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Self-Reported Periodontitis and Complications in Type 1 Diabetes Patients: A Brazilian Nationwide Survey

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This study aimed to evaluate the possible association between periodontitis and systemic complications in a Brazilian type 1 diabetes population. A multicentre, sectional study was carried out in 28 public clinics located in 20 Brazilian cities. Data from 3,591 patients were obtained (56.0% females, 57.2% Caucasians), with an average age of 21.2 ± 11.7 years and whose mean duration of type 1 diabetes was 9.6 ± 8.1 years. Periodontitis was evaluated through self-report. Odds ratios (OR) and 95% confidence intervals were calculated to evaluate the association between periodontitis and systemic diabetes complications (chronic micro and macrovascular complications and hospitalizations by hyperglycemia and diabetic ketoacidosis). The prevalence of periodontitis was 4.7% (n=170). Periodontitis patients had mean age of 27.4 ± 12.9. This group was older ($p<0.001$), exhibited longer diabetes duration ($p<0.0001$) and had elevated total cholesterol ($p<0.05$), triglycerides ($p<0.001$) and lower HDL ($p<0.05$) values than patients without periodontitis. Systolic and diastolic blood pressures were significantly increased in periodontitis patients ($p<0.01$). Periodontitis patients had increased odds of microvascular complications (2.43 [1.74-3.40]) and of hospitalizations related to hyperglycemia (2.76 [1.72-4.42]) and ketoacidosis (2.72 [1.53-4.80]). In conclusion, periodontitis was associated to systemic complications in Brazilian type 1 diabetes patients.

Key Words: periodontitis, type 1 diabetes mellitus, diabetes complications, association

Introduction

Diabetes mellitus is a cluster of chronic metabolic disorders characterized by abnormal metabolism of glucose caused by defects in insulin production and/or action (1). International Diabetes Federation estimates indicate that 382 million people worldwide present diabetes (2). Cost estimates in the Brazilian Public Health System evince diabetes as a serious economic threat to public authorities and all social sectors (3). Periodontitis is a biofilm-induced chronic inflammatory condition affecting teeth-supporting tissues (4). According to National Health and Nutrition Examination Survey data 8.5% of the adult U.S. population presented severe periodontitis, which may cause tooth loss (5).

Several studies have established the relationship between periodontitis and diabetes, which seems to be bidirectional. Diabetes is an established risk factor for periodontitis, as well as periodontitis influences metabolic control and the development of diabetic complications (1). Furthermore, periodontal treatment may reduce glycated hemoglobin in diabetics (6). The link between both diseases is not fully understood. Current findings point to pro-inflammatory response in determining periodontitis susceptibility and progression in patients with diabetes. In addition, locally activated inflammatory mediators could impair insulin signaling and impact on diabetes (1).

The majority of research has focused on the relationship between type 2 diabetes and periodontitis. However, type 1 diabetes (T1D) also increase the risk of periodontitis (7). Dakovic and Pavlovic (8) have found increased odds for periodontitis in type 1 diabetes patients (odds ratio = 2.78; 95% confidence interval: 1.42 - 5.44). Likewise, TID patients have higher odds for increased number of missing teeth in comparison with non-diabetic patients (9). The association between periodontitis and diabetes complications in T1D patients has been even less studied. In a follow-up study, significantly increased prevalence of proteinuria and cardiovascular complications were observed in T1D patients with severe periodontitis compared to T1D patients with no/minor periodontitis (10).

Thereby, the scientific evidence on this topic is scarce. We hypothesized that as periodontitis is associated to a low-grade systemic inflammation and an impairment of insulin signaling (1), T1D patients with periodontitis would have an increased odds of having diabetes chronic complications. Thus, this cross-sectional study evaluated the possible association between periodontitis and systemic complications in a Brazilian T1D population.

