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Alveolar and mandibular cortex bone status in individuals with type 1 diabetes mellitus: a cross-sectional paired study

Francisco Ivison Rodrigues Limeira[1] | Armando Baia Guiomarino Neto[2] | Diandra Costa Arantes[2]

[1]Faculdade Presidente Antônio Carlos, Teófilo Otoni, Minas Gerais, Brasil.
[2]Faculdade de Odontologia, Universidade Federal do Pará, Belém, Pará, Brasil.

Aim: This study compared alveolar bone loss, teeth with furcation, and mandibular cortical modification between individuals with type 1 diabetes mellitus (T1DM) and nondiabetic individuals.

Methods: Radiographs of 50 T1DM individuals and 100 nondiabetic individuals were examined to evaluate the presence of teeth with furcation, alveolar bone loss, and mandibular cortical modifications. The Mann-Whitney, Chi-square, and Student's t tests were used to analyze personal characteristics and bone status. Linear and logistic regression was performed to explore associations.

Results: A significant difference was observed in the average number of teeth with furcation and in the median of alveolar bone loss between T1DM and the nondiabetic participants. T1DM individuals are more likely to have alveolar bone loss (OR = 3 2.250), teeth with furcation (OR = 8.903), and mandibular cortical modification (OR = 15.667) than are nondiabetic individuals. Among T1DM individuals, the glycemic control has a high influence in mandibular cortical modifications ($p < 0.05$).

Conclusions: A high association between uncontrolled blood glucose and mandibular cortical modifications was observed among T1DM individuals. Alveolar bone loss of T1DM individuals was associated with age, time of diagnosis, glycemic control, and the existence of chronic complications.

Uniterms: diabetes mellitus, type 1; alveolar bone loss; furcation defects; glycemic control.

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INTRODUCTION

Diabetes mellitus (DM) is a metabolic disease of multiple etiologies characterized by chronic hyperglycemia. It is caused by problems in insulin secretion, in insulin action, or a combination of these two factors[1]. The main categories of DM are type 1 diabetes mellitus (T1DM) and type 2 diabetes mellitus (T2DM). T1DM is an autoimmune disease in which beta-pancreatic cells are destroyed by cells of the immune system, resulting in insulin deficiency. It represents only 5-10% of patients with DM. T2DM is the most common form of diabetes, whose characteristic is insulin resistance. Insulin production in this case is deficient and cannot overcome resistance to the hormone[2]. In 2045, it is estimated that the number of people between 18-99 years of age living with DM will be 693 million[3]. Complications of DM include problems with microvascularization, retinopathy, neuropathy, nephropathy, and changes in bone metabolism[4]. It is suggested that the degree of glycemic control is proportional to the level of severity of DM complications[5].

One of the characteristics of periodontitis is the loss of alveolar bone. A meta-analysis has shown that diabetics have a higher degree of periodontal disease than do non-diabetics[6]. T1DM subjects are twice as likely to be affected by periodontal disease when compared to those with normal blood glucose levels[7]. Inflammation is the main pathogenesis that links T1DM with periodontal disease[8] and alveolar bone loss, since the increase in inflammation mediators in

Autor para Correspondência:
Francisco Ivison Rodrigues Limeira
Rua Engenheiro Célso Murta, 600, Olga Correa, Teófilo Otoni, Minas Gerais. CEP: 39.803-087. Telefone: 55 31 9 9280 6835
E-mail: ivisonodontoce@hotmail.com

DM is proportional to the imbalance in the activity of osteoblasts and osteoclasts[4].

It is well known that metabolic changes in DM are responsible for affecting the bone quality and quantity of diabetic individuals[4]. In such cases, there is an increased risk of fracture due to bone fragility[9]. One study evaluated the trabecular and cortical bone condition of the tibia in adolescents and concluded that bone density is reduced in T1DM[10]. The evaluation of the mandibular bone condition can be performed by panoramic radiographs using radiomorphometric indices, such as the mandibular cortical index (MCI), panoramic mandibular index (PMI), and mandibular cortical width (MCW)[11–13]. There are few studies in the literature relating the mandibular bone condition to T1DM. Clinically, it is important to recognize, evaluate, and associate systemic disorders with bone conditions for planning periodontal treatment and oral surgical procedures.

