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BRIEF REPORT

Is chronic periodontitis premature in systemic lupus erythematosus patients?

Débora Cerqueira Calderaro[1] · **Gilda Aparecida Ferreira**[2] · **Jôice Dias Corrêa**[3] · **Santuza Maria Souza Mendonça**[4] · **Tarcília Aparecida Silva**[5] · **Fernando Oliveira Costa**[5] · **Antônio Lúcio Teixeira**[6]

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Abstract The aim of this study was to compare the frequency and severity of chronic periodontitis (CP) in systemic lupus erythematosus (SLE) patients with individuals without rheumatic diseases. Seventy-five patients with SLE were compared to 75 individuals without rheumatic diseases (control group) matched for age, educational level, and income. The activity of SLE was assessed with the *Systemic Lupus Erythematosus Disease Activity Index* 2000. *Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index for Systemic Lupus Erythematosus* evaluated SLE-related damage. Dental evaluation included measuring plaque index and parameters of periodontal disease (probing depth, clinical attachment level, and bleeding on probing). Fifty-one (68 %) SLE patients and 42 (56 %) control individuals had CP (p = 0.13). Periodontal status was similar in both groups. Considering only individuals with CP, SLE patients were younger than controls (40.7 ± 9.8 versus 46.14 ± 12.5 years of age, p = 0.02). CP was not associated with activity or therapeutics in SLE patients. Severity of periodontal parameters was similar in SLE patients and control subjects; however, CP occurred earlier in SLE patients.

Keywords Chronic periodontitis · Comorbid diseases · Periodontal diseases · Systemic lupus erythematosus

✉ Débora Cerqueira Calderaro
dccalderaro@gmail.com

[1] Rheumatology Service, Hospital das Clínicas, Universidade Federal de Minas Gerais, Rua Dona Nancy de Vasconcelos Gomes, 125/401, Sagrada Família, Belo Horizonte, Minas Gerais CEP: 31030-071, Brazil

[2] Department of Locomotor System, Faculdade de Medicina, Universidade Federal de Minas Gerais, Belo Horizonte, Brazil

[3] Cellular Biology Post-graduation Program, Instituto de Ciências Biológicas, Universidade Federal de Minas Gerais, Belo Horizonte, Brazil

[4] Faculdade de Odontologia, Centro Universitário Newton Paiva, Belo Horizonte, Brazil

[5] Faculdade de Odontologia, Universidade Federal de Minas Gerais, Belo Horizonte, Brazil

[6] Department of Internal Medicine, Faculdade de Medicina, Universidade Federal de Minas Gerais, Belo Horizonte, Brazil

Introduction

Systemic lupus erythematosus (SLE) is a chronic inflammatory disease which is considered a prototypical autoimmune disease. Chronic periodontitis (CP) is a chronic infection of periodontal tissues that leads to systemic and local inflammatory responses and immune-mediated destruction of supporting tissues of the teeth and alveolar bone. Association between CP and rheumatic diseases, such as rheumatoid arthritis, has been shown, but the association between SLE and CP remains debatable [1].

The reported frequency of periodontal disease in SLE patients is variable, ranging from 60 to 93.8 % [2]. The severity of periodontal parameters in SLE patients in comparison with healthy controls was addressed in different studies, with conflicting results. The influence of SLE treatment on CP was assessed in one study with juvenile SLE patients with a positive correlation between the cumulative dose of glucocorticoids and worse periodontal parameters [3]. Conversely, the influence of CP treatment on SLE activity has been addressed by a randomized controlled trial that enrolled 49 SLE patients with CP. Patients on periodontal treatment group showed a significant decrease in SLEDAI score that was not observed in the untreated group [4]. Comparative studies of adult SLE

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patients and controls did not investigate the associations between SLE features and periodontal parameters.

The present study aims to compare the frequency and severity of CP in adult SLE patients with individuals without rheumatic diseases (controls), and to evaluate whether there is any association between SLE features and periodontal parameters.

Patients and methods

Subjects of the study

SLE patients (according to ACR 1982/1997 revised classification criteria [5] with regular follow-up at the Rheumatology Outpatient Clinic of Hospital das Clínicas of Universidade Federal de Minas Gerais, Belo Horizonte, Brazil) were evaluated for the inclusion on the present study.

Patients with SLE were compared to subjects without SLE or other known rheumatic diseases (control group), matched for age, educational level, and monthly income. Control group included randomly assigned subjects from a population with demographic, social, and educational backgrounds similar to SLE patients, recruited during domiciliary visits regularly performed by allied health personnel, with no dental complaints. Their medical history was obtained from an interview.