Material and Methods

This multicenter, cross-sectional study was performed

in 28 public ambulatory outpatient clinics from secondary or tertiary levels of care, situated in 20 Brazilian cities in four regions (north/northeast, southeast, south, and mid-west) between December 2008 and December 2010. Detailed methods of data collection have been previously described (11). Briefly, all patients received health care from the Brazilian Health Care System. The participating centers possessed a diabetes clinic with at least one endocrinologist and data from a minimum of 50 consecutive patients presenting an initial diagnosis of T1D regularly attending the clinic. Inclusion criteria consisted of a diagnosis of T1D by a physician based on the typical clinical presentation, such as weight loss, polyuria, polydipsia and polyphagia, and the need for continuous insulin use since T1D diagnosis. All patients were diagnosed between 1960 and 2010.

The following variables were assessed during the clinical visit: age, race, educational level, economic status, smoking status (current smoking should smoke more than one cigarette/day at the moment of the interview), height, weight, mean systolic (sBP) and diastolic blood pressures (dBP) (three consecutive measurements in one day were performed using a standard sphygmomanometer). Age at diagnosis, duration of diabetes, modality of diabetic treatment, comorbidities, hospitalization due to hyperglycemia or diabetic ketoacidosis (DKA), and frequency of self-monitoring of blood glucose were also gathered. Levels of glycated hemoglobin (HbA1c), fasting plasma glucose (FPG) and lipid profile on the last clinical visit were obtained from medical records. Screenings for retinopathy, using fundoscopy; nephropathy, according to microalbuminuria; and foot examinations in patients with diabetes duration equal or greater than five years were noted when these procedures were performed within one year of the study assessment. Analysis of diabetic chronic microvascular complications was not performed in patients with diabetes for less than five years (n=1,160, 32.3%).

The Brazilian Economic Classification Criteria was used to assess the economic status (16). This classification also considers education level, which is classified as illiterate/incomplete primary education, complete primary education/incomplete secondary education, complete secondary education/incomplete high school, complete high school/some college or complete college education. The following classes of economic status were considered in the study: very low, low, middle and high (12). The study was approved by each local ethics committee. The Brazilian Diabetes Society monitored and reviewed study-related documents and approved all amendments and publications. Each center's coordinator reviewed the chart form prior to final approval. All patients or their parents when necessary signed an informed consent.

Hypertension in adults was defined as sBP≥140 mmHg and/or dBP≥90 mmHg, measured during the last clinical visit (13) or self-report; in children and adolescents, hypertension was defined as sBP or dBP≥95th percentile, according to age, sex and height of the patient (14). ADA criteria were used to define microalbuminuria and clinical nephropathy (15). Overweight and obesity were defined according to established BMI cutoffs for adults and children and adolescents (15).

Methods used to measure HbA1c levels were collected from the medical charts. HbA1c measurements were obtained for 3,099 patients (86.2%) using methods that were certified by the National Glycohemoglobin Standardization Program; of these, 51.3% (n=1,766) were evaluated using high-performance liquid chromatography, whereas 46.6% (n=1,601) were evaluated using turbidimetry. FPG, triglycerides, HDL and total cholesterol were assessed using enzymatic techniques. LDL levels were calculated using Friedewald's equation (16). Patients were classified as children (≤ 13 years of age), adolescents (≥ 13 years and ≤ 18 years) and adults (>18 years) (15).

A detailed description of the study sample calculation has been described previously. Sample size was calculated based on the estimated prevalence of T1DM in Brazil and the population density of each geographic region (11).

Periodontitis was evaluated through self-report after giving a brief explanation about what periodontitis is. The following question was asked to all patients 'Do you think you have gum disease?' Whenever available, medical records were checked for a possible diagnosis of periodontitis.

Data are presented as means (±standard deviation) for continuous variables and as frequencies for categorical variables. Comparisons between numeric variables were performed using independent t-tests and z-tests for discrete variables with a normal approximation to binomial distribution. Odds ratios and 95% confidence intervals (CI) were calculated with periodontitis (yes/no) as independent variable and chronic complications and hospitalizations (hyperglycemia and ketoacidosis) as dependent variables. Analyses were performed using SPSS version 16.0 (Statistical Package of Social Sciences, Chicago, Illinois, USA). A p-value less than 0.05 was considered significant.