The aim of this cross-sectional study was to assess the alveolar and the mandibular cortex bone condition of individuals with T1DM and compare them with the ones of non-diabetic individuals. The null hypothesis was that the prevalence of alveolar bone loss, teeth with furcation, and mandibular cortical modification were not different between individuals with T1DM and nondiabetics.

MATERIALS AND METHODS

This cross-sectional paired study was approved by the ethics committee (protocol number: 446307). All patients signed informed consent, in accordance with 466/12 resolution of the Brazilian National Health Council and with Helsinki Declaration. This study was reported according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement[14].

Individuals with diagnosis of T1DM based on the criteria established by the American Diabetes Association[15] and who were undergoing medical treatment at the local university hospital of the Federal University of Campina Grande, Brazil, were recruited to take part in this study. The inclusion criteria were as follows: minimum age of 18 years, T1DM monitored by the reference service, more than a year of T1DM diagnosis, a complete medical record, having at least eight remaining teeth, and absence of conditions or illnesses related to bone mass alterations (renal, endocrine, or rheumatologic disease history; menopause; or malignant tumors in any organ). Participants were included by convenience through nonprobability sampling. Nondiabetic patients from the dental and radiology clinic at the school of dentistry of a public university in Campina Grande, Brazil, were age and sex matched with diabetics in a 2:1 proportion.

Information regarding the history and the current status of T1DM was collected from the medical records of each participant (date of diagnosis, fasting blood glucose levels, glycated hemoglobin [HbA1c], and the presence of chronic complications associated with T1DM). According to the American Diabetes Association, fasting blood glucose levels recommended for adults are between 80–130 mg/dL and 90–130 mg/dl for adolescents[15]. The recommended HbA1c for adults is 7.0% and 7.5% for adolescents, corresponding to good glycemic control[15].

Periapical status was diagnosed on the basis of the examination of the digital panoramic radiographs of the jaws. The radiographs were acquired using the same equipment (Orthophos XG5; Sirona Dental Systems, Bensheim, Germany) operated by the same radiographic technician. The exposure parameters were chosen following the manufacturer's recommendations according to patients' size and weight (70–90 kVp, 10–15 mA, and 14 seconds of exposure). All original images were saved in Tagged Image File Format (TIFF) using Sidexis XG version 2.6 (Sirona Dental Systems, Bensheim, Germany). The images were calibrated with zero magnification and image resolution of 276 dpi. All analyses were performed bilaterally by two double-blinded clinicians calibrated using RadioImp® software, version 2.0 (Radio Memory Ltda., Belo Horizonte, Minas Gerais, Brazil). The recording of parameters was calibrated: the results were compared with those of the radiologist ("gold standard") and the interexaminer agreement was calculated (k = 0.79). The intraobserver agreement (k = 0.82) was calculated by repeating the analysis of the 10 panoramic radiographic images one month after the first examination.

The Mandibular Cortical Index (MCI) refers to the inferior mandibular cortex quality by observing the region between the mental foramen and the antegonial region. This is divided into three categories according to the classification of Klemetti, Kolmakov, and Kröger[16]:

- Normal cortex (C1): the endosteal margin of the cortex is even and sharp;
- Mild to moderately eroded cortex (C2): the endosteal margin shows semilunar defects or endosteal cortical residues;
- Severely eroded cortex (C3): the cortical layer is clearly porous and with reduced thickness.

Alveolar bone loss was assessed by measuring from the alveolar bone crest to the cemento-enamel junction, at the mesial and distal sites of each tooth, excluding the third molars[17]. Evidence of bone loss measuring ≥ 2 mm was considered. The analysis of teeth with furcation involvement was performed by identification and measurement of vertical bone loss from the roof of the furcation apically[18].

All analyses were performed using the statistical software SPSS Statistics (Version 23.0, Armonk, NY: IBM Corp), at a 5% level of significance. The Mann-Whitney, Chi-square, and Student's t tests were used to analyze possible differences concerning personal characteristics and bone status between participants with T1DM and nondiabetic participants.

