Type 1 diabetes mellitus and periodontal disease: Relationship to different clinical variables

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Abstract
Objective: This study is designed to evaluate the frequency of periodontal disease in a group of patients with type 1 diabetes mellitus and how this relates with diabetes metabolic control, duration of diabetes, and presence of diabetic complications.

Methods: A comparison was made of periodontal parameters (plaque index, bleeding index, pocket depth and attachment loss) in a group of diabetic patients (n=90) versus a group of non-diabetics (n=90). Logistic regression analysis was performed to evaluate relationship between periodontal parameters and degree of metabolic control, the duration of the disease, and the appearance of complications.

Results: Diabetics had greater bleeding index (p<0.01), deeper periodontal pockets (p<0.01) and more periodontal attachment loss (p<0.01) than non-diabetics. Deficient metabolic control and presence of diabetic complication were associated with higher bleeding index and pocket depth (p≤0.02).

Conclusions: Patients with type 1 diabetes appear to show increased periodontal disease susceptibility, particularly those with poorer metabolic control or with diabetic complications.

Key words: Diabetes mellitus, periodontitis, evolution, complications.
Introduction
Diabetes mellitus (DM) and periodontal disease (PD) are among the most prevalent human disorders. Frequently these two medical problems are present concurrently in many people. For years, attempts have been made to relate these two processes, and PD has even been regarded as one of the multiple complications of DM (1-3). On 1997, the report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus has defined PD as a disease of very high prevalence in patients with DM (4). Different mechanisms have been proposed to explain this relationship such as periodontal chronic inflammation which produces increased circulating cytokines and inflammatory mediators, autoimmune response to the chronic periodontal infection that leads to endothelial dysfunction, or the presence of certain factors that lead to increased susceptibility to PD and DM vascular diseases simultaneously (5).

Different studies have contributed evidence that the prevalence, extent, severity and progression of PD are increased in patients with DM (6). On the other hand, prospective studies have shown that PD in diabetic patients may be associated with poorer diabetic metabolic control and number of chronic diabetic complications (7,8). It has been suggested that adequate periodontal treatment in diabetic patients may be beneficial in reducing diabetic complications (9-11).

The present study has been designed to emphasize the relationship between diabetes mellitus and periodontal disease and to analyze how diabetes metabolic control, diabetes complications and diabetes duration are related with periodontal parameters.

Material and Methods
Patients were recruited from the Endocrinology department of our hospital, and selected based on the following two criteria: aged between 18 and 50 years old, and with a diagnosis of type 1 DM. Patients were excluded if they had non-type 1 diabetes, any inflammatory diseases, renal impairment (blood creatinine: 130 mol/L), chronic liver disease, or were receiving medical treatments that could influence the studied parameters such as antibiotics, antiepileptic or immunosuppressive drugs.

As a control group we selected healthy individuals who matched the patients in both age and sex. These individuals were people related with patients receiving treatment in the Stomatology Unit of the same hospital. Informed consent was obtained in all cases, and the local research ethics committee approved the protocol.

Medical history was performed recording age, sex, toxic habits, weekly physical exercise, level of oral hygiene, diet, and existence of diabetes complications.

Oral clinical evaluation comprised gingival bleeding, based on gentle probing at four points of the gingival sulcus using a North Carolina probe (HuFriedy®) calibrated every millimeter, to determine the presence or absence of bleeding. Bleeding index was calculated and expressed in percentage of the total number of points examined.

The plaque index was determined according to the hygiene index of O’Leary et al. (12). The presence or absence of bacterial plaque was visually assessed at four points of each tooth, and the results were expressed as a percentage. Bacterial plaque was sampled by displacing a periodontal probe along the gum margins. Likewise, clinical attachment loss (CAL) of the total teeth present in the mouth was evaluated with a calibrated North Carolina probe at 6 exploratory points for each tooth. This parameter measures de distance from the cemento-enamel junction to the bottom of the periodontal pocket and it shows the amount of alveolar bone that has been lost due to periodontal disease.

