

Prevalence of oral mucosal lesions, dental caries, and periodontal disease among patients with systemic lupus erythematosus in a teaching hospital in Chennai, Tamil Nadu

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ABSTRACT

Background: The presence of oral symptoms and signs in many systemic diseases is not uncommon knowledge. Investigations that explore the relationship between systemic diseases and their oral manifestations are of particular interest to dentists, as this enables them to be better clinicians with an acumen to recognize, treat, or refer patients with the systemic disease to general physicians. This study was undertaken to understand the oral manifestations of systemic lupus erythematosus (SLE) with an emphasis on oral mucosal lesions, dental caries, and periodontitis. **Methods:** A single institutional cross-sectional survey was conducted from September 2017 to July 2018 on a sample of 500 SLE patients attending the Institute of Rheumatology, Rajiv Gandhi Government General Hospital, Chennai. The dentition status, periodontal status, and oral mucosal lesions were assessed by a single trained and calibrated examiner using the World Health Organization (WHO) proforma, 2013. Besides, disease activity in SLE patients was assessed by rheumatologists using the SLEDAI index with a cutoff score of more than 4 indicating the presence of active disease. Demographic characteristics including age, gender, occupation, monthly income, and education status were assessed using a questionnaire. Data were entered into an Excel Sheet and all statistical analyses were performed using SPSS for Windows version 20.0 (SPSS Inc., Chicago, IL, USA). **Results:** In the present study, the prevalence of dental caries was found to be 87.6% in patients with SLE. The prevalence of severe periodontitis defined as the presence of at least one tooth with a 6 mm or deeper pocket was found to be 85% and the prevalence of oral mucosal lesions was found to be 86%. The prevalence percentage for dental caries, periodontal disease, and oral mucosal lesions were found to be higher than the rates reported for the general population in India. Patients with active SLE had a higher prevalence of dental caries, periodontitis, and oral mucosal lesions than patients with inactive SLE. **Conclusion:** It can be concluded from the present study that SLE patients are more vulnerable to oral diseases than the general population. Furthermore, disease activity in SLE patients has a strong positive correlation with oral health status in SLE patients.

Keywords: Dental caries, oral health status, oral mucosal lesions, periodontitis, SLE

Introduction

It is common knowledge that a vast number of systemic diseases exhibit oral manifestations which is a well-explored topic in

dentistry.^[1] Systemic lupus erythematosus (SLE) is one such disorder that exhibits characteristic oral lesions, in addition to various systemic manifestations of the disease.

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SLE is a clinically heterogeneous autoimmune disorder wherein the presence of autoantibodies against nuclear antigens is a defining characteristic of the disease. In SLE, tolerance to self-antigens is impaired. Prevalence of SLE, in general, is high when

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compared with other autoimmune diseases and as much as one in 2500, get affected with SLE. SLE most commonly affects women, predominantly women of childbearing age. The male to female ratio for the incidence of SLE is 1:9.^[2]

Previous studies done on oral manifestations in SLE have generally shown a high prevalence of xerostomia, mucositis, glossitis, angular cheilitis, mucosal ulceration, temporomandibular joint dysfunction, dysgeusia, and increased incidence of dental caries and periodontitis.^[3-5]

SLE is a disorder with alternating stages of remission and flares. Patients exhibit symptoms and signs of SLE during flares or periods of active disease and remain relatively asymptomatic during periods of remission. So far, the existing literature on oral lesions due to SLE, do not give a clear indication of whether oral mucosal manifestations of SLE also occur during periods of active disease.

A study investigating the association between disease activity and oral manifestations indicates that oral lesions were generally associated with increased disease activity.^[6] However, this study uses an older system of evaluation to assess disease activity in patients and not the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) which is used presently. Hence, this study was done to determine the prevalence of mucosal lesions, dental caries, and periodontitis in SLE patients and also to understand if there is a correlation between disease activity and oral manifestations in SLE. Around 500 patients suffering from SLE and undergoing treatment at the Institute of Rheumatology, Rajiv Gandhi Government General Hospital, Chennai were examined for the presence of oral lesions in addition to a comprehensive dental examination using the WHO proforma (2013). The disease activity in these SLE patients was assessed using SLEDAI criteria.

