RIEE
ANIMAIS E HUMANOS

ARTIGO ORIGINAL

PERIODONTAL DISEASE AND SYSTEMIC LUPUS ERYTHEMATOSUS ACTIVITY

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Abstract

Because systemic lupus erythematosus (SLE) and periodontal disease share some pathogenetic similarities, a relationship between the two diseases might exist. This study aimed to assess SLE patients for the possible existence of a relationship between periodontal status and SLE disease activity. Fiveteen SLE patients had their disease activity index (SLEDAI), c-reative protein (CRP) serum levels and periodontal status determined. SLEDAI scores ranged from 0 to 11 and the CRP levels from 0.6 mg/l to 11.2 mg/l. The mean frequencies of periodontal sites with bleeding on probing and visible bacterial plaque were 8.79% (± 7.48) and 22.70% (± 26.32), respectively. The mean frequencies of sites with probing depths below 4 mm, between 4 and 6 mm and above 6 mm were 94.4% (± 10.87), 5.22% (± 10.07) and 0.38% (± 0.92), respectively. Statistical analysis showed significant correlation between the frequency of sites with visible bacterial plaque and C3 serum levels. Although not statistically significant, correlations between the periodontal condition with SLEDAI scores and CRP serum levels were found. This study suggests that there is a relationship between periodontal status and SLE disease activity and between periodontal status and CRP serum levels.

Keywords

Periodontal disease. Systemic lupus erythematosus. C-reactive protein.

1 INTRODUTION

Periodontal disease is a set of infections characterized by destruction of soft and hard tissues surrounding the teeth (KINANE; LINDHE, 1997). When inflammation involves only the gums, the situation is called gingivitis. If tooth-supporting tissues, i.e. cement, periodontal ligament and alveolar bone, are affected, the condition is called periodontitis (KINANE, 2001). Gingivitis, diagnosed through physical examination, is characterized by red swollen bleeding gums on periodontal probing. Besides the signs present in gingivitis, periodontitis is further characterized by loss of clinical insertion, with greater depths on gingival pocket probing, radiographically-detected bone loss and tooth mobility in more advanced cases (NYMAN; LINDHE, 1997).

Although periodontopathogenic bacteria (chiefly Gram-negative) are considered the main etiological factor in inflammatory periodontal disease (GREENSTEIN; HART, 2002), a combination of factors including environmental factors, acquired diseases and genetic predisposition is thought to influence disease pathogenesis, extension and severity (GREENSTEIN; HART, 2002; EBERSOLE et al., 2001). Periodontal tissue destruction is immunologically mediated (SIGUSCH et al*.,* 1998;) and thus related to host susceptibility to bacterial challenges (GUSTAFSSON et al*.,* 1997).

Identification of periodontal disease susceptibility criteria is paramount, as prevention, early diagnosis and treatment could then be reached (PEACOCK; CARSON, 1995). This is the rationale for studies that have been undertaken with patients with systemic conditions, such as systemic lupus erythematosus (SLE) that might influence periodontal health.

SLE is a chronic auto-immune inflammatory disease (AHSAN et al*.,* 2003) characterized by the production of a large number of antibodies and immune-complex formation (CARREÑO et al*.,* 2002; WAIS et al*.,* 2003) and more frequently affecting black women in the second and third life decades (RHODUS; JOHNSON, 1990; VOGEL, 1981). SLE etiology remains elusive and might be associated with hormonal, genetic, environmental and immunologic factors (RHODUS; JOHNSON, 1990; GONZALES; COLEMAN, 1999). Signs and symptoms vary widely according to disease severity and organ involvement (MUTLU et al.,1993).

