Association Between Dental Caries and Pneumonia in Patients with Systemic Lupus Erythematosus

VIRGINIA PASCUAL-RAMOS, CARLOS HERNÁNDEZ-HERNÁNDEZ, ARMANDO E. SOTO-ROJAS, ERIKA CELIS-AGUILAR, and JORGE SÁNCHEZ-GUERRERO

ABSTRACT. Objective. To establish the association between oral pathology and pneumonia in patients with systemic lupus erythematosus (SLE).

Methods. Thirty women with SLE, consecutively admitted for hospitalization because of pneumonia, and 60 noninfected controls with SLE (30 hospitalized and 30 ambulatory), matched by age, sex, and date of hospitalization to the cases, were enrolled. At entry, information about sociodemographic variables, traditional infection risk factors, SLE characteristics, treatment, and comorbidity was gathered by medical chart review. In every patient, one rheumatologist performed a complete physical examination, and assessed disease activity and chronic damage using validated indices; and one periodontist performed a standardized oral health evaluation including the use of 6 international oral health indices.

Results. Twenty-eight patients with community-acquired and 2 patients with nosocomial pneumonias were included. Age of the total study population was 38.8 ± 14.6 years, mean number of SLE criteria 6.3 ± 1.95, and disease duration 6.0 ± 7.2 years, with no differences among the 3 groups. Cases had greater disease activity and damage, and were taking higher doses of prednisone than ambulatory controls (p ≤ 0.03). Cases accrued more traditional infection risk factors than ambulatory controls and had lower levels of serum albumin than both control groups (p ≤ 0.04). Oral health was worse among the cases, including more periapical lesions, cervical and third-grade caries, and a higher mean number of caries/patient than controls (p ≤ 0.05). In the multivariate analysis, third-grade caries (odds ratio 7.5, 95% CI 2.05–27.3, p = 0.002) was strongly associated with pneumonia.

Conclusion. Poor oral hygiene and third-grade caries are common in patients with SLE who develop pneumonia. (First Release Sept 1 2006; J Rheumatol 2006;33:1996–2002)

Key Indexing Terms: SYSTEMIC LUPUS ERYTHEMATOSUS PNEUMONIA ORAL HEALTH CARIES

Systemic lupus erythematosus (SLE) is an autoimmune disease of complex etiology. Immunosuppression resulting from therapy, comorbidities, and the disease itself makes patients with SLE susceptible to severe infections. These occur in 14–45% of patients, and so are of major relevance for their prognosis. Pneumonia, one of the most common infections, occurs with variable frequency, clinical spectrum, and etiology.

During the past decade, several studies reported that oral health may be related to some systemic diseases. Dental plaque and poor oral health have been associated with nosocomial pneumonia and chronic obstructive pulmonary disease (COPD). Since community-acquired pneumonia and lung abscesses may be due to anaerobic bacteria, dental plaque would seem to be the logical source of these bacteria especially in patients with periodontal disease, acting as a reservoir of respiratory pathogens.

Few studies have assessed oral health in patients with autoimmune diseases. The American Heart Association recommends a standard regimen of antibiotic prophylaxis in patients with SLE undergoing dental procedures. Although oral mucosal lesions are more common in immunosuppressed patients than in healthy controls, there is no evidence of increased periodontal disease in patients with SLE. Oral health is also impaired in Behçet’s disease and correlates with disease severity.

We investigated the association between oral pathology and pneumonia in patients with SLE.

MATERIALS AND METHODS

Study population. The study was approved by the Institutional Committee of Biomedical Research and all patients gave signed, informed consent.