Methods

This study was a single institutional cross-sectional survey conducted on 500 outpatients diagnosed with SLE and undergoing treatment at the Institute of Rheumatology, Rajiv Gandhi Government General Hospital, Chennai.

Patients and Sample Collection

The study was conducted for 11 months from September 2017 to July 2018 until the desired sample size of 500 study subjects had been recruited. The sample size for the study was determined using the prevalence percentage of oral mucosal manifestations in SLE patients in a previously published article. With a prevalence percentage of 76% and an allowable error of 5%, the sample size was estimated to be 500 study subjects.

Patients diagnosed with SLE according to the American College of Rheumatology criteria (ACR, 2012) for the diagnosis of SLE and gave informed consent to participate in the study were

recruited for the study. The exclusion criteria were patients harboring viral infections such as cytomegalovirus, Epstein-Barr virus, human immunodeficiency virus, parvovirus, patients suffering from tuberculosis or a history of tuberculosis infection, and patients with malignant conditions such as non-Hodgkin's lymphoma, acute myeloid leukemia, and acute lymphoid leukemia.

The demographic characteristics such as age, gender, occupation, monthly income, and educational status were assessed using a questionnaire. A single examiner conducted all the intraoral examinations following the American Dental Association specified Type 3 examination guidelines, using mouth mirror, plain probe, CPI (community periodontal index) probe, and adequate natural light illumination. The World Health Organization (WHO) proforma for Oral Health Status Assessment (2013) was used to record the intraoral findings including oral mucosal manifestations, dental caries, and periodontal status. The intraexaminer reliability was assessed using Kappa statistics and the Kappa value was found to be above 0.8 for dentition status, periodontal status, and oral mucosal lesions.

The disease status was assessed by a rheumatologist using the SLEDAI criteria and recorded on individual case sheets which indicated whether a patient was in the active or inactive periods of the disease. A cutoff of more than 4 in the SLEDAI index was considered to be indicative of the presence of active disease.

Disease activity status was considered as the explanatory variable and dental caries, periodontal status, and oral mucosal lesions were the outcome variables with oral mucosal lesions being the primary outcome of interest.

Ethical approval

The nature and purpose of the study were explained to the Institutional Review Board of SRM Dental College and Hospital on 7-4-2017, Ramapuram, Chennai and ethical clearance was obtained with ethical approval number SRMDC/IRB/2016/MDS/No. 702. Ethical approval for the study was also obtained from the Institutional Ethics Committee, Madras Medical College with ethical approval number 28022017. Written informed consent was obtained from the study subjects after giving them a detailed explanation about the nature and purpose of the study. All procedures were done following the ethical principles established by the Helsinki Declaration 1975, revised in 2000.

Statistical analysis

Descriptive statistics including frequency distributions for discrete variables and mean (standard deviation) for continuous variables were calculated for all outcome variables. Bivariate analysis using Chi-square test was used to examine the relationship between disease activity and categorical outcome variables. Independent *t*-test and one-way ANOVA were used to examine the relationship between disease activity and

continuous outcome variables. The data were entered into an Excel sheet (MS Excel) and all statistical analyses were done using SPSS for Windows version 20.0 (SPSS Inc., Chicago, IL, USA). A *P* value of less than 0.05 was considered as statistically significant.

Results

In the present study, majority of patients were females (93.2%), the mean age of the study participants was found to be 31.7. Around 44 (*n* = 218) percentage of patients were found to have completed some level of schooling while 56 (*n* = 282) percent were found to have acquired a graduate or a post-graduate degree. The majority of patients had no source of monthly income (79.2%). About 35% (*n* = 176) of patients were found to have active SLE, whereas 65% (*n* = 324) of patients were found to have inactive SLE. The demographic characteristics of the study subjects are presented in Table 1. Bivariate analysis using Chi-square tests showed no significant association between gender and outcome variables of gingival bleeding, probing pocket depth (PPD), and clinical attachment loss (CAL) [Table 2]. Likewise, the *t*-test of independent means showed no significant association between gender and the mean number of decayed, missing, or filled teeth [Table 3].

