

Diabetes mellitus promotes periodontal destruction in children

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Abstract

Aim: The association between diabetes mellitus and periodontal attachment and bone loss is well established. Most of the prior literature has focused on adults, and studies in children have mostly reported gingival changes. Our aim was to assess the periodontal status of a large cohort of children and adolescents with diabetes.

Material and Methods: We examined 350 children with diabetes (cases) and 350 non-diabetic controls (6–18 years of age). Using three different case definitions for periodontal disease, which incorporated gingival bleeding and/or attachment loss findings, multiple logistic regression analyses adjusting for age, gender, ethnicity, frequency of prior dental visits, dental plaque, and examiner were performed.

Results: Subjects with diabetes had increased gingival inflammation and attachment loss compared with controls. Regression analyses revealed statistically significant differences in periodontal destruction between cases and controls across all disease definitions tested (odds ratios ranging from 1.84 to 3.72). The effect of diabetes on periodontal destruction remained significant when we separately analysed 6–11 and 12–18 year old subgroups.

Conclusions: These findings demonstrate an association between diabetes and an increased risk for periodontal destruction even very early in life, and suggest that programmes to address periodontal needs should be the standard of care for diabetic youth.

Key words: children; complications; diabetes; periodontitis

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Diabetes mellitus comprises a group of metabolic disorders marked by high levels of blood glucose, resulting from defects in insulin production, action, or both. In 2005, the total prevalence of diabetes in the US was estimated at 20.8 million people (CDC 2005). Multiple studies have demonstrated that the prevalence, severity, and progression of periodontal diseases are significantly increased in patients with diabetes; therefore, diabetes is recognized as an important risk factor for periodontitis

(Löe 1993, Papapanou 1996, Mealey 1999, Taylor 2001).

A number of reports on the relationship between diabetes and periodontal disease have included children and adolescents (Cianciola et al. 1982, Gusberti et al. 1983, Sastrowijoto et al. 1990, de Pommereau et al. 1992, Karjalainen & Knuutila 1996). The consensus has been that in patients with childhood-onset diabetes, periodontitis seems to ensue around puberty and to progress with age. In order to explore the periodontitis association in diabetic youth conclusively, we endeavoured to revisit this issue targeting a much larger cohort of children and expanding the analyses of data collected using fully adjusted regression models. We previously reported on the oral findings in a subgroup of 182 children and adolescents with diabetes (Lalla et al. 2006a). When compared with 160 non-diabetic con-

trols, children with diabetes exhibited significantly increased attachment loss. When controlling for important confounders, diabetes was a significant correlate of periodontal destruction, even in the younger subgroup of children 6–11 years of age. These findings suggested that periodontal destruction develops earlier in life than previously recognized.

The goal of the present study was to further explore the periodontal effects of diabetes using data from an expanded cohort of a total of 700 children and adolescents, 6–18 years of age.

Material and Methods

The study protocol was approved by the Columbia University Medical Center Institutional Review Board. Parents/legal guardians of participants provided informed consent.

Conflict of interest and source of funding statement

The authors declare that they have no conflict of interest.

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Study population

Three hundred and fifty patients with diabetes mellitus, 6–18 years of age, were recruited from among the patients followed at the Naomi Berrie Diabetes Center at the Columbia University Medical Center. Three hundred and fifty 6–18 year old subjects seen at the pediatric dental clinic at the Columbia University College of Dental Medicine who denied a history of diabetes served as controls. Children in both groups were excluded, if they were undergoing active orthodontic therapy.

Oral examination protocol

Participants and/or their guardians responded to questions concerning the participants' dental history. Periodontal assessments were performed by three calibrated examiners on one randomly assigned maxillary and the diagonally opposite mandibular quadrant.