Lastly, we evaluated the probing pocket depth (PPD) of each explored tooth, using the same calibrated probe as before, and measuring the distance from the gingival margin to the bottom of the pocket for each tooth and at the 6 aforementioned points. In order to obtain detailed information on the severity of the periodontal lesions, the pockets were classified into three groups according to depth: 1-3 mm (mild pockets), 4-5 mm (medium pockets) and ≥ 6 mm (deep pockets). The results were expressed as percentages, and the mean probing pocket depth was also calculated, to allow comparison of the two patient groups.

The degree of metabolic control was evaluated on the basis of the glycosylated hemoglobin value (HbA1c), determined by high pressure liquid chromatography (HPLC)(Adams TM (Menarini®)). The value at the time of the study was documented, along with the mean of the values determined in the previous two years (4 determinations per patient and year). Good metabolic control was taken to be represented by HbA1c ≤ 7%, while poor control was defined as HbA1c > 7%. Normality for the controls was taken to be HbA1c < 5.5%.

On the other hand, patients with long evolving diabetes were defined as those in whom the diagnosis had been made 10 or more years ago. The presence of diabetic retinopathy was determined on the basis of the yearly funduscopic examinations, using previously established criteria (13). The diagnosis of diabetic nephropathy was based on the presence of albumin in 24-hours urine (≥30 mg/24 hours). Finally, the presence of peripheral neuropathy was based on vibration perception using a neurotensiometer (128 Hz) and the application of monofilament pressure (10 g)(13).

The qualitative variables were described as frequencies and proportions, and the quantitative variables as the mean and standard deviation (SD). The Student t-test was used in the bivariate analysis to compared means. Statistical significance was accepted for p<0.05.

We performed a logistic regression analysis using the
forward stepwise method for selecting variables according to the statistic likelihood ratio, in order to assess the association of the independent variables with the probability of being a diabetic patient. The adjusted Ors with 95% CI (Confidence Interval) were estimated. Plaque index, bleeding index, mean PPD, mean CAL and age were considered for inclusion in the model.

**Results**

The study group consisted of 90 patients diagnosed with type 1 DM. The mean age was 32.54 years ± 8.02, with a range of 19-50 years. On grouping the patients by decades of age, most were seen to belong to the 21-30 and 31-40 years age intervals (35.56% and 42.22% of the total, respectively). The mean time elapsed from the diagnosis of diabetes was 12.66 ± 8.40 years.

The control group (n=90) presented a mean age of 31 years ±7.38, with a range of 18-50 years. Most belonged to the 21-30 and 31-40 years age intervals (40% and 38.80% of the total, respectively).

There were no statistical significant differences between the two groups in terms of variables such as age, sex, smoking, physical exercise, or oral hygiene.

In effect, on examining the periodontal conditions of the diabetics versus the control group, no statistical significant differences were observed in terms of the plaque index, so the conditions of oral hygiene were similar in both groups.

However, significant differences were recorded in bleeding index, pocket depth and attachment loss (Table 1). The diabetic group presented a mean distribution of mild, medium and deep pockets of 72.26%, 23.73% and 3.52%, respectively. In the case of the control group, the percentages were 88.21%, 8.36% and 3.53%.

The mean glycosylated hemoglobin value among the diabetic patients at the time of the study was 7.83% ±1.62 (range 4-13.1%). Mean value corresponding to the two previous years was 7.79%±1.62. Glycosilated hemoglobin was under 7% in 46 patients, while the remaining 44 diabetics presented mean values above 7%. On comparing the diabetics with poor metabolic control of the disease versus those with moderate or good control, significant differences were recorded in bleeding index (p=0.02) and periodontal pocket depth (p=0.01) (Table 2).