C-reactive protein (CRP) is an acute phase reactant produced by the liver in response to infection or inflammation (CARVALHO et al*.,* 2007; LOSS et al*.,* 2000). Serum CRP levels are routinely measured for identification of systemic inflammation (CARVALHO *et al.,* 2007; GOLDIE, 2004). Studies with conflicting data have analyzed serum CRP levels in SLE patients (BARNES et al., 2005; WILLIAMS et al*.,* 2005) and patients with periodontal disease (CZERNIUK et al*.,* 2006; D'AIUTO et al*.,* 2004; LALLA et al*,* 2007; PERSSON et al, 2005). The role of CRP in the pathogenesis of both diseases has not been defined.

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Because SLE and periodontal disease share some pathogenetic similarities, the two diseases might modify the clinical evolution of each other. This study aimed to assess SLE patients for the possible relationship of periodontal status, SLE disease activity and serum CRP levels.

2 MATERIALS AND METHODS

2.1 PATIENTS

The sample was composed of 15 adults from both sexes, aged from 22 to 53 years, diagnosed with SLE and seen at the Rheumatology Outpatient Unit of the University Hospital of the Federal University of Juiz de Fora (HU/UFJF), MG, Brazil. Patients were excluded if they were: edentate, smokers, on anticonvulsant drugs, pregnant or diagnosed with another systemic condition besides SLE.

After periodontal assessment, the study participants were divided in two groups: one with seven patients with periodontitis and another with eigth patients without periodontitis.

The study was approved by the Research Ethics Committee of the Federal University of Juiz de Fora. All the participants signed their informed consent.

2.2 SLE CLINICAL AND LABORATORY ASSESSMENT

Patient clinical and laboratory assessment for determination of SLE disease activity was undertaken by a single rheumatologist from the HU/UFJF. The SLE Disease Activity Index (SLEDAI), a validated and reliable tool, was used. This index is the result of the summation of points attributed to some clinical and laboratory variables, such as seizures, lupus headache, alopecia, arthritis, myositis, complement consumption, anti-dsDNA increase, thrombocytopenia and leukopenia. The index score varies from 0 to 105, with 0 indicating SLE inactivity and higher values pointing to more intense disease activity (BOMBARDIER et al*,* 1992).

2.3 CRP SERUM LEVEL DETERMINATION BY THE ULTRA-SENSITIVE METHOD

CRP serum levels were measured with a highly sensitive commercial assay (Dade Behring, Milton Keynes, United Kingdom), according to the manufacturer`s instructions.

Eigth-hour fasting blood samples were obtained and centrifuged for 5 min at 3,500 rpm in order to obtain serum samples that were subsequently stored under refrigeration at 3ºC for a maximum of three days until undergoing nephelometry analysis.

The minimum detectable level with the method is 0.05 mg/l and we considered 3 mg/l as the cut-off value for CRP.

2.4 PERIODONTAL CLINICAL EXAMINATION

All the patients underwent periodontal clinical examination performed by a single periodontist. A Williams-type periodontal probe (Newmar®, Brazil) was used to examine six sites (mesial-vestibular, vestibular, distal-vestibular, mesial-lingual, lingual and distal-lingual) of all the teeth according to the following criteria (RIBEIRO et al., 2005):

1) Presence or absence of visible bacterial plaque;
2) Presence or absence of bleeding on probing;
3) Probing depth: distance in millimeters from the free gingival margin to the most apical point reached with gentle probing of the gingival pocket.

For each patient, the frequencies of sites with visible bacterial plaque, bleeding on probing and probing depth below 4 mm, between 4 and 6 mm and above 6 mm were calculated. The same analyses were made for the group as a whole.

Subjects with periodontal sites with probing depths over 3 mm were considered to have periodontitis.

2.5 STATISTICAL ANALYSIS

The "Statistical Package for the Social Sciences"-SPSS®, v. 11.0, was used for statistical analysis of the clinical and laboratory data. Spearman`s correlation coefficient was calculated for assessment of the correlations among the clinical periodontal variables, CRP serum levels, SLEDAI scores and the laboratory components making up the SLEDAI. Significance was established at 5%.