The following were evaluated at four sites per tooth (mesio-buccal, disto-buccal, mesio-lingual, disto-lingual) for all fully erupted permanent teeth (third molars excluded), using a manual periodontal probe:

- Plaque index (PI); each site was given a score from 0 to 3, as described by Silness & Loe (1964).
- Gingival Index (GI); each site was given a score from 0 to 3, according to Loe & Silness (1963). In this index, a GI score of 2 or 3 denotes a bleeding site.
- Probing depth; defined as the distance between the gingival margin and the bottom of the probeable pocket to the nearest whole mm.
- Location of the gingival margin; the distance between the cemento-enamel junction (CEJ) and the gingival margin to the nearest whole millimeter. The distance was deemed non-readable, whenever the CEJ was obscured by dental restorations or was impossible to identify.

The last two parameters were used to compute clinical attachment level.

Diabetes-related variables

The following information was collected from medical records: type of diabetes and duration (years since diagnosis); insulin regimen (multiple daily insulin injections or continuous subcu-

Table 1. Demographic and periodontal characteristics of study population

	Controls N = 350	Cases N = 350	p-value
Age (years)	10.87 ± 2.53	11.33 ± 3.41	0.045
Gender, female	181 (52)	153 (44)	0.034
Ethnicity			<0.001
Hispanic	291 (83)	109 (31)	
Non-Hispanic	59 (17)	241 (69)	
Medical insurance, with coverage	338 (97)	330 (94)	0.148
Reported frequency of dental visits, per year	1.51 ± 1.04	1.54 ± 0.75	0.586
Reported age at first dental visit (years)	5.02 ± 2.49	3.97 ± 2.22	<0.001
Reported ever had red/inflamed gums	41 (12)	46 (14)	0.481
Reported ever had bleeding gums	107 (31)	99 (29)	0.659
Mean plaque index	1.20 ± 0.36	1.28 ± 0.36	0.006
Percent of sites with plaque (PI ≥ 2)	24.42 ± 22.93	29.90 ± 25.28	0.003
Mean gingival index	1.08 ± 0.29	1.14 ± 0.32	0.006
Percent of bleeding sites (GI ≥ 2)	13.61 ± 17.58	18.96 ± 21.38	<0.001
Mean attachment loss (mm)	0.71 ± 0.84	1.22 ± 1.11	<0.001
Percent of sites with attachment loss (> 2 mm)	7.57 ± 17.36	21.09 ± 29.08	<0.001

Data shown as mean ± SD, or n (%).

GI, gingival index; PI, plaque index.

taneous insulin infusion) and/or oral hypoglycaemic medications; and hemoglobin A1c (HbA1c) values over the 2-year period before inclusion into the study (excluding those that were within 3 months of diagnosis of diabetes).

Data and statistical analysis

Analyses were performed using SAS, version 9.1 (SAS Institute, Cary, NC), and the R statistical software, version 2.2.1. First, we directly compared cases and controls using unadjusted Student's *t*- or χ^2 tests. Then, we performed logistic regression analyses using three "definitions" of gingival/periodontal disease as the dependent variable, for the whole cohort and separately for two age subgroups (6–11 and 12–18 years of age). The first definition combined both attachment loss and gingival bleeding findings: at least two teeth with at least one site each with attachment loss > 2 mm and bleeding (i.e., GI ≥ 2) at the same site. The second definition was based on the presence of gingival bleeding only: at least two teeth with at least one bleeding site (i.e., GI ≥ 2). The third definition was based on attachment loss measurements only: at least two teeth with at least one site with attachment loss > 2 mm. Indeed, our attachment loss definition is in accordance with the "sensitive" case definition (i.e., inclusive of incipient cases) proposed by the recent European Workshop in Periodontology for use in risk factor research (Tonetti & Claffey

2005). Adjusting variables included age (continuous), gender, ethnicity (Hispanic, non-Hispanic), reported frequency of prior dental visits (log transformed to achieve a better fit), plaque index, and dental examiner. *p* < 0.05 (two sided) was considered to be statistically significant for all analyses.