Results

Demographic data for the study population are presented in Table 1. Demographic data were available for 3,591 patients. The majority of the patients evaluated were under age 30 (n=1,077, 30%). The mean age was 21.2 ±11.7.

The prevalence of periodontitis was 4.7% (n=170). Periodontitis patients were older (p<0.01) and showed both higher age at diagnosis and diabetes duration (p<0.001) than periodontally healthy patients. Periodontal patients also presented higher systolic and diastolic blood

pressure (p<0.01). Regarding to biochemical variables, patients with periodontitis exhibited increased total cholesterol (p=0.03), triglycerides (p<0.001) and lower HDL cholesterol (p<0.05) than patients with no periodontitis. Periodontitis patients presented higher frequencies of microvascular complications (p<0.001), hospitalizations by both hyperglycaemia (p=0.001) and diabetes ketoacidosis (p<0.01). These data are presented in Table 2.

Periodontitis patients presented ORs (95% CI) of 2.43 (1.74-3.40) and 2.48 (1.79-3.44) for microvascular and micro/macrovascular chronic complications, respectively. Regarding hospitalization, periodontitis patients showed increased ORs for hyperglycemia (2.76 [1.72-4.42]) and DKA (2.72 [1.53-4.80]) in comparison with patients with no periodontitis.

Discussion

This study aimed to assess the possible association between periodontitis and systemic complications in a Brazilian type 1 diabetes population. We assessed a range of diabetes chronic complications, both microvascular and macrovascular and comorbidities. To the best of our knowledge this is one the greatest studies in this field. This population presented a prevalence of periodontitis of 4.7% and it was significantly associated with age, duration of diabetes, diabetes-related chronic complications and other comorbidities.

Table 1. Demographic data of the studied population

Variable	
Age, years	21.2±11.7
Gender, female (n [%])	2,010 (56.0)
Age at diagnosis, years	10.0 (<1 to 44)
Age at diagnosis, years (n [%])	
0-4.9	667 (18.5)
5-9.9	961 (26.8)
10-14.9	941 (26.2)
≥15	1,022 (28.5)
Diabetes duration, years	9.6±8.1
Diabetes duration, years (n [%])	
0-4.9	672 (18.7)
5-9.9	961 (26.8)
10-14.9	941 (26.2)
≥15	1,017 (28.3)
Level of care, n (%)	
Secondary	995 (27.7)
Tertiary	2,596 (72.3)
Region (n [%])	
Southeast	1,424 (39.7)
North/northeast	1,113 (31)
South	820 (22.8)
Mid-west	234 (6.5)

The data are presented as means (±SD) and frequencies.

The reported prevalence of periodontitis in T1D patients has been variable. Studies have set the prevalence between 6 and 10% (17). Others studies have found prevalence of periodontitis as high as 57.9% in type 1 diabetics (7). Our study found a prevalence of 4.7%. Differences in age, duration of disease and level of metabolic control may account for these observed variations in prevalence (7,17). Different methods have been used to evaluate periodontitis (full and partial-mouth examinations, radiographs), which may also contribute to variations in prevalence. Our study used self-reported periodontitis and the question asked presents good validity (18).

In agreement with our result, Poplawska-Kita et al. (7) have also found higher age in diabetic patients with periodontitis. Regarding blood pressure and biochemical variables, we found higher sBP and dBP, total cholesterol, triglycerides and lower HDL cholesterol in periodontitis patients. Elevations in blood pressure were found in systemically healthy patients with periodontitis (19). Likewise, a worsening in lipid profile was shown in periodontitis (20). In T1D patients, Poplawska-Kita et al. (7) have found no significant difference in blood pressure and lipid profile between patients with and without periodontitis. Merchant et al. (21) have found non-significant increases in total cholesterol, LDL cholesterol and triglycerides in T1D patients with periodontal damage. On the other hand, periodontal inflammation was negatively associated with HDL levels in TID patients (22). These conflicting results might arise from differences in populations evaluated. Our population was younger than that from Poplawska-Kita and Passoja's studies and older than that from Merchant's study. Variations in duration of disease and level of metabolic control might also account for the differences. Our sample presented mean duration of diabetes of 9.6 years. Other studies have shown duration of disease of about 1 year (21) and 20 years (22).