3 RESULTS

Rheumatologic assessment identified 2 patients with a SLEDAI score of 0 (inactive SLE). The other patients had SLEDAI scores ranging from 2 to 11, compatible with active SLE. The SLEDAI scores for each patient are presented in figure 1.

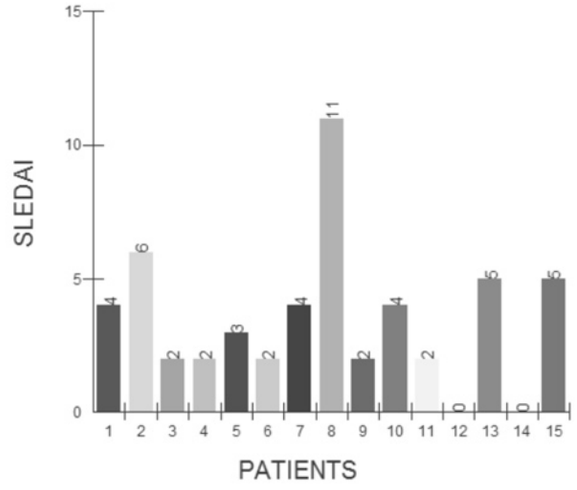

Figure 1: SLEDAI scores for each patient.

Mean SLEDAI scores did not significantly differ between those with and those without periodontal disease. The mean SLEDAI score for those with periodontitis was 3.42 (SD 1.62) and for those without periodontitis was 3.5 (SD 3.55), with p=0.678 (Figure 2).

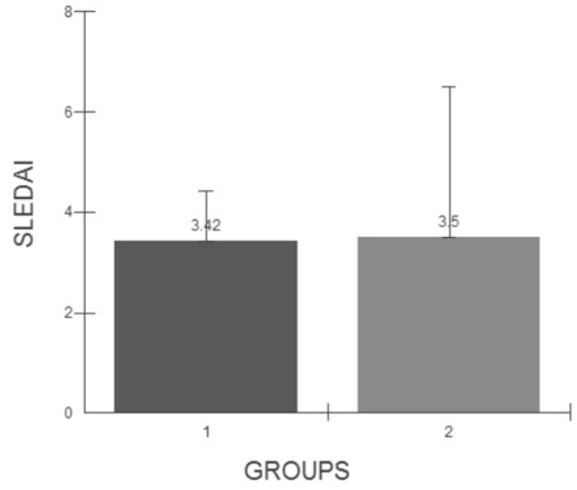

Figure 2: Mean SLEDAI values for patient with periodontitis (1) and patients without periodontitis (2).

CRP serum levels ranged from 0.6 mg/l to 11.2 mg/l. Five patients had serum CRP levels above 3 mg/l. Serum CRP levels for each patient are presented in figure 3.

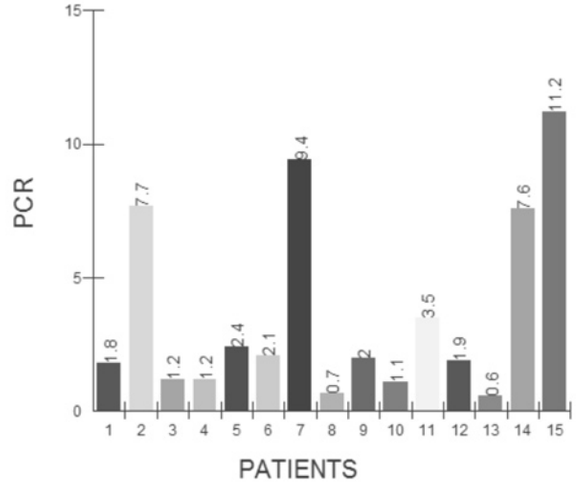

Figure 3: Serum CRP levels for each patient.