Results

The demographic and clinical periodontal parameters of the study population are presented in Table 1. Cases had a higher plaque index than non-diabetic controls (1.28 *versus* 1.20, respectively; unadjusted *p* = 0.006), and a higher percentage of sites with plaque (PI ≥ 2) (29.90% in cases *versus* 24.42% in controls; unadjusted *p* = 0.003). Children with diabetes had significantly more gingival inflammation than controls: mean GI was 1.14 *versus* 1.08, respectively (unadjusted *p* = 0.006), and the percentage of sites that bled upon examination was 19.0% *versus* 13.6%, respectively (unadjusted *p* < 0.001). Attachment loss, calculated as either a subject-based mean or as the percentage of sites with > 2 mm of attachment loss, was also significantly higher in diabetic children compared with non-diabetic controls (1.22 *versus* 0.71, and 21.09 *versus* 7.57, respectively; unadjusted *p* < 0.001 for both).

Diabetes-related variables in our cases are presented in Table 2. Ninety-three per cent of the cases had type 1

Table 2. Diabetes related variables for the case group ($N = 350$)

Diabetes type	
Type 1	325 (93)
Type 2	25 (7)
Duration (years)	3.96 ± 3.39
Treated with*	
Insulin only	326 (93)
Multiple daily injections	223 (64)
Continuous subcutaneous infusion	103 (29)
Oral hypoglycemic medication(s) only	8 (2)
Both	11 (3)
Mean HbA1c over past 2 years (%) [†]	8.49 ± 1.74
<7.5%	97 (29)
7.5–9.5%	170 (50)
>9.5%	73 (21)

Data shown as n (% of total) or mean \pm SD.

*Data available for 345 subjects.

[†]Data available for 340 subjects.

Table 3. Estimated odds ratios from logistic regression analyses for periodontal changes in cases over controls*

	OR	95% CI	p -value
All subjects ($N = 700$)			
≥ 2 teeth with ≥ 1 site with AL > 2 mm and bleeding at same site	2.72	(1.32, 5.60)	0.006
≥ 2 teeth with ≥ 1 site with bleeding	1.84	(1.10, 3.07)	0.020
≥ 2 teeth with ≥ 1 site with AL > 2 mm	3.72	(1.98, 6.97)	<0.001
6–11 years old subjects ($N = 401$)			
≥ 2 teeth with ≥ 1 site with AL > 2 mm and bleeding at same site	3.74	(1.23, 11.43)	0.021
≥ 2 teeth with ≥ 1 site with bleeding	2.15	(1.08, 4.28)	0.030
≥ 2 teeth with ≥ 1 site with AL > 2 mm	4.45	(1.87, 10.54)	0.001
12–18 years old subjects ($N = 299$)			
≥ 2 teeth with ≥ 1 site with AL > 2 mm and bleeding at same site	2.63	(0.94, 7.34)	0.066
≥ 2 teeth with ≥ 1 site with bleeding	1.57	(0.71, 3.51)	0.268
≥ 2 teeth with ≥ 1 site with AL > 2 mm	3.84	(1.46, 10.12)	0.007

*Adjusted for age, gender, ethnicity, reported frequency of dental visits, plaque index, and dental examiner.

AL, attachment loss; OR, odds ratio; CI, confidence interval.

diabetes and were treated with insulin only. Twenty-nine per cent of our cases were on continuous subcutaneous insulin infusion (insulin pump). Mean HbA1c over the 2 years before the examination was $8.49\% \pm 1.74$, and 79% of the children had HbA1c $\leq 9.5\%$.

As shown in Table 3, using three different case definitions for gingival/periodontal disease (which incorporate gingival inflammation and/or attachment loss findings), formal regression analyses adjusting for several relevant variables revealed significantly increased odds of gingival/periodontal disease in cases compared with controls. Importantly, when we separately assessed subjects in the two age subgroups (under 12 years of age, or 12 years and older) the effect of diabetes on periodontal status remained significant across all definitions of periodontal disease in the younger children, and for the

attachment loss definition in the older children.

Figure 1 graphically shows the probability (estimated from the logistic regression analyses) of a subject having periodontal changes according to the attachment loss plus bleeding (a), bleeding only (b), and attachment loss only (c) definitions described above, by age. It is obvious from this figure that cases had significantly more periodontal disease than controls. Although this is not based on longitudinal data, it appears that bleeding peaks around puberty (13–14 years of age) and then decreases again; however, when attachment loss is included in the definition, the peak occurs later at approximately 16 years of age.