Subjects included were at least 18 years of age and had eight erupted teeth. Exclusion criteria were SLE overlapping other rheumatic diseases (except for secondary Sjögren syndrome), treatment of periodontal disease within the last 6 months, use of orthodontic appliances, use of antibiotics within the last 3 months, need for antibiotics for infective endocarditis prophylaxis during dental procedures, chronic renal insufficiency requiring dialysis or after kidney transplantation, pregnancy or lactation, acute or chronic infectious conditions at the time of the study visit, and diagnosis of neoplasia within the last 5 years.

The following laboratory tests, performed according to standard routine techniques, were registered: erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), complement (C3 and C4) serum levels, and urinalysis. Anti-ds-DNA antibodies were detected by indirect immunofluorescence using *Crithidia luciliae* as substrate. The activity and damage of SLE disease were assessed, respectively, by the Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI 2k) [6] and the Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index for Systemic Lupus Erythematosus (SDI) [7]. High activity of SLE was defined as SLEDAI 2k ≥6 [8]. The presence of organ damage in SLE was defined as SDI ≥1 [9]. Renal disease was defined as proteinuria >0.5 g/24 h or the presence of cell casts, or renal biopsy compatible with lupus nephritis.

This study was carried out in compliance with the Helsinki Declaration and approved by the Institutional Ethics Committee (CAAE: 03128012.0.0000.5149/2012). All participants understood the study and provided written informed consent (signing the informed consent form approved by the Institutional Ethics Committee).

Dental evaluation

Dental evaluation was performed in all subjects included in the study (SLE patients and controls). Clinical periodontal indices, probing depth (PD), clinical attachment level (CAL), and bleeding on probing (BOP) were measured using a calibrated periodontal probe (Hu-Friedy, PCP 15, North Carolina University, Chicago, IL, USA). Probing depth (PD) is the depth of a sulcus or periodontal pocket determined by measuring the distance from the gingival margin to the base of the sulcus or pocket. Clinical attachment level (CAL) is the distance between the gingival margin and the cementoenamel junction. Bleeding on probing (BOP) is the bleeding that is induced by the manipulation of the gingival sulcus [10].

PD, CAL, and BOP were recorded from four locations per tooth (mesial, distal, lingual, and buccal), for each subject, by two calibrated examiners (JDC, SMSM).

The definition of periodontitis was based on the criteria proposed by Eke et al. (2012) no evidence of periodontitis; mild periodontitis ≥2 interproximal sites with CAL ≥3 mm, and ≥2 interproximal sites with PD ≥4 mm (not on the same tooth) or one site with PD ≥5 mm; moderate periodontitis ≥2 interproximal sites with CAL ≥4 mm (not on the same tooth), or ≥2 interproximal sites with PD ≥5 mm (not on same tooth); severe periodontitis: ≥ 2 interproximal sites with CAL ≥ 6 mm (not on same tooth) and ≥1 interproximal site with PD ≥5 mm [10].

Patients with CP were referred to periodontists for specialized treatment.

Statistical analysis

Statistical Package for the Social Sciences program (SPSS) for windows 17.0 was used. Descriptive analyses were performed, and data are presented as mean, median, standard-deviation (SD) and percentiles. Paired and independent Student's *t* test or Mann-Whitney's test were applied. Spearman or Pearson's correlation analyses were used to investigate a potential association among variables. Chi-square or Fisher's exact test was used to investigate associations among categorical variables. Binary logistic regression models were designed to determine the most significant associations. Significance level was determined as $p < 0.05$.

Results

Initially, 336 patients with SLE were invited to participate in the study, but 213 were excluded, with 62 patients excluded due to less than eight teeth. Finally, 75 patients with SLE and 75 control subjects were enrolled in the study.

Demographic features and periodontal status of the 75 SLE patients and the 75 subjects integrating the control group are shown in Table 1. Clinical SLE findings at the time of study entry were cutaneous lesions in 16 (21 %), serositis in 3 (4 %), oral ulcers in 5 (7 %), nephritis in 12 (16 %), seizures in 1 (1 %), arthritis in 5 (7 %), myocardial involvement in 1 (1 %), and hematological abnormalities (lymphopenia ≤1500/mm^3; leukopenia ≤4000/mm^3; hemolytic anemia or thrombocytopenia ≤100,000/mm^3) in 38 (51 %) patients. Thirty (40 %) patients had low complement (C3 or C4) levels and 24 (32 %) had anti-ds DNA positivity. Twenty-three (31 %) patients had high SLE activity (SLEDAI 2K ≥ 6) and 36 (48 %) had organ damage (SDI ≥ 1).