There was no significant difference (p=0.49) when mean CRP serum levels of patients with periodontitis (3.94 mg/l; SD 3.92) were compared with those of patients without periodontitis (3.35 mg/l; SD 3.34), as seen in figure 4.

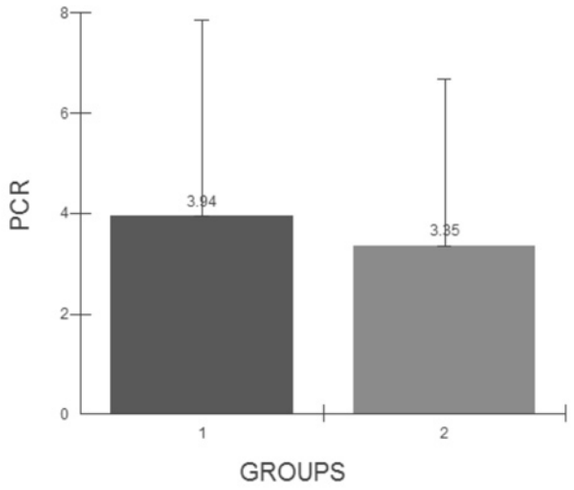

Figure 4: Mean serum CRP levels for patients with periodontitis (1) and patients without periodontitis (2).

Clinical periodontal assessment showed 94.40% (SD 10.87) of sites with depths below 4 mm, 5.22% (SD 10.07) with depths between 4 and 6 mm and 0.38% (SD 0.92) with depths over 6 mm. Furthermore, the mean frequencies of sites with bleeding on probing and visible bacterial plaque were 8.79% (SD 7.48) and 22.70% (SD 26.32), respectively, as seen in figure 5. Seven patients were diagnosed with periodontitis, with probing depths over 3 mm. Of these, three had sites with probing depths over 6 mm.

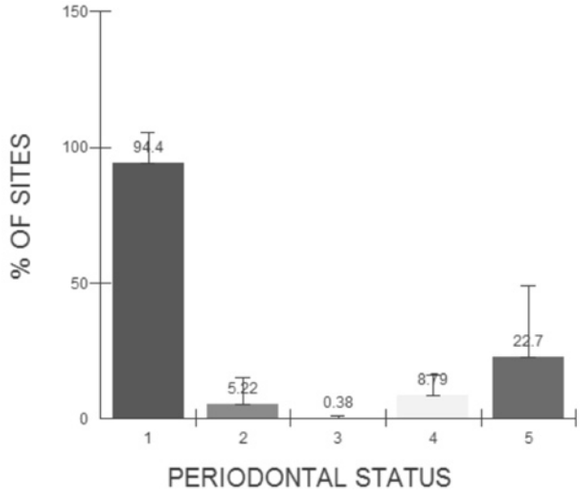

Figure 5: Mean frequencies of sites with probing depths below 4 mm (1), between 4 and 6 mm (2), over 6 mm (3), with bleeding on probing (4) and with visible bacterial plaque (5).

There was no significant correlation between the SLEDAI scores and periodontal status. Table 1 shows Spearman`s correlation coefficients between the SLEDAI scores and the frequencies of sites with probing depths below 4 mm, between 4 and 6 mm and over 6 mm, with visible bacterial plaque and bleeding on probing. In all cases we obtained p>0.05.

Table 1: Spearman`s correlation coefficients between the SLEDAI scores and the frequencies of sites with probing depths below 4 mm, between 4 and 6 mm and over 6 mm, with visible bacterial plaque and bleeding on probing.

Clinical eriodontal parameter	Frequency of sites with probing depth below 4 mm	Frequency of sites with probing depth between 4 and 6 mm	Frequency of sites with probing depth over 6 mm	Frequency of sites with visible bacterial plaque	Frequency of sites with bleeding on probing
Spearman`s correlation coefficients	-0,178	0,178	0,29	0,36	0,37
p values	0,57	0,57	0,30	0,19	0,17

There was no significant correlation between CRP serum levels and SLEDAI scores and between CRP serum levels and periodontal status. Table 2 shows the Spearman`s correlation coefficients between these variables, with the corresponding "p" values. In no case was $p \leq 0.05$ obtained.