Finally, we also assessed the pattern of periodontal changes by focusing on the tooth level (data not shown). Similar to what was found on the subject level, the odds of periodontal destruction were

statistically significantly higher in cases versus controls, and this was consistent irrespective of the disease definition used or the tooth type (anterior versus posterior).

Discussion

Our results from a cohort of 700 young individuals (ages 6–18) demonstrate an association between diabetes and an increased risk for periodontal destruction even very early in life. This is the first report of this magnitude to address periodontal conditions in children and adolescents with diabetes.

In studying young individuals, it is important to assess periodontal changes both at the gingival level and the connective tissue attachment/bone level. However, as there is no consensus on the extent or severity of periodontal destruction necessary for clinically significant gingival/periodontal disease in children, we used different definitions that included gingival bleeding and/or attachment loss findings. Importantly, using multiple logistic regression models, a significant effect of diabetes was seen across all definitions of disease used for the whole population, and even separately for the 6–11 year old subgroup. These results extend and validate our previous findings in a subset of 342 subjects (Lalla et al. 2006a).

Further, we calculated a subject-based bleeding/plaque ratio (number of sites that bled over number of sites that harboured plaque, data not shown), as it has previously been demonstrated that an increased ratio may identify periodontitis-susceptible individuals and act as a prognostic indicator for future periodontal breakdown (van der Velden et al. 1985; Abbas et al. 1986). This concept is relevant in the setting of diabetes as studies have previously suggested that the subgingival bacterial challenge in diabetes does not differ from that in the non-diabetic state (Thorstensson et al. 1995; Ciantar et al. 2005; Lalla et al. 2006b), and that it is an exaggerated inflammatory response that drives the accelerated breakdown observed in affected individuals (Mealey 1999; Lalla et al. 2001; Salvi et al. 2005). When using this measure of gingival inflammation, regression results were consistent [odds ratio (OR) 1.81, $p = 0.013$ for the whole group; OR 2.18, $p = 0.017$ for the young subgroup; OR 1.37, $p = 0.389$ for the older subgroup].