Chi-square tests revealed a significant association between age and the presence of gingival bleeding and CAL at *P* < 0.05 [Table 2]. No significant association was found for explanatory variables of income and education status with gingival bleeding, PPD, CAL, or oral mucosal lesions in the bivariate analysis using Chi-square tests. One-way ANOVA to compare a mean number of decayed, missing and filled teeth revealed significant differences for mean decayed and missing teeth between different age groups of patients at *P* < 0.05 [Table 3]. One-way ANOVA yielded significant results for mean missing and filled teeth between varying income status and for mean decayed, missing, and filled teeth between patients with differing education status at *P* < 0.05 [Table 3].

With disease activity being considered as the explanatory variable, the Chi-square test showed highly significant results with a *P* value of less than 0.001 for outcome variables of gingival bleeding, PPD, CAL, and oral mucosal lesions [Table 4].

The *t*-test of independent means showed a significant relationship between disease activity and the mean number of decayed teeth at *P* < 0.05 [Table 5]. Out of 176 patients with active SLE, 78.4% (*n* = 138) were found to have at least one mucosal lesion in the oral cavity. In patients with inactive SLE, oral mucosal lesions were present in only 8% (*n* = 26). Around 51.1% of patients with active SLE presented with an aphthous ulcer in the oral mucosa. Other than the presence of ulceration, macules, and papules in the oral mucosa was seen in 3.4% of patients with active SLE. The presence of multiple oral lesions including aphthous ulcers, macules, and papules were seen in 36% of patients with active SLE. The

percentage of patients with single and multiple oral mucosal lesions in active and inactive SLE is represented in Figure 1. The sites where mucosal lesions were present in the oral cavity is represented in Figure 2.

Discussion

In the present study, an overwhelming majority of patients suffering from SLE were found to be females (93.2%). This is following the trends observed in the occurrence of SLE through decades with a noted predilection for women to be affected more than men.^[7] The increased prevalence of SLE in women has been attributed to differences in the way sex hormones are

Table 1: Demographic characteristics of study subjects (n=500)

Total (n=500)	n	Percentage
Gender		
Males	34	6.8%
Females	466	93.2%
Age in years		
15-30	247	49.4%
31-40	193	38.6%
41-50	51	10.2%
51 and above	9	1.8%
Educational Status		
Post graduate	94	18.8%
Graduate	188	37.6%
High Secondary Completed	37	7.4%
High Secondary Partially Completed	29	5.8%
Middle School Completed	4	0.8%
Middle School Partially Completed	19	3.8%
Primary School Completed	70	14%
Primary School Partially Completed	59	11.8%
Monthly Income		
Nil	396	79.2%
Up to INR 5,000	10	2%
INR 5,000-15,000	27	5.4%
INR 15,001-25,000	39	7.8%
Above INR 25,000	28	5.6%
Disease Status		
Active	176	35.2%
Inactive	324	64.8%

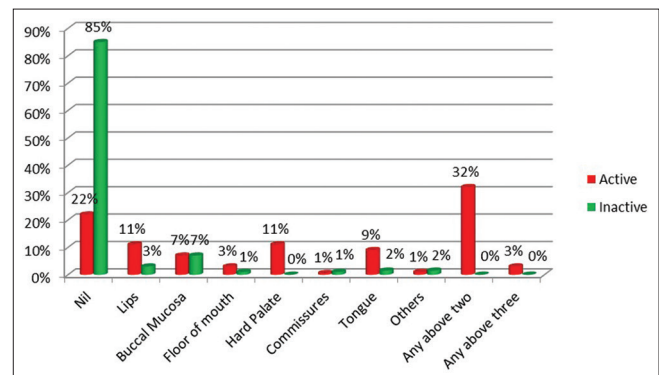


Figure 1: Site-specific distribution of patients with oral mucosal manifestations in active and inactive cases of SLE

Table 2: Chi-square analysis of the effect of gender, age, income, and education on oral health status including the presence of gingival bleeding, PPD, and CAL

	Gingival Bleeding	P	PPD	P	CAL	P
Gender		0.412		0.738		0.869
Males	22		18		14	
Females	268		216		173	
Age in Years		0.036*		0.124		0.001*
15-30	133		107		86	
31-40	113		91		70	
41-50	36		30		25	
51 and Above	8		6		6	
Monthly Income		0.724		0.819		0.743
Nil	233		192		155	
Up to INR 5,000	7		5		4	
INR 5,000-15,000	13		11		9	
INR 15,001-25,000	21		15		11	
Above INR 25,000	16		11		8	
Education		0.230		0.248		0.285
PG	49		35		28	
G	105		87		69	
HSC	18		14		10	
HSP	20		16		14	
MSC	2		1		1	
MSP	15		12		7	
PC	45		39		33	
PP	36		30		25	