Bivariate logistic regression analysis was performed to explore the association between individuals with/without T1DM with alveolar bone loss (< 2 mm and > 2 mm), the presence of teeth with furcation, and the presence of mandibular cortical modification. Bivariate linear regression analysis was run to infer association between age, gender, smoking status, T1DM diagnosis time, glycemic control, and the presence of other chronic complications, among individuals with T1DM, with the amount of alveolar bone loss and the number of teeth with furcation. For these dependent variables, multivariate linear regression was performed with the independent variables, considering $p \leq 0.20$ in the bivariate linear regression, applying the hierarchical model. The model with the highest R^2 obtained was considered for results.

Multinomial logistic regression was conducted to examine the association of age, gender, smoking status, T1DM diagnosis time, glycemic control, and the presence of other chronic complications, among individuals with T1DM, with the degree of mandibular cortical modification.

RESULTS

Among the 50 individuals with T1DM, 23 were male and 27 were female, aged 18 to 45 (27.94 ± 6.60) years. Among the 100 nondiabetic individuals, 46 males and 54 females, ages ranged from 18 to 45 (27.94 ± 6.57) years as well. This sample represents 0.99 statistical power, estimated by the mean of difference and standard deviation data for alveolar bone loss, teeth with furcation, and mandibular cortical modification between T1DM and non-diabetic patients (Power and Sample Size Calculation, Vanderbilt University, Nashville, TN, USA).

No significant difference was found in age, gender, and smoking status between the T1DM and the nondiabetic participants. A significant difference was observed in the average number of teeth per participant between the T1DM and the nondiabetic participants, as well as in the average number of teeth with furcation and in the median of alveolar bone loss (Table 1).

Table 1. Personal characteristics and bone status of T1DM and nondiabetic participants.

	With T1DM (n = 50)	Without T1DM (n = 100)	Total (n = 150)	*p*-value
Age				
Mean ± SD	27.94 ± 6.60	27.94 ± 6.57	27.94 ± 2.50	1.000*
Gender, *n* (%)				
Male	23 (46)	46 (46)	69 (46)	1.000#
Female	27 (54)	54 (54)	81 (54)	
Smoking, *n* (%)				
Never	8 (16)	20 (20)	28 (18.7)	0.659#
Yes (present or past)	42 (84)	80 (80)	122 (81.3)	
Number of teeth				
Mean ± SD	21.58 ± 2.19	25.45 ± 1.41	24.16 ± 2.50	< 0.001*
Mandibular Cortical Index, *n* (%)				
Normal cortex (C1)	25 (50)	92 (92)	117 (78)	< 0.001#
Moderately eroded cortex (C2)	19 (38)	8 (8)	27 (18)	
Severely eroded cortex (C3)	6 (12)	0 (0)	6 (4)	
Alveolar Bone Loss (mm)				
Median [IR]	3.66 [1.25]	1.02 [0.68]	1.47 [2.26]	< 0.001+
Teeth With Furcation				
Median [IR]	2.00 [2.00]	0.00 [1.00]	0.00 [2.00]	< 0.001+

*t test; #Chi-square; +Mann-Whitney; IR = interquartile range; SD = standard deviation; T1DM = type 1 diabetes mellitus.

Bivariate logistic regression suggested that individuals with T1DM are more likely to have alveolar bone loss (odds ratio [OR] = 32.250, p < 0.001, confidence interval [CI] = 12.550-82.871), teeth with furcation (OR = 8.903, p < 0.001, CI = 3.952-20.059), and mandibular cortical modification (OR = 15.667, p < 0.001, CI = 5.797-42.340) than are nondiabetic individuals (Table 2).

Table 2. Bivariate logistic regression analysis of association of alveolar bone loss, teeth with furcation, and mandibular cortical modification with the independent variable T1DM status.

