)	3 (4.8)	6 (15.4)	
Adipose infiltration (n = 102)	Absent	45 (44.1)	27 (42.9)	18 (46.1)	0.088
	Discreet	47 (46.1)	32 (50.8)	15 (38.5)	
	Moderate	10 (9.8)	4 (6.3)	6 (15.4)	
Germinal center (n = 95)	Absent	94 (98.9)	63 (100)	31 (96.9)	0.359[a]
	Present	1 (1.1)	0 (0)	1 (3.1)	
LE infiltrate (n = 93)	Absent	89 (95.7)	57 (98.3)	32 (91.4)	0.127[a]
	Present	4 (4.3)	1 (1.7)	3 (8.6)	

NA not available, *LE* Lymphoepithelial

[a] Fischer's Exact Test was applied (categories with n < 5 or n < 10 with 1 df)

to other studies [17, 27], therefore, the subtype of anti/Ro was not evaluated.

The frequency of dryness symptoms was high in patients with SLE, with or without SS. Either, nearly half of the patients with SLE had salivary dysfunction (WUFS ≤ 0.1 ml/min in 48.3%) and a third showed lacrimal dysfunction (ST I ≤ 5 mm in 30% and OSS ≥ 5 in 28.5%). Unlikely symptoms, glandular dysfunction was a predictor, with a 2.6 to 7.5 more chance of SS. Considering the high frequency of symptoms, the dissociation between symptoms and the diagnosis of SS, and the greater chance of SS in patients with glandular dysfunction, gland function should be routinely assessed in patients with SLE, with dryness and/or positive anti-Ro.

Half of the patients with SLE had some histological alteration including nonspecific inflammatory infiltrate, acinar atrophy, ductal dilatation, adipose infiltration, and lymphoepithelial lesion. The frequency of glandular histological abnormalities could explain the high frequency of glandular dysfunction in SLE without SS. Patients with SLE associated with SS had a higher degree of inflammation and focal lymphocytic sialadenitis. However, SSp patients have a greater prevalence of some histological features such as ductal spongiosis, periductal fibroplasia, acinar fibrosis, and focal lymphocytic sialadenitis with a focus score ≥ 1 than SLE patients [30]. In our study, focal lymphocytic sialadenitis with a focal score ≥ 1 occurred in 18 (17.2%) of SLE sample, and 17 (44%) of SS/SLE patients. Of those with focal lymphocytic sialadenitis, 22% showed lymphoepithelial lesions.

Among the limitations of this study are the losses, approximately half of the sample (120 patients) was excluded, due to death, non-attendance, not accepting to participate, or presenting incomplete data. Furthermore, it was not possible to evaluate the Anti/Ro subtypes.

Conclusion

The prevalence of SS was 23% based on the 2002 AECG criteria and 35% using the ACR-EULAR 2016 criteria. Glandular dysfunction, salivary biopsy, and anti/Ro were predictors of SS. The greatest advantage of the new ACR-EULAR 2016 criteria is to enable an early diagnosis and identify patients who present an association of the two diseases, thus providing individualized treatment. However, the ACR-EULAR criteria are not yet validated for secondary SS and this study is a pioneer in investigating prevalence based on the new criteria.