A total of 49 patients had been diagnosed with diabetes over 10 years previously, while 41 had suffered the disease for shorter periods of time. On relating the periodontal conditions of the patients with long evolving disease versus those with a short duration of diabetes, significant differences were seen in bleeding index (p<0.01) and

### Table 1. Comparison of mean values of periodontal parameters between the two study groups.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Diabetic Group</th>
<th>Control Group</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plaque index (%)</td>
<td>63.34±25.3</td>
<td>63.17±31.2</td>
<td>0.61</td>
</tr>
<tr>
<td>Bleeding index (%)</td>
<td>50.54±26.4</td>
<td>18.36±18.5</td>
<td>&lt;0.01*</td>
</tr>
<tr>
<td>Pocket depth (mm)</td>
<td>3.12±0.8</td>
<td>2.18±0.5</td>
<td>&lt;0.01*</td>
</tr>
<tr>
<td>Attachment loss (mm)</td>
<td>2.36±1.1</td>
<td>1.29±0.4</td>
<td>&lt;0.01*</td>
</tr>
</tbody>
</table>

### Table 2. Relationship between periodontal parameters and different aspects of diabetes.

<table>
<thead>
<tr>
<th>Metabolic control</th>
<th>Disease duration</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poor</td>
<td>Disease duration</td>
<td>Complications</td>
</tr>
<tr>
<td>Plaque index (%)</td>
<td>short</td>
<td>long</td>
</tr>
<tr>
<td>Bleeding index (%)</td>
<td>69.6±23.3</td>
<td>61.3±24</td>
</tr>
<tr>
<td>Pocket depth (mm)</td>
<td>49.4±27.5</td>
<td>44.2±24*</td>
</tr>
<tr>
<td>Attachment loss (mm)</td>
<td>3.4±0.6</td>
<td>2.9±0.8**</td>
</tr>
</tbody>
</table>

* p<0.05; ** p<0.01 between each group

### Table 3. Variables associated with the probability of belonging to the diabetic group according to a stepwise logistic regression analysis.

<table>
<thead>
<tr>
<th>Covariate</th>
<th>Adjusted OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bleeding index (%)</td>
<td>1.026</td>
<td>1.005 - 1.047</td>
</tr>
<tr>
<td>Pocket depth (mm)</td>
<td>2.465</td>
<td>1.058 - 5.741</td>
</tr>
<tr>
<td>Attachment loss (mm)</td>
<td>2.969</td>
<td>1.179 - 7.476</td>
</tr>
</tbody>
</table>

OR odds ratio
CI confidence interval
periodontal attachment loss (p<0.01) (Table 2). Twenty-six patients (28.8%) suffered one or more chronic complications of the disease, while 64 (71.1%) experienced no complications. Between these two patient subgroups, differences were recorded in bleeding index (p<0.01) and periodontal pocket depth (p=0.02) (Table 2).

The results of the logistic regression analysis (Table 3) showed that bleeding index, periodontal pocket depth and attachment loss, all were positively and independently associated with the probability of being a diabetic patient.

Discussion
In recent decades, many studies have reported that the presence of diabetes mellitus (DM) increases the incidence and severity of periodontal disease (PD). There appears to be a relationship between the two processes, whereby the consequences of DM serve as modifiers of the expression of periodontal pathology (14). However, there are many aspects of this relationship that remain unclear. In this context, it has not been clarified whether good metabolic control influences the success of periodontal treatment or vice versa. Likewise, it remains to be determined whether the mechanisms involved are the same in both type 1 and type 2 DM (15,16).

The present study investigated 90 type 1 diabetics between 18 and 50 years of age, with absence of concomitant diseases. This homogeneous diabetic population was compared with a healthy group of 90 age- and sex-matched controls. Individuals under 18 years of age were excluded, in an attempt to avoid bias inherent to the duration of the disease (much shorter in younger individuals), together with patients over 50 years of age - in order to avoid the appearance of many complications specific of the disease. The two groups had healthy life styles and presented similar oral hygiene - thus contributing to homogenize the study series.

In coincidence with other authors (17,18), we recorded a mean glycosylated hemoglobin value of 7.83%, which was very similar to the value recorded in the two years prior to the study (7.8% on average). This showed the HbA1c values to be stable, and indicated that metabolic control among these individuals at the time of the study was representative of the usual metabolic conditions in most of them.