Dependent variables	T1DM		
	p value	OR	95% CI
Alveolar bone loss	< 0.001	32.250	12.550-82.871
Teeth with furcation	< 0.001	8.903	3.952-20.059
Mandibular cortical modification	< 0.001	15.667	5.797-42.340

CI = confidence interval; OR = odds ratio; T1DM = type 1 diabetes mellitus. Alveolar bone loss status: 0 = <2mm and 1 = > 2mm; Teeth with furcation status: 0 = absent and 1 = present; Mandibular cortical modification status: 0 = absent and 1 = present.

Bivariate linear regression showed that, among the T1DM participants, there was an association of age, time of diagnosis, glycemic control, and existence of other chronic complications with alveolar bone loss. There was also an association of age, history of smoking, time of diagnosis, glycemic control, and existence of other chronic complications with the presence of at least one teeth of furcation (Table 3).

Table 3. Bivariate linear regression analysis of independent variables of participants with T1DM (age, gender, smoking, T1DM diagnosis time, glycemic control, presence of chronic complications) association with alveolar bone loss and teeth with furcation.

Independent Variables	Alveolar bone loss			Teeth with furcation		
	β	p	R^2	β	p	R^2
Gender	0.296	0.352	0.018	0.626	0.108	0.053
Age	0.059	0.012	0.125	0.125	< 0.001	0.361
Smoking	- 0.415	0.336	0.019	- 1.952	< 0.001	0.278
Diagnosis time	1.254	< 0.001	0.293	1.481	< 0.001	0.268
Glycemic control	- 0.999	0.004	0.159	- 1.541	< 0.001	0.248
Chronic complications	1.005	0.001	0.197	1.387	< 0.001	0.246

In the multivariate linear regression model for alveolar bone loss, the diagnosis time (p = 0.002) and the glycemic control (p = 0.014) remained significant. This model explained 38.1% of the variation in the amount of the alveolar bone loss. Glycemic control also maintained significance (p = 0.001) in the multivariate linear model for teeth with furcation, as well as gender, age, and smoking status. This model explained 61.6% of the variation in the number of teeth with furcation (Table 4).

Table 4. Multivariate linear regression, including alveolar bone loss and teeth with furcation as dependent variables.

Variables	Adjusted model[#]		
	β	*p*	Adjusted R^2
Alveolar bone loss			
Diagnosis time	0.984	0.002	0.381
Glycemic control	- 0.745	0.014	
Chronic complications	0.356	0.240	
Teeth with furcation			
Gender	0.628	0.014	
Age	0.057	0.048	
Smoking	- 1.048	0.008	0.616
Diagnosis time	0.403	0.270	
Glycemic control	- 1.073	0.001	
Chronic complications	0.276	0.364	

[#] The model with the highest R^2 obtained by hierarchical model was considered.

Bivariate multinomial regression model for mandibular cortical modification suggested that, among the T1DM participants, glycemic control highly influences mandibular cortical modifications ($p < 0.05$). The chance of an individual with moderately eroded cortex not having glycemic control is 17.4 times the chance of an individual with glycemic control having a moderately eroded cortex, compared to individuals with a normal mandibular cortex. The chance of an individual with a severely eroded cortex not having glycemic control is 48 times the chance of an individual with glycemic control having a severely eroded cortex, as compared to individuals with normal mandibular cortex (Table 5). However, these results must be interpreted with caution due to the wide confidence interval.

Table 5. Bivariate multinomial regression analysis of independent variables of participants with T1DM (age, gender, smoking, T1DM diagnosis time, glycemic control, presence of chronic complications) associated with mandibular cortical modification.

Independent Variables	Mandibular Cortical Modification[#]		
	p	OR	95% CI
Gender (male)			
Moderately eroded cortex (C2)	0.406	1.667	0,500 – 5.559
Severely eroded cortex (C3)	0.657	1.500	0.251 – 8.977
Age (years)			
Moderately eroded cortex (C2)	0.237	1.072	0.955 – 1.202
Severely eroded cortex (C3)	0.003	1.474	1.138 – 1.909
Smoking (never)			
Moderately eroded cortex (C2)	0.428	2.156	0.323 – 14.410
Severely eroded cortex (C3)	0.026	11.500	1.331 – 99.329
Diagnosis time (up to 10 years)			
Moderately eroded cortex (C2)	0.831	0.831	0.256 – 2.989
Severely eroded cortex (C3)	-	-	-
Glycemic control (without control)			
Moderately eroded cortex (C2)	0.011	17.455	1.938 – 157.203
Severely eroded cortex (C3)	0.004	48.000	3.482 – 661.609
Chronic complications (without)			
Moderately eroded cortex (C2)	0.179	0.426	0.123 – 1.480
Severely eroded cortex (C3)	-	-	-

CI = confidence interval; OR = odds ratio; - = there was no data for comparison. [#]The reference category is "normal cortex".