Periodontal status was similar in both groups, even after adjusting for gender and diabetic status (Table 1). However, in the comparative analysis of SLE patients and control subjects with CP, SLE patients were significantly younger than controls (mean (SD) 40.7 (9.8) versus 46.1 (12.5) years of age, $p = 0.02$) (Fig. 1). The likelihood of developing CP was systematically higher in SLE patients, especially at younger ages, despite the overlapping of confidence intervals (odds ratio (OR) = 2.92 (CI 0.998–5.98), $p = 0.06$) (Fig. 2).

The five SLE patients with arthritis had moderate periodontitis ($p = 0.02$). Other SLE features were not associated to periodontal status.

Table 1 Comparison of demographic characteristics and periodontal status between SLE patients and control group

	SLE patients ($n = 75$)	Control group (n = 75)	p Value [5]
Females	68 (91 %)	58 (77 %)	0.03
Age (years)	38 ± 9.8	41 ± 13.9	0.26
Ethnicity (White/non-White)	20 (27 %)/55 (73 %)	30 (40 %)/45 (60 %)	0.08
Income (minimum-wage[a]/month)[b]	3 (2–4)	3 (2–5)	0.1
Educational level (years of formal education)[b]	11 (8–11)	11 (8–13)	0.13
Diabetes mellitus	9 (12 %)	1 (1 %)	0.02
Current smoking	8 (11 %)	8 (11 %)	1.0
Disease duration (years)[c]	11.31 (7.42	–	–
Current use of corticosteroids[d]	62 (83 %)	–	–
Current use of immunosuppressants[e]	59 (79 %)	–	–
Current use of antimalarials[f]	47 (63 %)	–	–
Cumulative prednisone dosec (mg)[c]	38,692.42 (28,019.68)	–	–
SLEDAI 2 K[b]	4 (2–7)	–	–
SDI[b]	0 (0–2)	–	–
PD (mm)[b]	1.9 (1.72–2.16)	1.93 (1.67–2.32)	0.9
CAL (mm)[b]	2.1 (1.88–2.51)	2.02 (1.8–2.51)	0.41
Periodontitis	51 (68 %)	42 (56 %)	0.13
Mild periodontitis	2 (3 %)	1 (1 %)	1.0
Moderate periodontitis	36 (48 %)	28 (37 %)	0.19
Severe periodontitis	13 (17 %)	13 (17 %)	1.0

SLE systemic lupus erythematosus, *Anti-dsDNA* anti-double stranded DNA antibody, *SLEDAI 2K* Systemic Lupus Erythematosus Disease Activity Index 2000, *SDI* SLICC/ACR damage index, *PD* probing depth, *CAL* clinical attachment level, *BOP* bleeding on probing

[a] At the time of the study, one minimum wage corresponded to US$ 350,00

[b] Median (range)

[c] Mean (SD)

[d] Median (range): 7.5 (4–20) mg of prednisone/day

[e] Azathioprine: 25. Methotrexate: 10. Cyclophosphamide: 10. Mycophenolate: 8. Cyclosporine: 5

[f] Chloroquine Diphosphate or Hydroxychloroquine

[g] *P*-value was assessed using Mann-Whitney or Student's *t* test according to the normal distribution of numerical variables. Categorical variable associations were assessed using Chi-Square or Fisher's Exact Test. The significance level was established as $p < 0.05$