Table 2: Spearman´s correlation coefficients between CRP serum levels and SLEDAI scores and frequencies of sites with probing depths below 4 mm, between 4 and 6 mm and over 6 mm, with visible bacterial plaque and bleeding on probing.

Variable	SLEDAI	Frequency of sites with probing depth below 4 mm	Frequency of sites with probing depth between 4 and 6 mm	Frequency of sites with probing depth over 6 mm	Frequency of sites with visible bacterial plaque	Frequency of sites with bleeding on probing
Spearman´s correlation coefficients	-0,09	-0,27	0,27	0,34	0,41	0,22
p values	0,75	0,32	0,32	0,22	0,13	0,44

There was a significant negative correlation between C3 levels and the frequency of sites with visible bacterial plaque (correlation coefficient = -0.570; p=0.026). For the other SLEDAI variables no correlation was found (Table 3).

Table 3: Spearman´s correlation coefficients between SLEDAI variables and the frequencies of sites with probing depths below 4 mm, between 4 and 6 mm and over 6 mm, with visible bacterial plaque and bleeding on probing.

		Frequency of sites with probing depth below 4 mm	Frequency of sites with probing depth between 4 and 6 mm	Frequency of sites with probing depth over 6 mm	Frequency of sites with visible bacterial plaque	Frequency of sites with bleeding on probing
Hematuria	Coef.	0,374	-0,374	-0,492	0,146	-0,293
	"p"	0,170	0,170	0,063	0,604	0,289
Proteinuria	Coef.	0,033	-0,033	-0,130	0,088	0,161
	"p"	0,907	0,907	0,643	0,756	0,558
Pyuria	Coef.	0,441	-0,441	-0,413	0,005	0,027
	"p"	0,100	0,100	0,126	0.985	0,924
C3	Coef.	0,294	-0,294	-0,087	-0,570	-0,200
	"p"	0,287	0,287	0,758	0,026*	0,475
C4	Coef.	0,190	-0,190	0,033	-0,415	-0,061
	"p"	0,498	0,498	0,907	0,124	0,830
CH100	Coef.	0,025	-0,025	0,023	-0,375	0,025
	"p"	0,929	0,929	0,935	0,168	0,930
Anti-DNA	Coef.	-0,249	0,249	0,263	0,155	0,273
	"p"	0,370	0,370	0,343	0,581	0,342
Leukocyte	Coef.	-0,190	0,190	0,350	-0,118	0,059
	"p"	0,498	0,498	0,201	0,675	0,835
Thrombocyto	Coef.	0,196	-0,196	0,105	0,045	0,186
	"p"	0,485	0,485	0,710	0,874	0,508

* Statistically significant negative correlation between C3 levels and the frequency of sites with visible bacterial plaque.

4 DISCUSSION

The SLE patients in this study had good periodontal status in general. There were 94.40% (SD 10.87) of the periodontal sites with probing depths below 4 mm, 5.22% (SD 10.07) with depths between 4 and 6 mm, and only 0.38% (SD 0.92) with depths over 6 mm. Furthermore, the mean frequencies of sites with bleeding on probing and visible bacterial plaque were 8.79% (SD 7.48) and 22.70% (SD 26.32), respectively. Seven participants, with probing depths over 3 mm, were diagnosed with periodontitis. Of these, only three had depths over 6 mm. The frequency of subjects with periodontitis in this study was 46.7%, considerably lower than the 93.8% found by Rhodus & Johnson (1990) in their SLE population. Kobayashi et al. (2003) diagnosed periodontitis in 70% of 60 SLE patients in their study. Novo et al. (1999) found periodontitis in 60% of the SLE patients they examined, a finding which is closer to ours. Souza (2006), assessing 16 patients with juvenile SLE, also found good periodontal status, although the frequencies of periodontal sites with bleeding on probing (33.2% ± 15.7) and visible bacterial plaque (33.1% ± 18.8) were higher than the ones we found.