Thirty women with a diagnosis of SLE, consecutively admitted for hospitalization because of pneumonia, were enrolled. Pneumonia was diagnosed based on the presence of clinical signs and symptoms (fever, dyspnea, cough, tachypnea), laboratory abnormalities (leukocytosis, neutrophilia, low oxygen saturation), characteristic radiographic patterns (focal, multicentric, or atypical lesions), and the attending physician’s judgment; it was classified as nosocomial or community-acquired according to standard definitions.
As controls, 2 patients with SLE (one consecutively admitted for hospitalization and one ambulatory, chosen at random) free of infection were included, matched by age (± 5 years), sex, and date of hospitalization (± 1 week) to the cases. Hospitalized controls were admitted due to severe lupus activity (n = 18), surgical procedures (n = 6), and miscellaneous (n = 6). All participants were evaluated within 24 hours of study enrolment by a single rheumatologist and a single periodontist, blinded to patient’s allocation group.

Clinical evaluation. One rheumatologist (VPR) performed a physical examination, and scored SLE activity using the SLE Disease Activity Index (SLEDAI) and Mex-SLEDAI29,30, and chronic disease using the Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index (SLICC/ACR-DI)31. Biochemical abnormalities associated with higher risk of infection, i.e., serum creatinine > 3 mg/dl, erythrocyte sedimentation rate (ESR) > 50 mm/h, urine albumin excretion > 3.5 g/dl, low C3 levels, and low serum albumin, were purposely investigated at the index date32.

Clinical information was gathered from the medical charts using a standardized form, including sociodemographic data (age, sex, socioeconomic status, years of education, etc.), behavioral habits (past/current smoking tobacco index, alcohol consumption, and drug abuse), SLE characteristics (American College of Rheumatology criteria accrual, date of first and fourth criteria, disease duration, and length of follow-up), weight, height, and body mass index (BMI; kg/m²). History of pneumonia and/or recent hospitalization (occurring within one year from the index date) were intentionally explored. We also recorded the use and mean dose of immunosuppressive treatment (IT), corticosteroids (as equivalent dose of prednisone), and any other medication taken during the month before the evaluation.

Oral health evaluation. A standardized questionnaire for sicca symptoms33, oral hygienic habits (brushing frequency; use, frequency, and trademark of toothpaste; use of antiseptic and other hygienic devices), treatment of xerostomia, and comorbidity factors for periodontal disease (PD) was applied by an experienced periodontist. Xerostomia was assessed using the wafer test (WT) and nonstimulated whole salivary flow rate (NSWFR) as previously published34,35. Two 100 mm visual analog scales (VAS), one related to the patient’s oral health and another for xerostomia, were scored by each patient.

The periodontal examination included the description, type, location, and number of any lesions on the tongue, lips, commissures, hard and soft palate, oral mucosa, alveolar ridge, gums, and salivary glands; in addition, the number and location of teeth, missed teeth, filled teeth, and teeth alterations (peri- coronitis, periapical lesions, periodontal pocket and furcation lesions) were identified. The number and location of caries with emphasis on third-grade caries were also recorded. Six international indices to assess oral health were scored in every patient: the dental plaque index (DPI), the simplified oral hygiene index (OHI-S, 6 teeth evaluated), the retention index (RI), the total dental index (TDI), the periodontal screening recording index (PSR), and the decayed, missing and filled teeth index (DMFT); for definitions and scoring see below. All together, these indices evaluate the oral health and define the presence of PD and dental plaque.

Specifically, the PSR index was performed by a single certified periodontist and the PSR scores were recorded by sextants. Intraoral sextants were designated S1–S6 beginning in the right maxillary sextant (S1), proceeding clockwise and finishing in the right mandibular sextant (S6). A color coded probe 12 was used throughout the study since it limits false reading from over-measurement of probing depths. The CP 12 probe was gently inserted into the gingival sulcus of each tooth until light resistance was met and then the probe was walked around the tooth’s circumference. The PSR score was recorded from the greatest probe depth of each sextant of the mouth.

Recommendations related to oral health were offered to each patient after the evaluation.