*Indicates results are significant at $P < 0.05$, advancing age was associated with a higher proportion of patients exhibiting gingival bleeding, probing pocket depth (PPD) and clinical attachment loss (CAL), PG - Post Graduate, G - Graduate, HSC - Higher secondary completed, HSP - Higher secondary partially completed, MSC - Middle school completed, MSP - Middle school partially completed, PC - Primary school completed, PP - Primary school partially completed

Table 3: Effect of gender, age, income, education on the mean number of decayed, missing, and filled teeth

	Decayed	P	Missing	P	Filled	P
Gender		0.150 ^(f)		0.447 ^(f)		0.515 ^(f)
Males	5.35±3.44		0.88±1.57		0.06±0.34	
Females	4.63±2.72		1.11±1.70		0.13±0.63	
Age in years		0.001 ^(f)		0.010 ^(f)		0.785 ^(f)
15-30	4.47±2.84		0.81±1.32		0.15±0.67	
31-40	4.95±2.61		1.11±1.64		0.12±0.64	
41-50	5.19±2.84		1.96±2.36		0.01±0.14	
51 and above	2.00±2.59		3.44±3.32		0.00±0.00	
Monthly Income		0.647 ^(f)		0.025 ^(f)		0.001 ^(f)
Nil	4.69±2.72		1.14±1.71		0.08±0.49	
Up to INR 5,000	5.20±3.01		2.20±2.97		0.00±0.00	
INR 5,000-15,000	5.19±2.57		1.33±1.75		0.04±0.19	
INR 15,001-25,000						
Above INR 25,000	4.56±3.44		0.69±1.20		0.51±1.27	
	4.11±2.95		0.46±1.14		0.36±0.99	
Education		0.003 ^(f)		0.002 ^(f)		0.03 ^(f)
PG	3.86±3.12		0.73±1.35		0.31±0.94	
G	4.53±2.63		0.76±1.23		0.16±0.71	
HSC	3.92±2.74		0.86±1.29		0.03±0.16	
HSP	4.31±2.71		0.76±1.62		0.00±0.00	
MSC	4.89±2.28		1.00±1.15		0.00±0.00	
MSP	7.25±1.71		1.47±1.84		0.00±0.00	
PC	5.66±2.41		1.64±1.90		0.04±0.36	
PP	5.80±2.75		2.29±2.57		0.00±0.00	

Mean±Standard Deviation, *t*-unpaired *t*-test, F- One-way Analysis of variance, PG - Post Graduate, G - Graduate, HSC - Higher secondary completed, HSP - Higher secondary partially completed, MSC - Middle school completed, MSP - Middle school partially completed, PC - Primary school completed, PP - Primary school partially completed

metabolized and differences in gonadotropin-releasing hormone signaling in women.^[8] The majority of the patients in the present study were aged between 20–30 years of age (49.4%), followed

by patients in the age range of 31–40 years of age (38.6%). This finding is concurrent with studies conducted on the age-specific occurrence of SLE.^[9,10]

Table 4: Effect of disease activity on gingival bleeding, probing pocket depth, clinical attachment loss, and oral mucosal lesions in patients with SLE

	Active SLE	Inactive SLE	P
Gingival Bleeding			
Present	151	139	0.02 ^(x)
Absent	25	185	
Probing Pocket Depth			
Nil	36	230	0.001 ^(x)
4-5 mm	23	34	
6 mm or above	117	60	
Clinical Attachment Loss			
Nil	56	257	0.046 ^(x)
4-5 mm	3	7	
6-8 mm	32	30	
9-11 mm	85	29	
12 mm or above	0	1	
Oral Mucosal Lesions			
Nil	38	275	0.001 ^(x)
Aphthous ulcers	90	24	
Macules	6	0	
Papules	6	1	
Aphthous ulcers with others	36	1	

*x- Chi-square test

Table 5: Effect of disease activity on the mean number of decayed, missing, and filled teeth in SLE patients

Disease status	Decayed	P	Missing	P	Filled	P
Active	5.69±2.87	0.001 ^(*)	1.15±1.72	0.54 ^(*)	0.03±0.32	0.20 ^(*)
Inactive	4.13±2.58		1.06±1.67		0.17±0.73	