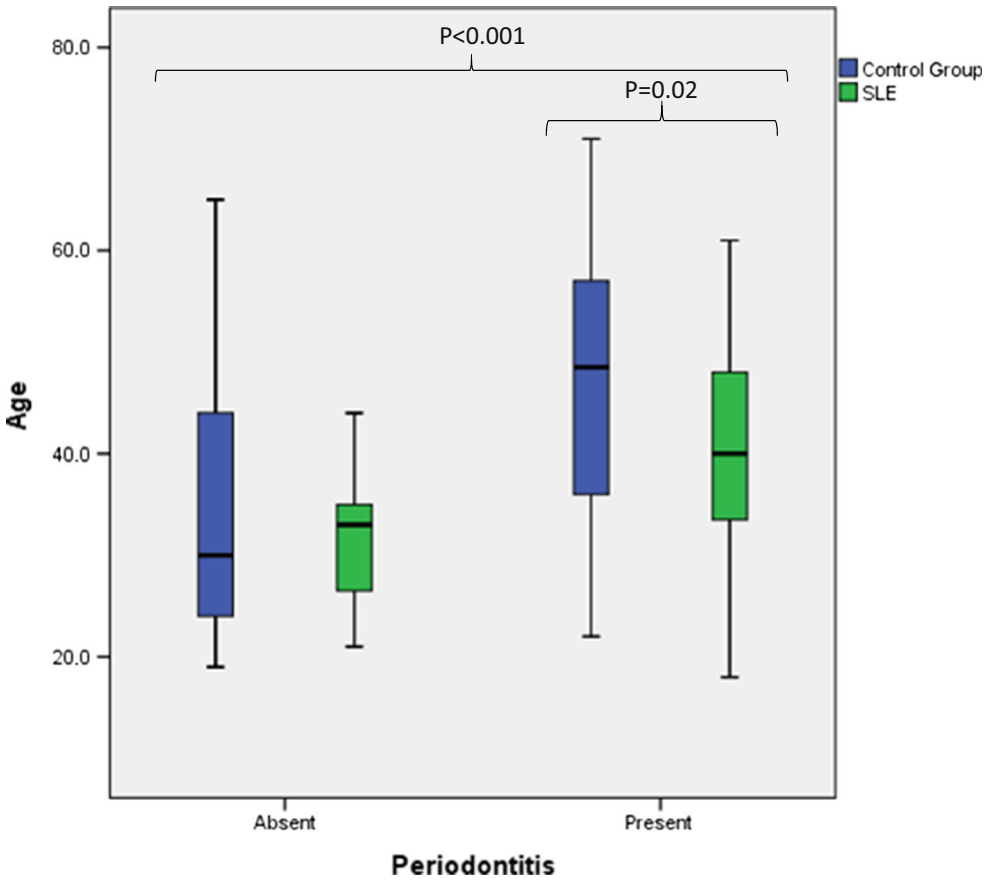

Fig. 1 Distribution of 75 SLE patients and 75 control subjects with and without chronic periodontitis according to age. *SLE* systemic lupus erythematosus

Correlation analyses among periodontal parameters and clinic-demographic data of SLE patients are shown in Table 2. Current smokers presented greater PD (median (range) 2.35 (1.86–2.52 mm) versus 1.9 (1.7–2.1 mm), p = 0.008) and CAL (median (range) 2.7 (2.43–3.22 mm) versus 2.09 (1.88–2.42 mm)) than non-smokers. There were no associations between periodontal status and gender, ethnicity, current use of corticosteroids, immunosuppressants or antimalarials, clinical and laboratory parameters, and SLEDAI 2K.

SLE patients with CP had a longer length of SLE (12.6 ± 7.8 versus 8.59 ± 5.8 years, p = 0.03) and a greater cumulative prednisone dose (42,473.54 ± 31,171.37 versus 30,657.55 ± 17,737.57 mg, p = 0.04) than SLE patients without CP.

In the SLE group, multivariate analysis using a binary logistic regression model that included CP as the dependent variable, age was the only variable independently associated with CP in SLE patients (OR 1.12; 95 % CI 1.04–1.19, p = 0.001, Hosmer and Lemeshow test 0.6).

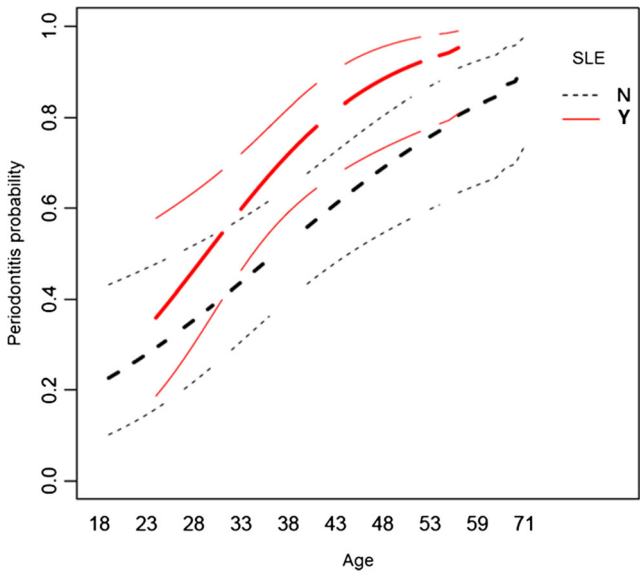

Fig. 2 Chronic periodontitis probability according to age in SLE patients and control subjects. *SLE* systemic lupus erythematosus, *Y* Yes, *N* No