No differences were observed between the two groups in terms of bacterial plaque, and the level of oral hygiene was similar.

In the present study we found that despite similar plaque indexes in both groups, the diabetics showed a significantly higher bleeding index - this being suggestive of greater periodontal vulnerability. These observations are in concordance with most studies that consider diabetics to show greater periodontal inflammation in response to the irritation generated by the accumulation of bacterial plaque (19).

We also recorded more periodontal attachment loss and more pathological periodontal pockets in the diabetic patients than in the control group - in coincidence with the observations of Oliver et al. (20). Regression analysis also showed the association between severity of the periodontal parameters and the probability of being diabetic subject. This could be interpreted as simply another complication of the disease, secondary to increased inflammation and alterations in tissue repair due to the impact of advanced glycosylation end products (AGEs) in the membrane of the fibroblasts within the periodontal pocket - a situation that would alter collagen stability and gingival vascular integrity (21). Likewise, the immune response is deficient in these patients (22), with an increase in interleukins such as IL-6 and IL-1β, together with tumor necrosis factor alpha (TNFα) and prostaglandin E2 (PGE2). As reported by Salvi et al. (23), these factors would act at crevicular level, stimulating the periodontal inflammatory response.

On the other hand, it appears to be a relationship between metabolic control and periodontal status. In the present study we found poorer control of diabetes to be associated with deeper periodontal pockets, in coincidence with other investigators (24). However, these data have not been corroborated by all authors (25).

High blood glucose sustained over time appears to give rise to a situation of chronic inflammatory mediator secretion, and thus to an exaggerated periodontal response. However, from the opposite perspective, it could be postulated that the severity of PD could affect DM control despite adequate integral treatment and patient cooperation (1).

It is also important to examine the relationship between the time elapsed from DM diagnosis and PD, since some authors have reported a correlation between a longer duration of DM and increased severity of PD. Thus, in young type 1 diabetics, Firatli et al. (26) observed a clear relationship between the years of evolution of the disease and clinical attachment loss. In the present study involving similar mean ages, a correspondence was found between the duration of DM and attachment loss. However, a more in-depth evaluation of this variable is required to establish its true influence, since age is an acknowledged PD risk factor, and this could alter the results obtained. Among the younger diabetics, a duration of DM of over 10 years tended to influence both attachment loss and pocket depth. In this group of younger diabetics, age as a risk factor for PD would not have been able to exert an influence.

In the present study we observed a positive relationship between bleeding index and the presence of periodontal pockets with complications of DM. Rylander et al. (27) in turn reported a correlation between complica-
tions inherent to DM, such as diabetic retinopathy or nephropathy, and an increased degree of periodontal inflammation. Thorstensson et al. (7) and Scannapieco (28) related the existence of cardiovascular and renal complications, and infections, to the severity of PD and epithelial attachment loss - in contraposition to earlier studies (29) where no association was recorded between the periodontal parameters and the complications inherent to diabetes. A relationship has been described between PD and the development of systemic diseases in young (30). Noma et al. (31) described a significant relationship between the severity of periodontal disease and diabetic retinopathy, with high IL-6 concentrations in the retinal vitreous fluid of the studied patients. Although the reasons for this increase have not been established, the presence of immune alterations in these patients, with the subsequent increase in inflammatory mediator production, could be responsible for the damage observed both at periodontal level and elsewhere.

In conclusion, we observed increased periodontal susceptibility in our type 1 diabetic patients compared with the non-diabetic controls. A greater periodontal inflammatory tendency corresponded to those individuals with poorer metabolic control or with complications, while longer durations of DM were associated with greater periodontal attachment loss. In the presence of similar bacterial plaque indexes, type 1 diabetic patients are comparatively more vulnerable to periodontal problems. We therefore consider that other factors must be responsible for this increased periodontal sensitivity, possibly related to the low high degree inflammation that characterizes diabetes.

References