Among T1DM participants, the age was also an important factor for developing severely eroded cortex modification (OR = 1.474), as compared to the normal cortex. The chance of an individual having a severe modification in the mandibular cortex with each passing year is 1.4 times the chance of having a normal cortex (Table 5).

DISCUSSION

The present study aimed to evaluate the alveolar and cortical mandibular bone condition of individuals with T1DM. The results of this study showed that diabetic individuals are more likely to have alveolar bone loss, teeth with furcation, and changes in the mandibular cortex. Alveolar bone loss and teeth with furcation were associated with age, time of diagnosis, glycemic control, and chronic complications. The glycemic control heavily influenced mandibular cortical modifications in participants with T1DM.

In this study, MCI was used to assess the condition of the cortical bone of the mandible of individuals with T1DM and to investigate possible associations with the degree of erosion of this cortical with diabetes. Analyzing the association between the degree of mandibular erosion and glycemic control, it was noted that the chance of individuals with moderate mandibular erosion not having controlled glycemia is greater than the chance of individuals with controlled glucose having this mandibular modification. Furthermore, the chance of individuals with severe mandibular erosion not having positive glycemic control is higher than the chance of

individuals with controlled glucose having this mandibular modification. These findings can be explained by the increase in the expression of advanced glycation end products (AGES) and AGE receptor (RAGES) characteristic of DM, which induce the apoptosis of osteoblastic cells[19] and the reduction of transcription factors that regulate the cellular differentiation of osteoblasts[20]. A study in rats with induced T1DM suggested that the elevated expression of cathepsin K in the exposed group is indicative of increased osteoclast activity[21]. All of these factors result in an imbalance in the activity of osteoblasts and osteoclasts, causing problems in bone remodeling.

There is a lack of studies in the literature associating the mandibular cortical index with the bone condition of diabetic patients. Munhoz et al.[12] used MCI to assess the influence of T2DM on bone mineral density in postmenopausal women. In the present study, diabetic and non-diabetic participants showed statistically significant differences between the MCI values. Kurşun-Çakmak and Bayrak[13] compared the radiomorphometric indices of diabetic individuals (T1DM and T2DM) with those of non-diabetic individuals by means of panoramic radiographs. There was no significant difference between the MCI of individuals with T1DM when compared to non-diabetics, which differs from the results of the present study. This divergence may be due to the sample size, reported as a limitation by the authors themselves. In addition, the inclusion criteria for the sample were different for the two studies. More studies using the same type of index and with different methodologies should be conducted, analyzing possible changes in the mandibular cortex of different populations (osteoporosis, osteogenesis imperfecta, and rickets), as this method has excellent reproducibility, accuracy, and specificity.

Several studies have been published in the literature suggesting an association between DM and alveolar bone loss. However, most studies are conducted with individuals with T2DM[7]. The few studies relating T1DM may be due to the lower prevalence of cases when compared to T2DM. Plessas et al.[22], when evaluating bitewing radiographs of diabetic nonsmokers and comparing them with radiographs of non-diabetics, found greater alveolar bone loss in the T1DM group. These data corroborate the association between alveolar bone loss and T1DM found in the present study. Alveolar bone loss can be stimulated by the elevated expression of pro-inflammatory factors observed in DM, such as IL-1β, IL-6, and TNF-α.[23] Smoking is a factor that influences the alveolar bone condition, as confirmed by Rosa et al.[24] in a prospective study comparing the alveolar bone of young smokers and non-smokers. Smokers showed an increase in areas of low density over time and a reduction in the height of the alveolar bone when compared to non-smokers. In the present study, the difference between smokers and non-smokers proved to be insignificant when comparing the diabetic and non-diabetic groups. Thus, the smoking variable does not interfere with the interpretation of the results.