This study adds significant knowledge to the field, as it showed significantly higher frequencies, as well as higher odds ratios of microvascular and micro/macrovascular complications and hospitalizations by both hyperglycaemia and diabetes ketoacidosis in TID patients reporting periodontitis. In a case-control study, 2 groups of insulin-dependent diabetics, 1 with severe periodontitis and 1

Table 2. Demographic, clinical and laboratorial data of the patients presenting or not periodontitis

Variables	Periodontitis*		p value
	Yes (%)	No (%)	
n (%)	170 (4.7)	2,649 (73.8)	-
Age, years	27.4±12.9	20.7±11.5	< 0.001
Age at diagnosis, years	14.4±8.9	11.3±7.8	< 0.001
Gender, Female n (%)	93 (54.7)	1,500 (56.6)	0.6
Diabetes duration, years	12.9±9.1	9.5±8.0	< 0.001
Race, n (%)			0.5
Caucasian	96 (56.5)	1,562 (59.0)	
Non-Caucasian**	74 (43.5)	1,087 (41.0)	
Economic Status, n (%)***			0.048
High	7 (4.1)	192 (7.5)	
Medium	31 (18.2)	610 (23.9)	
Low	59 (34.8)	871 (34.1)	
Very Low	73 (42.9)	883 (34.5)	
BMI (kg/m2)	22.6±4.2	21.6±4.2	0.004
Overweight/obesity, n (%)	48 (28.2)	837 (31.6)	0.3
Fasting glycaemia (mg/dL)	186.0±117.8	181.8±104.3	0.3
HbA1c (%)	9.2±2.2	9.2±2.3	0.9
HbA1c at goal, n (%)	20 (14.2)	463 (19.0)	0.15
sBP (mmHg)	115.3±20.1	110.1±16.5	< 0.001
dBP (mmHg)	73.5±13.4	70.7±11.4	< 0.003
Total Cholesterol (mg/dL)	177.6±43.9	170.0±41.5	0.03
HDL cholesterol (mg/dL)	49.7±14.2	52.9±14.7	0.02
LDL cholesterol (mg/dL)	105.2±36.5	99.5±33.0	0.059
Triglycerides (mg/dL)	115.8±100.5	91.7±69.9	< 0.001
Smoking status			< 0.001
Current smoker, y (%)	10 (5.9)	112 (4.2)	
Ex-smoker, y (%)	27 (15.9)	187 (7.1)	
Never smoker, y (%)	133 (78.2)	2255 (85.1)	
Dose of insulin (U/Kg/day)	0.9±0.4	0.9±0.3	0.13
Number of clinical visits to physician (previous year)	3.6±1.6	4.1±1.6	< 0.001
Number of clinical visits to dentist (previous year)	1.8±1.5	1.7±1.4	0.3
Chronic Complications, n (%)			
Microvascular	58 (42.3)	464 (26.1)	<0.0001
Macrovascular	12 (8.8)	84 (5.1)	0.06
Micro and macrovascular	63 (46.0)	507 (28.5)	<0.0001
Hospitalization, n (%)			
Hyperglycemia	23 (16.8)	142 (8.0)	0.001
DKA	15 (10.9)	91 (5.5)	0.008
Severe hypoglycaemia, n (%)	22 (25.6)	210 (17.7)	0.13