Definitions. Community-acquired pneumonia: pneumonia in a patient attending the emergency room or the outpatient clinic, presenting with typical signs, symptoms, and a characteristic radiographic pattern, and who lacks a history of recent hospital admission36,37. Nosocomial pneumonia: pneumonia occurring in a hospitalized patient whenever symptoms developed 48 hours after the admission, following an invasive procedure such as bronchoscopy, or within a week after hospital discharge36. IT: use of corticosteroids, azathioprine, cyclophosphamide, methotrexate, chloroquine or hydroxychloroquine, mycophenolate mofetil, cyclosporine, or any other drug considered as immunosuppressant. Socioeconomic classification: composed of 7 levels according to income, level 1 (lowest) to level 7 (highest). Third-grade caries: caries of dentin with or without pulpal involvement. DPE: assesses the prevalence and severity of plaque buildup. Scores ranges from 0, no plaque, to 3, abundance of soft matter within the gingival pocket and/or on the gingival and adjacent surfaces37. OHI-S: the simplified version of the OHI evaluates 6 teeth instead of 12. It assesses oral hygiene or cleanliness. It has 2 components: the Simplified Debris Index, scored from 0 (no debris or stain present) to 3 (soft debris covering more than two-thirds of the exposed surface), and the Simplified Calculus Index, scored from 0, no calculus present, to 3, supragingival calculus covering more than two-thirds of the exposed tooth surface, or a continuous heavy band of subgingival calculus around the cervical portion of the tooth38. RI: combines the evaluation of open caries calculus as well as restoration overhangs into one index combining all plaque-retaining factors. It is ranked from 0, no plaque, to 3, the highest amount of plaque over the dental surface37. TDI: describes the severity of 4 different entities: caries (scored from 0 to 3), periodontitis (scored from 0 to 3), periapical lesions (scored from 0 to 3), and pericoronitis (scored as 0 if absent or 1 if present). TDI is ranked from 0, no abnormalities, to 10, the highest abnormalities in the 4 lesions described39. PSR: a quick diagnostic tool for the early detection of PD. It ranks from code 0, no PD, to 4, severe PD, defined as clinical attachment level above 5.5 mm. Code X denotes edentulous sextant; code * denotes clinical abnormalities, including but not limited to furcation invasion, mobility, mucogingival problems, or recession, extending to the colored area of the probe, 3.5 mm or greater40. DMFT index: assesses the prevalence of coronal caries. It is obtained as the sum of all the decayed teeth, teeth missing or extracted due to decay, and filled teeth with either a permanent or a temporary restoration because of caries. The maximum DMFT score is either 28, or 32 if the wisdom teeth are included. It ranges from 0, healthy teeth, to 28/32, unhealthy teeth41.

Statistical analyses. Descriptive statistics, one-way ANOVA, Student’s t-test, chi-square or Fisher’s exact test were used as needed. All the variables with p ≤ 0.10 in the univariate analysis were entered in the multivariate analysis using logistic regression. p was set at ≤ 0.05 level. Analysis was performed using the Stata 5.0 computer program (Stata Corporation, College Station, TX, USA).

RESULTS

Population characteristics. Ninety women with SLE were included in the study, 30 per group. The mean age of the study population was 38.8 ± 14.6 years and was comparable among the 3 groups; mean formal education was 11.1 ± 14.3 years, but cases had lower educational level than ambulatory (p = 0.01) and hospitalized controls (p = 0.06). BMI was lower in cases than in ambulatory controls (p = 0.02), and 88% of the patients were classified in the lower socioeconomic levels (1 to 3) with no differences among groups. Current smoking, alcohol use, and drug abuse were similar among the study groups, but cases referred past smoking more frequently than ambulatory controls (p = 0.05). Recent hospitalization took place more frequently in cases than in ambulatory (p = 0.003) and hospitalized controls (p = 0.06), but history of pneumonia was similar among the 3 groups (Table 1).