Gianordoli *et al. Advances in Rheumatology*   (2023) 63:11

Page 7 of 8

Declarations

Ethics approval and consent to participate
This study was approved by Research Ethics Committee of the University Hospital of the Federal University of Espírito Santo (HUCAM/UFES), on July 31, 2016 (approval number 1.655.292). All patient consent terms were signed and the confidentiality term was presented and signed by the authors.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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References
1. Pan HF, Ye DQ, Wang Q, Li WX, Zhang N, Li XP, Xu JH, Dai H. Clinical and laboratory profiles of systemic lupus erythematosus associated with Sjögren syndrome in China: a study of 542 patients. Clin Rheumatol. 2008;27:339–43.
2. Heaton JM. Sjögren's syndrome and systemic lupus erythematosus. Br Med J. 1959;21(1):466–9.
3. Pons-Estel GJ, Catoggio LJ, Cardiel MH, Bonfa E, Caeiro F, Sato E, Massardo L, Molina-Restrepo JF, Toledano MG, Barile-Fabris LA, Amigo MC, Acevedo-Vásquez EM, Abadi I, Wojdyla D, Alarcón-Riquelme ME, Alarcón GS, Pons-Estel BA. GLADEL. Lupus in Latin-American patients: lessons from the GLADEL cohort. Lupus. 2015;24:536–45.
4. Rus V, Maury EE, Hochberg MC. The epidemiology of systemic lupus erythematosus. Dubois lupus erythematosus. 7th ed. Philadelphia: Lippincott Williams & Wilkins; 2007.
5. Borba EF, et al. Systemic lupus erythematosus consensus. Braz J Rheumatol. 2008;48(4):196–207 (**in Portuguese**).
6. Jonsson H, Nived O, Sturfelt G, Silman A. Estimating the incidence of systemic lupus erythematosus in a defined population using multiple sources of retrieval. Br J Rheumatol. 1990;29:185–8.
7. Yee CS, Su L, Toescu V, Hickman R, Situnayake D, Bowman S, Farewell V, Gordon C. Birmingham SLE cohort: outcomes of a large inception cohort followed for up to 21 years. Rheumatology (Oxford). 2015;54:836–43.
8. Seror R, Ravaud P, Bowman SJ, Baron G, Tzioufas A, Theander E, Gottenberg JE, Bootsma H, Mariette X, Vitali C, EULAR Sjögren's Task Force. EULAR Sjogren's syndrome disease activity index: development of a consensus systemic disease activity index for primary Sjogren's syndrome. Ann Rheum Dis. 2010;69(6):1103–9. https://doi.org/10.1136/ard.2009.110619. Erratum in: Ann Rheum Dis. 2011;70:880.
9. Valim V, et al. Prevalence of primary Sjögren syndrome in an important metropolitan area in Brazil. Braz J Rheumatol. 2013;53(1):29–34 (**in Portuguese**).
10. Gilboe IM, Kvien TK, Uhlig T, Husby G. Sicca symptoms and secondary Sjögren's syndrome in systemic lupus erythematosus: comparison with rheumatoid arthritis and correlation with disease variables. Ann Rheum Dis. 2001;60:1103–9.
11. Pasoto SG, Adriano de Oliveira Martins V, Bonfa E. Sjögren's syndrome and systemic lupus erythematosus: links and risks. Open Access Rheumatol. 2019;11:33–45.
12. Alani H, Henty JR, Thompson NL, Jury E, Ciurtin C. Systematic review and meta-analysis of the epidemiology of polyautoimmunity in Sjögren's syndrome (secondary Sjögren's syndrome) focusing on autoimmune rheumatic diseases. Scand J Rheumatol. 2018;47:141–54.
13. Aggarwal R, Anaya JM, Koelsch KA, Kurien BT, Scofield RH. Association between secondary and primary Sjögren's syndrome in a large collection of lupus families. Autoimmune Dis. 2015;2015:298506.
14. Andonopoulos AP, Skopouli FN, Dimou GS, Drosos AA, Moutsopoulos HM. Sjögren's syndrome in systemic lupus erythematosus. J Rheumatol. 1990;17:201–4.
15. Manoussakis MN, Georgopoulou C, Zintzaras E, Spyropoulou M, Stavropoulou A, Skopouli FN, Moutsopoulos HM. Sjögren's syndrome associated with systemic lupus erythematosus: clinical and laboratory profiles and comparison with primary Sjögren's syndrome. Arthritis Rheum. 2004;50:882–91.
16. Baer AN, Maynard JW, Shaikh F, Magder LS, Petri M. Secondary Sjogren's syndrome in systemic lupus erythematosus defines a distinct disease subset. J Rheumatol. 2010;37:1143–9.
17. Yao Q, Altman RD, Wang X. Systemic lupus erythematosus with Sjögren syndrome compared to systemic lupus erythematosus alone: a meta-analysis. J Clin Rheumatol. 2012;18:28–32.
18. Shiboski CH, Shiboski SC, Seror R, Criswell LA, Labetoulle M, Lietman TM, Rasmussen A, Scofield H, Vitali C, Bowman SJ, Mariette X, International Sjögren's Syndrome Criteria Working Group. 2016 American College of Rheumatology/European League Against Rheumatism classification criteria for primary Sjögren's syndrome: a consensus and data-driven methodology involving three international patient cohorts. Ann Rheum Dis. 2017;76:9–16.
19. Whitcher JP, Shiboski CH, Shiboski SC, Heidenreich AM, Kitagawa K, Zhang S, Hamann S, Larkin G, McNamara NA, Greenspan JS, Daniels TE, Sjögren's International Collaborative Clinical Alliance Research Groups. A simplified quantitative method for assessing keratoconjunctivitis sicca from the Sjögren's Syndrome International Registry. Am J Ophthalmol. 2010;149:405–15.
20. Giovelli RA. Retrospective histological analysis of minor salivary gland in patients with dry syndrome. Master's thesis, Federal University of Espírito Santo; 2013 (**in Portuguese**).
21. Le Goff M, Cornec D, Jousse-Joulin S, Guellec D, Costa S, Marhadour T, Le Berre R, Genestet S, Cochener B, Boisrame-Gastrin S, Renaudineau Y, Pers JO, Saraux A, Devauchelle-Pensec V. Comparison of 2002 AECG and 2016 ACR/EULAR classification criteria and added value of salivary gland ultrasonography in a patient cohort with suspected primary Sjögren's syndrome. Arthritis Res Ther. 2017;6(19):269.
22. Grennan DM, Ferguson M, Ghobarey AE, Williamson J, Dick WC, Buchanan WW. Sjogren's syndrome in SLE: Part 2. An examination of the clinical significance of Sjogren's syndrome by comparison of its frequency in typical and atypical forms of SLE, overlap syndromes and scleroderma. N Z Med J. 1977;86:376–9.
23. Cervera R, García-Carrasco M, Font J, Ramos M, Reverter JC, Muñoz FJ, Miret C, Espinosa G, Ingelmo M. Antiphospholipid antibodies in primary Sjögren's syndrome: prevalence and clinical significance in a series of 80 patients. Clin Exp Rheumatol. 1997;15:361–5.
24. Witte T, Hartung K, Sachse C, Matthias T, Fricke M, Kalden JR, Lakomek HJ, Peter HH, Schmidt RE. Rheumatoid factors in systemic lupus erythematosus: association with clinical and laboratory parameters. SLE study group. Rheumatol Int. 2000;19:107–11.
25. Lee CW, Kang SG. Recurrent annular erythema in Sjögren's/lupus erythematosus overlap syndrome: an additional case from Korea. J Dermatol. 1996;23:431–2.