*t-unpaired t-test

So far, studies reporting the prevalence of periodontitis in SLE patients have shown higher rates of chronic periodontitis in SLE patients in comparison to healthy controls. A study conducted in China on 108 SLE patients found that SLE patients had an odd's ratio of 13.98 for the presence of chronic periodontitis in comparison to healthy controls.^[11] In the present study, the presence of severe periodontitis with the presence of at least one tooth with a pocket of 6 mm or more was seen in 85% of patients. This is comparatively higher than the national prevalence percentage of severe periodontitis in India which was found to be 7.8% in 35–44 year olds and 18.1% in 65–74 year olds.^[12]

In this study, a significant association was found between disease activity and the presence of a probing pocket depth of more than 6 mm. PPD of more than 6 mm was found in 66.5% of patients with active SLE in comparison to 18.5% of patients with inactive SLE. This finding is similar to a study conducted by Al-Mutairi *et al.* (2015) who found that patients with active SLE exhibited deeper periodontal pockets with multiple sites of gingival bleeding.^[13] However, no correlation between SLEDAI scores and periodontitis was observed in a study conducted by Calderaro DC *et al.* (2017).^[14] Gofur *et al.* (2019) in a study on SLE patients revealed a strong association between periodontitis score, SLEDAI score, and anti-dsDNA antibody levels in

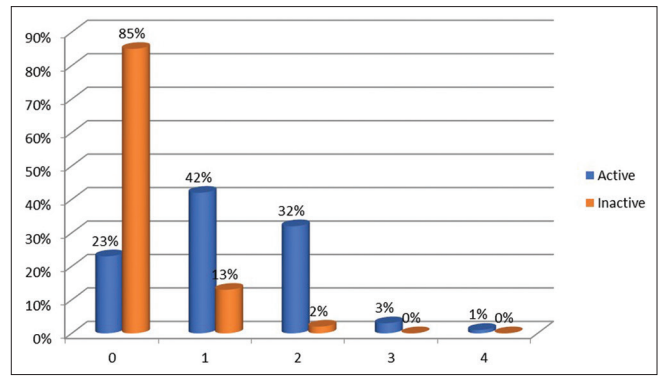


Figure 2: Percentage distribution of the number of oral mucosal lesions in active and inactive cases of SLE

SLE patients.^[15] The mechanism to explain the occurrence of periodontitis more frequently in SLE has been attributed to the intake of anti-inflammatory and immunosuppressive drugs which may have a detrimental effect on periodontal tissues. The immunosuppressants taken systemically may cause exaggerated growth of periodontal pathogens due to suppression of the immune system. Pessoa *et al.* (2019) studied the interactions between host immune response and microflora of the oral cavity in SLE patients and concluded that the generalized low-level inflammation that persists in active SLE also leads to an increase in severe periodontal pathogens such as *Treponema denticola* and *Tannerella forsythia*.^[16]

The prevalence of dental caries in SLE patients was found to be 87.6% in the present study. This is higher than the prevalence percentage reported for dental caries in all WHO index age groups in India, which is 60% in 15-year-olds, 78% in 35–44 year olds, and 84% in 65–74 year olds.^[17]

In the present study, statistically significant differences were observed in the occurrence of dental caries in patients with active and inactive SLE. The mean number of decayed teeth was 4.13 in patients with inactive SLE and 5.69 in patients with active SLE. This finding is similar to studies conducted by Rodriguez *et al.* (2016) on 60 SLE patients, where the caries prevalence was found to be 100% among patients with active disease and 85% among patients with inactive disease.^[18] Increased caries occurrence in SLE patients is attributed to reduced salivary flow rates, pH, buffering capacity, and loss of microbial diversity resulting in a state of disequilibrium between pathogenic and commensal bacteria that play a role in the development of dental caries.^[19]

The overall prevalence of mucosal lesions in the present study was found to be 86% which is comparatively higher to the prevalence percentage reported for oral mucosal lesions in studies done in India. A study by Kamala *et al.* (2017) reported the prevalence of oral mucosal lesions among 1500 outpatients attending a dental hospital in western Maharashtra to be 39.1%.^[20] Similarly, Mathew *et al.* (2008) found the prevalence of oral mucosal lesions to be 41.2% among dental outpatients in Karnataka.^[21]