*Missing cases 772 (21.5%). **African-Brazilians, Mulattos, Asians, and Native Indians. ***Missing cases: 93 (3.3%). BMI, body mass index; sBP, systolic blood pressure; dBP, diastolic blood pressure; HDL, high density lipoprotein; LDL, low density lipoprotein; DKA, diabetes ketoacidosis. Overweight and obesity were considered together. The data are presented as means (±SD) and frequencies.

with no/minor periodontitis, were followed for a median time of 6 years. The authors have found significantly higher prevalence of proteinuria and cardiovascular complications such as stroke, angina, myocardial infarction, transient ischemic attacks, and intermittent claudication in patients with severe periodontitis (10). Also, greater percentage of ketoacidosis, retinopathy and neuropathy in insulin-dependent diabetes mellitus patients with periodontitis. These results are in agreement with our findings.

Severe periodontitis was associated with higher risk of cardiorenal mortality (combination of diabetic nephropathy and ischemic heart disease) in patients with type 2 diabetes (23). Likewise, periodontitis was shown to predict the development of overt nephropathy and end-stage renal disease in type 2 diabetic patients with little or no pre-existing kidney disease in a dose-dependent way (24). The authors proposed systemic inflammation, which may lead to endothelial dysfunction, as the mechanism responsible for the relationship of periodontitis and kidney disease. Although it was not verified in our study, we speculate that systemic inflammation may also be the link between periodontitis and systemic complications in TID patients. Serum interleukin-6 and osteoprotegerin levels have been associated with periodontal inflammation in patients with TID (25).

The major strengths of this study are its large sample size and the nationwide aspect comprising a broad range of ethnic and socioeconomic backgrounds. One shortcoming includes the lack of clinical periodontal evaluation, which might have led us to

misclassification. However, due to our large sample size self-reported periodontitis was used. Self-report has been shown to be useful and valid for the assessment of periodontitis and the question we used in the study has been shown to have good validity (18). It is noteworthy that non-differential misclassification of periodontitis could result in underestimation of the associations. Because of the cross-sectional nature, it is not possible to establish temporality and, thus, causality might not be drawn. Prospective studies are warranted to investigate the assumptions made in this study.

In summary, periodontitis was associated to diabetes-related chronic systemic complications in Brazilian type 1 diabetes patients. Periodontitis should be more carefully observed in diabetic patients, since they are more prone to systemic complications.

Resumo

Esse estudo objetivou avaliar a possível associação entre periodontite e complicações sistêmicas em uma população brasileira com diabetes tipo 1. Foi realizado um estudo transversal, multicêntrico em 28 clínicas públicas em 20 cidades brasileiras. Dados de 3.591 pacientes foram obtidos (56% mulheres, 57,2% caucasianos), com idade média de 21,2±11,7 anos, em que a duração média da diabetes tipo 1 foi 9,6±8,1 anos. Periodontite foi avaliada através de auto-relato. Odds ratio (OR) e intervalos de confiança 95% foram calculados para avaliar a associação entre periodontite e complicações sistêmicas da diabetes (complicações crônicas micro e macrovasculares e hospitalizações por hiperglicemia e cetoacidose diabética). A prevalência de periodontite foi 4,7% (n=170). Pacientes com periodontite apresentaram idade média de 27,4±12,9 anos. Esse grupo foi mais velho (p<0,001), exibiu duração mais longa de diabetes e tinha colesterol total (p<0,05) e triglicerídeos (p<0,001) elevados e menor HDL (p<0,05) que pacientes sem periodontite. Pressões sanguíneas sistólica e diastólica foram significativamente aumentadas em pacientes com periodontite (p<0,01). Pacientes com periodontite apresentaram OR aumentada para complicações microvasculares (2,43 [1,74-3,40]) e para hospitalizações relacionadas à hiperglicemia (2,76 [1,72-4,42]) e cetoacidose (2,72 [1,53-4,80]). Concluindo, periodontite foi associada a complicações sistêmicas em pacientes brasileiros com diabetes tipo 1.

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