Gianordoli *et al. Advances in Rheumatology*   (2023) 63:11

Page 8 of 8

26. Szántó A, Kiss E, Sas A, Szegedi G, Zeher M. Association of systemic lupus erythematosus and Sjögren's syndrome. Orv Hetil. 2005;11(146):2533–8 (**in Hungarian**).

27. Xu D, et al. Patients with Sjögren's syndrome-onset lupus have distinct clinical manifestations and a benign prognosis: a case-control study. Lupus. 2010;19:197–200 (**in Portuguese**).

28. Ghillani P, André C, Toly C, Rouquette AM, Bengoufa D, Nicaise P, Goulves-tre C, Gleizes A, Dragon-Durey MA, Alyanakian MA, Chretien P, Chollet-Martin S, Musset L, Weill B, Johanet C. Clinical significance of anti-Ro52 (TRIM21) antibodies non-associated with anti-SSA 60kDa antibodies: results of a multicentric study. Autoimmun Rev. 2011;10:509–13.

29. Yoshimasu T, Hiroi A, Ohtani T, Uede K, Furukawa F. Comparison of anti 60 and 52 kDa SS-A/Ro antibodies in the pathogenesis of cutaneous lupus erythematosus. J Dermatol Sci. 2002;29:35–41.

30. Bologna SB, Cavalcante WS, Florezi GP, Souza MM, Nico MMS, Lourenço SV. Distinct salivary gland features in Sjögren's syndrome and lupus erythematosus sialadenite. Am J Dermatopathol. 2020;42:407–13.

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