SLE characteristics. All but 3 patients (2 hospitalized controls and one ambulatory control) met 4 or more SLE criteria28. The other 3 patients met 3 criteria, and a diagnosis of SLE was made by their attending rheumatologist.
The mean time from the onset of the first SLE criterion, to clinical evaluations was 9.7 ± 8.9 years for the entire population, being comparable among groups. Among the 87 patients who fulfilled SLE criteria, disease duration (time between the onset of the fourth SLE criterion and the evaluation) was 6.6 ± 7.2 years, being similar among groups. The length of follow-up for the whole population was 6.3 ± 7.6 years; however, cases had shorter follow-up than ambulatory controls (p = 0.004). The mean number of SLE criteria in the study population was 6.3 ± 1.95, being equal among the groups, and SLE manifestations, as per ACR criteria, were also similar among the groups, except that low C3 and C4 serum levels ever, were more common among cases than ambulatory controls (p = 0.02 and p = 0.009, respectively). Disease activity and chronic damage, as per the SLEDAI, Mex-SLEDAI, and SLICC indices, were higher among the cases than ambulatory controls (p = 0.001, p = 0.0007, and p = 0.01, respectively). Finally, cases were taking a higher mean dose of prednisone and a lower mean dose of azathioprine compared to ambulatory controls (p = 0.01 and p = 0.03, respectively). No other differences regarding immunosuppressive treatment were found (Table 2).

**Pneumonia characteristics.** According to radiological findings, pneumonia was classified in condensation pattern (20 patients), multiple focus pattern (9 patients), and atypical pattern (one patient). Twenty-eight were community-acquired and 2 nosocomial pneumonias. Sputum and blood cultures were performed in 21 and 23 patients and they were positive in 3 and 2 patients, respectively. Pleural effusion was detected in 4 patients. All the patients improved after antibiotic treatment, but 3 required mechanical ventilation.

**Traditional infection risk factors (Table 3).** At the index date,
more cases had high serum creatinine and ESR, and low serum C3 levels ever, than ambulatory controls (p = 0.006, p = 0.001, and p = 0.04, respectively). In addition, cases had the lowest mean serum albumin values of all patients (p ≤ 0.04 for all group comparisons).

**Oral health and periodontal evaluations (Table 4).** Mouth dryness, as assessed by questionnaire and VAS, was more common among cases than ambulatory controls (p = 0.04 and p = 0.001, respectively); salivary flow, according to the NSWSF rate and WT, was lower among cases than ambulatory controls (p ≤ 0.02 for both); and regular professional dental care was less frequent among cases than hospitalized controls (p = 0.003).

Periapical lesions and cervical and third-grade caries were more frequent among cases than hospitalized (p = 0.05, p = 0.01, and p = 0.003, respectively) and ambulatory controls (p = 0.004, p = 0.01, and p = 0.02, respectively). Cases also had a higher mean number of caries/patient (4.3 ± 3.7) than ambulatory (2.5 ± 2.8, p = 0.04) and hospitalized controls (2.6 ± 3.1, p = 0.06).

The scores of the DPI, OHI-S, RI, TDI, PSR, and DMFT indices were comparable among the 3 groups. The proportion with ≥ 1 pockets greater than 5 mm (cases 3%, hospitalized controls 3%, and ambulatory controls 13%, p = 0.36) and the percentage of teeth with pockets greater than 5 mm (< 1% for all) were similar among the 3 groups. Nonetheless, a significant difference was found between cases and both control groups regarding the subset of the DMFT index that quantifies the number of decayed teeth.

**Multivariate analysis.** Several multivariate models were constructed in which demographic variables (age, BMI, socioeconomic status, education), SLE characteristics (SLEDAI, SLICC, complement levels), treatment (steroids), traditional infection risk factors (ESR, high serum creatinine levels, serum albumin levels), and oral findings (NSWSF rate, caries, periapical lesions) were included. In the final model, some traditional infection risk factors were associated with pneumonia, high serum creatinine [odds ratio (OR) 7.8, 95% CI 1.4–42.9, p = 0.02], ESR > 50 (OR 3.1, 95% CI 1.03–9.21, p = 0.04), and low serum albumin levels (OR 5.1, 95% CI 1.97–13.68, p = 0.001); however, as in the other models, third-grade caries remained as one of the strongest variables associ-

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### Table 3. Distribution of traditional infection risk factors among the patient groups.