Discussion

This is the first study to suggest CP occurs earlier in SLE patients than controls. The link between SLE and the early occurrence of different comorbid diseases, such as accelerated atherosclerosis [11], osteoporosis [12], cognitive dysfunction [13], and cataract [14], has been well described in the literature. The development of premature CP in SLE patients may be explained by multiple factors in common between both

Table 2 Correlations among periodontal parameters and demographic-clinical features in SLE patients (Spearman's correlation analyses)

	PD	CAL	BOP
Age (years)	$r = 0.22$; $p = 0.05$	$r = 0.5$; $p = 0.00$	$r = 0.09$; $p = 0.43$
Educational level (years of formal education)	$r = -0.29$; $p = 0.01$	$r = -0.37$; p = 0.01	$r = -0.17$; $p = 0.14$
SLE duration (years)	$r = 0.32$; $p = 0.005$	$r = 0.35$; $p = 0.002$	$r = 0.14$; $p = 0.25$
SLEDAI 2K	$r = 0.072$; $p = 0.54$	$r = 0.11$; $p = 0.37$	$r = -0.11$; $p = 0.35$
SDI	r = 0.22; $p = 0.058$	$r = 0.31$; $p = 0.006$	$r = 0.09$; $p = 0.41$
Cumulative prednisone dose (mg)	$r = 0.30$; $p = 0.008$	$r = 0.23$; $p = 0.049$	$r = 0.22$; $p = 0.058$

SLE systemic lupus erythematosus, *SLEDAI 2K* Systemic Lupus Erythematosus Disease Activity Index 2000, *SDI* SLICC/ACR damage index, *PD* probing depth, *CAL* clinical attachment level. *BOP* bleeding on probing

diseases, including shared genetic vulnerability [2], environmental predisposing factors (e.g., smoking) [15] and comorbidities such as metabolic syndrome and *diabetes mellitus* [16]. Furthermore, immune dysfunction associated with SLE and immunosuppressive treatment might play a role in the initiation and/or development of CP, a chronic infection with local and systemic inflammatory effects.

The frequency of CP in SLE patients found in this study is in agreement with previous studies [2] and similar to the control group. Since CP is a common condition either in SLE or in general population, a larger sample would be necessary to show any difference in the frequency of CP between both groups. Interestingly, a significant proportion of SLE patients was excluded from our initial sample as they had less than eight teeth, preventing CP evaluation. It is tempting to speculate that previous CP was responsible for dental loss in some of these excluded patients, indicating that the true incidence of CP during SLE is higher than reported.

The severity of periodontal parameters was similar between SLE patients and controls, which is also in line with some previous reports, but contradicts others [2]. These conflicting findings might be ascribed to differences in genetic and environmental backgrounds of the studied populations.

The present study found an association between arthritis in SLE patients and the occurrence of moderate periodontitis. This finding confirms a possible relationship between periodontitis and non-rheumatoid autoimmune arthritis, as suggested by experimental studies [17, 18].

Periodontal parameters were associated with organ damage-related variables in SLE (SLE duration, cumulative prednisone dose, SDI). Fernandes et al. [3] also described the association between the severity of periodontal parameters (i.e., BOP) and the cumulative prednisone dose in juvenile SLE patients. It would be possible to speculate that earlier dental evaluation and institution of periodontal treatment might contribute to reduce the development of SLE-associated damage and prevent premature dental loss.

This study is a pilot cross-sectional research. Due to its design, it is not possible to draw any definite conclusion on the temporal or causal relationship between SLE and CP. Further studies, with longitudinal design, involving a higher number of patients, are mandatory to corroborate these findings and to address the direction of the association between these two conditions.

The main contribution of this study was to suggest that CP is premature in SLE patients. The limitations were mostly the cross-sectional design and the number of SLE patients evaluated.

Conclusions

CP seemed to develop earlier in SLE patients and was associated with features related to organ damage. Accordingly, early reference to dentist's evaluation and periodical assessments, with emphasis on periodontal status, should become the standard care for physicians and other healthcare professionals dealing with SLE patients.

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Compliance with ethical standards

Disclosures None.

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