As smoking could be a confounding variable and a potential risk of bias, the ideal alternative would be to control the sample by this factor, however this was not feasible. Alveolar bone loss and teeth with furcation may also be influenced by oral hygiene, which was not evaluated in the present study. Within the limitations, the results of this study allow one to infer an association between T1DM and the alveolar and mandibular bone condition. However, this is a cross-sectional study, which makes it impossible to infer any causal relationship between the variables of interest. Despite this, the association of bone condition with diabetes mellitus, by means of radiographic images, is important so that the professional in his clinical practice can identify bone alterations influenced by T1DM in these radiographs and refer them for diagnosis and treatment. It should be noted that the most suitable imaging test for the analysis of alveolar bone loss is the interproximal radiograph. In addition, the importance of identifying bone changes caused by T1DM is due to the fact that these individuals are more susceptible to fractures[9] and have lower bone turnover rates[25]. Therefore, when perceiving this sign, the professional must be cautious when performing procedures that can affect the mandibular structure of these patients.

CONCLUSION

This study proved the high association of the uncontrolled blood glucose with mandibular cortical modifications, including both moderately and severely eroded cortexes, among T1DM individuals. Individuals with T1DM are also more likely to have alveolar bone loss and teeth with furcation than are nondiabetic individuals. Moreover, the alveolar bone loss of these individuals was associated with their age, time of diagnosis, glycemic control, and existence of other chronic complications.

CRediT – AUTHORSHIP CONTRIBUTION STATEMENT

Francisco Ivison Rodrigues Limeira: Conceptualization, Methodology, Validation, Investigation, Resources, Data Curation, Writing - Original Draft, Funding acquisition.

Armando Baia Guiomarino Neto: Writing - Original Draft, Funding acquisition.

Diandra Costa Arantes: Formal Analysis, Writing - Original Draft, Supervision, Funding acquisition

CONFLICT OF INTEREST

None

ORCID

Francisco Ivison Rodrigues Limeira https://orcid.org/0000-0002-3540-9178
Armando Baia Guiomarino Neto https://orcid.org/0000-0002-8484-8169
Diandra Costa Arantes https://orcid.org/0000-0001-9220-987X

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Condição óssea alveolar e da cortical mandibular em indivíduos com diabetes mellitus tipo 1: um estudo transversal pareado

Objetivo: Comparar a perda óssea alveolar, a presença de dentes com lesão de furca e a alteração da cortical óssea entre indivíduos com DMT1 e indivíduos não-diabéticos.

Métodos: Foram examinadas radiografias de 50 indivíduos diabéticos e de 100 não-diabéticos para avaliar a presença de dentes com lesão de furca, perda óssea alveolar e alteração cortical mandibular. Para analisar as características individuais e as condições ósseas foram usados os testes de Mann-Whitney, Qui-quadrado e t de Student. Regressões linear e logística foram realizadas para identificar associações.

Resultados: Foi encontrada diferença significativa na média de dentes com lesão de furca e na mediana da perda óssea alveolar entre diabéticos e não-diabéticos. Indivíduos com DMT1 possuem mais chance de apresentar perda óssea alveolar (OR = 32,250), lesão de furca (OR=8,903) e alteração da cortical mandibular (OR = 15,667) em comparação aos indivíduos não-diabéticos. Entre os diabéticos, o controle da glicemia possui grande influência nas alterações da cortical mandibular ($p < 0,05$).

Conclusões: Existe uma alta associação entre os níveis de glicemia descontrolada e alterações na cortical mandibular entre os indivíduos com DMT1. A perda óssea alveolar de indivíduos com DMT1 foi associada aos fatores idade, tempo de diagnóstico, controle da glicemia e a presença de complicações crônicas.

Descritores: diabetes mellitus tipo 1; perda do osso alveolar; defeitos da furca; controle glicêmico.