<table>
<thead>
<tr>
<th></th>
<th>Cases, n = 30</th>
<th>Controls</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hospitalized, n = 30</td>
<td>Ambulatory, n = 30</td>
<td></td>
</tr>
<tr>
<td>Patients with serum creatinine &gt; 3 mg/dl, (%)</td>
<td>30</td>
<td>13.3</td>
<td>3.3</td>
</tr>
<tr>
<td>Patients with ESR &gt; 50, (%)</td>
<td>63.3</td>
<td>46.7</td>
<td>23</td>
</tr>
<tr>
<td>Patients with low C3 levels, (%)</td>
<td>36.7</td>
<td>43.3</td>
<td>13.3</td>
</tr>
<tr>
<td>Serum albumin: mean ± SD, (mg/dl)</td>
<td>2.3 ± 0.58</td>
<td>2.7 ± 0.89</td>
<td>3.7 ± 0.41</td>
</tr>
</tbody>
</table>

<sup>a</sup> Cases vs ambulatory controls (p = 0.006 for high serum creatinine and p = 0.001 for high ESR).
<sup>b</sup> Cases vs ambulatory controls (p = 0.04). Hospitalized vs ambulatory controls (p = 0.02). <sup>c</sup>p ≤ 0.04, for all intergroup comparisons.

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### Table 4. Results of oral health and periodontal evaluations in the study groups.

<table>
<thead>
<tr>
<th></th>
<th>Cases</th>
<th>Controls</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hospitalized</td>
<td>Ambulatory</td>
<td></td>
</tr>
<tr>
<td>Patients with mouth dryness, %</td>
<td>26.7</td>
<td>30</td>
<td>6.7</td>
</tr>
<tr>
<td>VAS related to sicca symptoms, mean ± SD, mm</td>
<td>4.7 ± 3.5</td>
<td>4.3 ± 3.5</td>
<td>1.9 ± 2.7</td>
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<tr>
<td>Patients without regular professional care, %</td>
<td>83</td>
<td>46.6</td>
<td>80</td>
</tr>
<tr>
<td>Values of NSWSF, mean ± SD, ml</td>
<td>0.23 ± 0.17</td>
<td>0.21 ± 0.16</td>
<td>0.42 ± 0.42</td>
</tr>
<tr>
<td>Patients with abnormal wafer test, %</td>
<td>76.7</td>
<td>66.7</td>
<td>46.7</td>
</tr>
<tr>
<td>Patients with periapical lesions, %</td>
<td>43.3</td>
<td>20</td>
<td>10</td>
</tr>
<tr>
<td>Patients with cervical caries, %</td>
<td>56.6</td>
<td>23.3</td>
<td>23.3</td>
</tr>
<tr>
<td>Patients with third-degree caries, %</td>
<td>56</td>
<td>20</td>
<td>26.6</td>
</tr>
<tr>
<td>No. caries/patient, mean ± SD</td>
<td>4.3 ± 3.7</td>
<td>2.6 ± 3.1</td>
<td>2.5 ± 2.8</td>
</tr>
</tbody>
</table>

<sup>a</sup> Cases vs ambulatory controls (p = 0.04). Hospitalized vs ambulatory controls (p = 0.02). <sup>b</sup> Cases vs ambulatory controls (p = 0.001). Hospitalized vs ambulatory controls (p = 0.004). <sup>c</sup> Cases vs ambulatory controls (p = 0.003). Hospitalized vs ambulatory controls (p = 0.007). <sup>d</sup> Cases vs ambulatory controls (p = 0.02). Hospitalized vs ambulatory controls (p = 0.01). <sup>e</sup> Cases vs ambulatory controls (p = 0.01). <sup>f</sup> Cases vs ambulatory controls (p = 0.004 for periapical lesions, p = 0.01 for cervical caries and p = 0.02 for third-degree caries). Cases vs hospitalized controls (p = 0.05 for periapical lesions, p = 0.01 for cervical caries and p = 0.003 for third-degree caries). <sup>g</sup> Cases vs ambulatory controls (p = 0.04), vs hospitalized controls (p = 0.06). VAS: visual analog scale; NSWSF: non-stimulated whole salivary flow; WT: wafer test.
disorder, and pneumonia when either the mean score of the PSR index, and serum albumin levels, and ESR > 50 mm/h are expected, patients with pneumonia had a less favorable health status than controls, including a higher frequency of traditional risk factors for severe infection, such as decreased renal function and serum albumin levels, and ESR > 50 mm/h. Nevertheless, in the different multivariate models constructed, third-grade caries remained one of the variables with the strongest association with pneumonia.