Studies conducted by Menzies *et al.* (2018), Meyer *et al.* (1997), and Jonsson *et al.* (1984) have determined the prevalence of oral mucosal lesions in SLE patients to be 50%, 48%, and 45%, respectively.^[22-24] In the present study, the prevalence of oral mucosal lesions was found to be 78.4% among patients with active SLE and 8% among patients with inactive SLE. A higher prevalence percentage observed in this study might be attributed to larger sample size. Previous studies unanimously reported prevalence percentage in a sample of fifty or lesser patients with SLE.^[22-24] The mechanism through which these oral lesions occur has been attributed to circulating antigen-antibody complexes which lead to degeneration of keratinocytes present in the basement membrane of the oral mucosa.^[25]

A significant correlation was observed between disease activity and the presence of mucosal lesions in the present study. This is similar to studies conducted by Urman *et al.* (1978) where the presence of oral mucosal lesions was accompanied by a rise in clinical disease activity.^[6] A study was done by Jonsson *et al.* (1984) on SLE patients who reported the presence of mucosal lesions only in patients with active disease.^[24] Barrio Diaz *et al.* (2020) has also demonstrated that certain lesions such as pigmented macules and gingival telangiectasia were found in patients who had active cutaneous lupus and systemic lupus, respectively.^[26]

The most common oral mucosal lesion observed in SLE patients in the present study was the occurrence of aphthous ulcer. The prevalence of ulcers in patients with active SLE and inactive SLE was found to be 51.1% and 7.4%, respectively. This finding is similar to studies conducted by Urman *et al.* (1978) and Khatibi *et al.* (2012) where mucosal ulcers were the most commonly observed oral lesion in SLE patients; however, it was contrary to the study conducted by Jonsson *et al.* (1984) which reported a prevalence percentage of only 3% for mucosal ulcers in SLE patients.^[6,4,24]

Some of the integral components of primary care are health maintenance, health promotion, disease prevention and diagnosis, and treatment of chronic illnesses in varied healthcare setups. Primary care providers constitute the first point of contact for patients seeking care, aside from dentists who examine the oral cavity regularly, physicians can also include an oral examination in patients suspected of having an underlying disorder. As many systemic diseases present with lesions in the oral cavity which may sometimes be a marker or only sign of disease, it is important to know the clinical oral manifestations of systemic diseases such as SLE. Prompt diagnosis of these conditions by primary care providers can then enable the patient to obtain specialized care at an earlier period before fulminant disease develops and exposes the patient to suffering, loss of productivity, and decreased quality of life.

The limitations of the present study are that this study was done in a state-based referral center for SLE and the study sample may not be truly representative of the population. This study also did not use a comparison control group to understand whether healthy subjects exhibited significant differences than

patients with SLE. Owing to this reason, national prevalence rates for dental caries and periodontitis reported in national oral health survey (2002–2003) and prevalence rates reported in published literature including cross-sectional studies, systematic reviews, and meta-analysis were used for comparison between the general population and patients with SLE. The proportion of patients with active and inactive SLE was not equal in the present study which may have reflected in the study results. As this was a hospital-based study, the true prevalence rate of SLE and oral manifestations of SLE in the general population cannot be reliably estimated from this study.

Conclusion

From this study, it can be concluded that SLE patients have a higher prevalence of oral diseases such as dental caries and periodontitis in comparison to the prevalence of oral diseases in the general population. SLE patients also have a higher propensity to exhibit mucosal lesions in the oral cavity, most commonly with the presence of ulcers. In this study, SLE patients with active disease had poorer oral health status with an increase in dental caries occurrence and poor periodontal status with deeper periodontal pockets. Oral lesions were also found to occur more commonly in patients with active disease than in patients with inactive disease. Oral manifestation in SLE patients showed a high degree of positive correlation with SLEDAI scores. With such a high prevalence of oral lesions in SLE, it becomes important for primary care providers to know the various oral lesions that commonly occur in SLE. This would facilitate diagnosis at the level of the primary care center and further referral to specialized centers of care. Further research is recommended in this area with parameters such as salivary flow rate and microbiological assays of oral microbiota being included as studies assessing the association between disease activity and oral manifestations are scarce in the field of SLE and oral health research.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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