There are literature reports suggesting that anti-inflammatory and immunosuppressive drugs commonly used in SLE might both protect against and favor periodontal destruction, the latter argument being based on immune suppression and subsequent overgrowth of periodontopathogenic bacteria. Because there was wide variation of drug types and dosages in our sample, we could not analyze the relationship between anti-SLE immunosuppressive therapy and periodontal status. However, SLE treatment might have protected our patients against periodontal disease, accounting for the low frequencies of periodontal disease founded. Moreover, Meyer et al. (2000) stated that controlled immunosuppressed patients have no significant periodontal changes. Our sample might have included controlled immunosuppressed individuals without significant periodontal changes.

Serum CRP levels ranged from 0.6 mg/l to 11.2 mg/l. Five patients had serum CRP levels over 3 mg/l, the cut-off value. There was no statistically significant difference when CRP levels between patients with and without periodontitis were compared. Likewise, correlation between clinical periodontal parameters and CRP levels was not statistically significant. There are no literature reports of the relationship between serum CRP levels and periodontal status of SLE patients, but only of systemically healthy subjects or those with a different systemic disease. Our data are in accordance with those of Bretz et al. (2005), Yamazaki et al. (2005) and Czerniuk et al. (2006), who did not find any association between the extension of periodontal disease and serum CRP levels. On the other hand, Ebersole et al. (1997) reported increased CRP levels in adults with periodontitis compared with healthy controls, with higher levels found in those with more aggressive periodontal disease. Loss et al. (2000) also found higher CRP levels in those with generalized periodontitis compared with those with localized periodontitis. The latter also had higher levels than healthy controls. Significant correlation between serum CRP levels and extension and severity of periodontal disease was also reported by Slade et al. (2000), D'Aiuto et al. (2004), Dye et al. (2005) and Pitiphat et al. (2008).

Although not statistically significant, a negative correlation was found between serum CRP levels and the frequency of sites with probing depths below 4 mm and a positive correlation between serum CRP levels and the frequency of sites with probing depths equal to or above 4 mm. This observation suggests a relationship between periodontal status and serum CRP levels: as serum CRP levels increase the periodontal status deteriorates with reduction of the frequency of sites with probing depths below 4 mm and an increase in the frequency of sites with probing depths equal to or over 4 mm.

We could not find any study of a possible relationship between the periodontal status and SLE disease activity in adults. A study of adolescents with juvenile SLE did not find any relationship between periodontal probing depths and SLE disease activity. Likewise, we could not find any statistically significant association between the periodontal status and SLE disease activity as determined by the SLEDAI. Additionally, when the SLEDAI components were individually analyzed, only C3 levels presented a statistically significant negative correlation with the frequency of sites with visible bacterial plaque. This correlation suggests that as the amount of bacterial plaque increases, serum C3 levels decrease, a finding that may be related to C3-consuming systemic inflammation. Although not statistically significant, a negative correlation between the SLEDAI scores and the frequency of sites with probing depths below 4 mm and a positive correlation between the SLEDAI score and the frequency of sites with depths equal to or over 4 mm were found. This observation suggests a relationship between the periodontal status and SLE disease activity. As the SLEDAI score increases (and SLE becomes more severe) the frequency of sites with depths below 4 mm decreases, and the frequency of those with depths equal to or above 4 mm increases, indicating that the periodontal disease also becomes more severe.

The lack of statistically significant correlation among the variables analyzed may be due to a periodontal status which is not severe enough to produce relevant systemic effects in our population. Yet, data from this study suggest a relationship between periodontal status and SLE disease activity, and between the periodontal status and serum CRP levels.

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