No relationship was found between periodontal disease and pneumonia when either the mean score of the PSR index, the number of patients with deep pockets, or the percentage of teeth with deep pockets were compared among the 3 groups. Since periodontal disease occurs mostly in subjects older than 35 years of age and almost 50% of our population was younger than that, this may explain this negative result.

Our results were consistent with several reports where oral hygiene was associated with increased periodontal disease and pneumonia. Periodontal disease has been associated with coronary heart disease and atherosclerosis, stroke, subclinical cardiovascular disease, and preterm delivery and low-birthweight infants. In the institutionalized elderly, dental plaque and poor oral health were associated with nosocomial pneumonia and chronic obstructive pulmonary disease, and oral care was found to reduce the risk of pneumonia and serious infections.

Different mechanisms have been proposed to explain the potential role of oral bacteria in the pathogenesis of respiratory infections. Among them are the aspiration of oral pathogens into the lungs; the modification of mucosal surfaces by periodontal disease-associated enzymes that promote adhesion and colonization by respiratory pathogens; the destruction of salivary pellicles by periodontal disease-associated enzymes that modify clearance of pathogenic bacteria from the mucosal surface; and alteration of the respiratory epithelium by cytokines originating from periodontal tissues to promote infection by respiratory pathogens.

Few studies have evaluated oral health in patients with SLE, with contradictory results. To our knowledge, no one has correlated third-grade caries with pneumonia. Meyer, et al determined the frequency of oral, dental, and periodontal findings in 147 immunosuppressed patients, of whom 46 had SLE diagnosis, and compared the results to those of 50 healthy subjects. They found more oral mucosal lesions in the group of patients than in the control group. Mutlu, et al failed to demonstrate a predisposition to increased periodontal disease in patients with SLE compared to healthy controls. Jensen, et al found a reduced NSWF rate and higher oral microbial counts in patients with SLE compared to healthy controls. We also found an impaired salivary flow rate, which is considered a risk factor for dental caries, in patients with pneumonia when compared to ambulatory controls.

Some potential limitations of our study need to be considered. The cross-sectional design of the study allowed us to describe an association between dental caries and pneumonia, but precluded affirming a cause-effect relationship. Although the dental care specialist who evaluated the patients was blinded to the diagnosis of pneumonia, he was aware of the hospitalized/ambulatory status of the patients and in some circumstances could guess who had pneumonia, so this could have influenced his oral health scoring. Since pneumonia was confirmed by appropriate cultures only in 3 patients, a diagnosis of lupus pneumonitis cannot be ruled out. However, all patients improved with antibiotics, and although the dose of prednisone was also increased in 14 patients, the dose was higher than 0.5 mg/kg in only 7 patients. Therefore we consider that they truly had pneumonia. This is a single-center study; therefore, the association between third-grade caries and pneumonia in other lupus populations needs to be confirmed.

The evidence gathered to date suggests that poor oral health may serve as a significant but potentially modifiable risk factor for lower respiratory tract infections, especially in immunosuppressed patients. Despite the beneficial aspects...
of newer therapeutic interventions to improve clinical outcomes in patients with SLE, major infections are still a leading cause of morbidity-mortality. Thus, an increased patient and physician awareness of the medical relevance of oral health would improve the outcome of SLE and other immunosuppressed patients.

We conclude that poor oral hygiene and third-grade caries are common in patients with SLE who develop pneumonia. Whether a cause-effect relationship exists still needs to be determined.

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