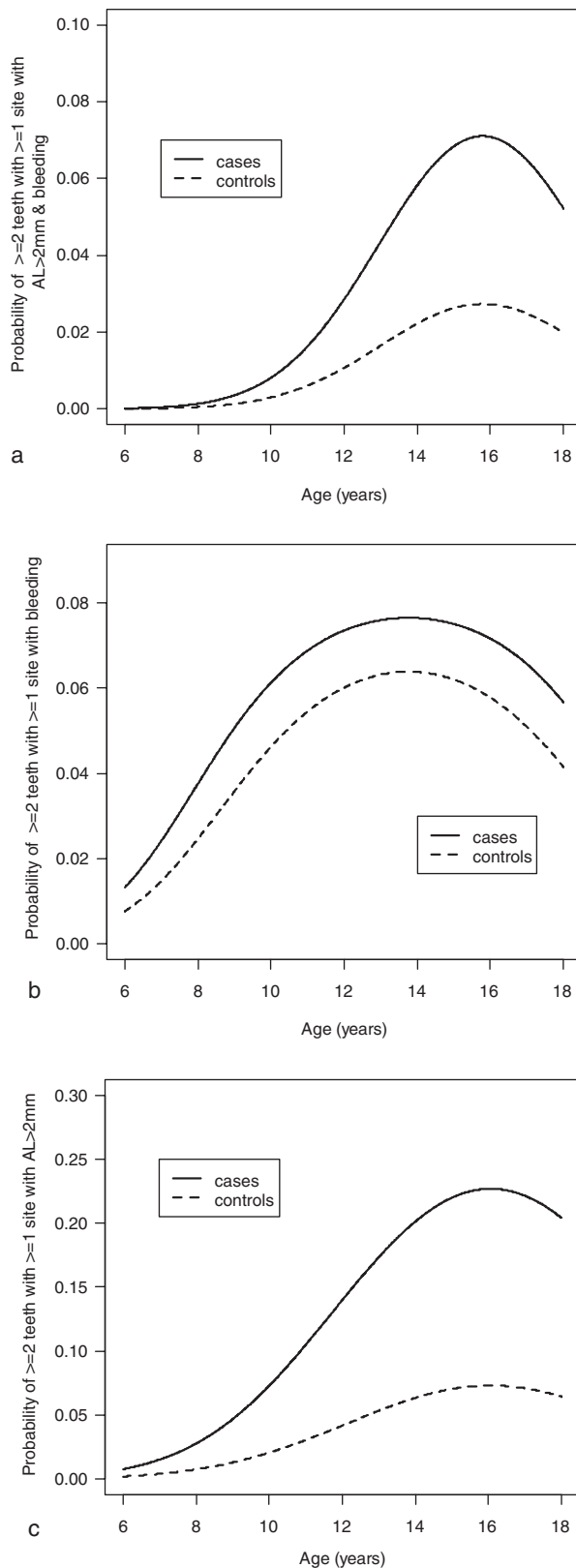


Fig. 1. Probability (estimated from logistic regression analyses) of a subject having periodontal changes, using three different definitions of gingival/periodontal disease, in diabetic subjects (solid line, $N = 350$) and controls (interrupted line, $N = 350$) by age. (a) at least two teeth with at least one site each with attachment loss > 2 mm and bleeding (at same site), (b) at least two teeth with at least one bleeding site each, and (c) at least two teeth with at least one site each with attachment loss > 2 mm.

Analysis of the effects of diabetes on the periodontal status by age revealed some interesting findings. First of all, diabetes was a significant correlate of periodontal destruction irrespective of disease definition in the young (< 12 years) age group (ORs of cases over controls from 2.18 to 4.45). This implicates diabetes as an important systemic modifier for periodontitis earlier in life than previously recognized (Cianciola et al. 1982, Iughetti et al. 1999). In the older group (12–18 years of age), the effect of diabetes was significant for the attachment loss (OR 3.84, $p = 0.007$), but not for the bleeding-only definition. This finding is probably due to the overwhelming confounding effect of puberty on gingival inflammation (Kinane et al. 2001). Consistent with this, in the combined periodontitis definition of at least two teeth with AL > 2 mm and bleeding at the same sites, the OR for cases over controls was 2.63 and approached statistical significance [95% confidence interval (CI): 0.94, 7.34; $p = 0.066$].

When age was examined as a continuous variable (Fig. 1), interesting trends emerged. Across all ages, and irrespective of the definition of periodontal disease, cases were significantly more affected than controls. This analysis was not based on longitudinal data and thus needs to be interpreted with caution. However, it appeared that in both groups, bleeding peaked around puberty and then decreased again; when AL was included in the definition, the peak occurred a few years later. The effects of hormonal/puberty-related changes, and diabetes-related parameters (such as duration, age at diagnosis, and level of glycemic control) might account for these observations. Further study of these associations and the underlying mechanisms is warranted.

A limitation of the current study is that a better match of the two groups was not possible and formal measures of socioeconomic status (SES), such as family income and parent education, were not available for our study participants. However, we can make some inferences based on the information we collected on ethnicity, medical insurance, and dental care history (reported in Table 1). We had significantly more Hispanic children in our control group compared with our cases. However, most children in both groups had medical coverage and, similarly, there were no differences between the two groups with regards to reported frequency of

prior dental visits. Moreover, it is important to note that (a) in our formal logistic regression analyses, we adjusted for important variables that might impact on the oral health status of our subjects and (b) if our non-diabetic controls were indeed of lower SES, that would only further support, and certainly not invalidate, our finding that children with diabetes have more gingival/periodontal disease than those without diabetes.

Periodontal diseases are largely preventable even in susceptible individuals, and progression of destruction can be best arrested when the disease is identified in the early stages. Moreover, evidence suggests that control of periodontal infections in adults with diabetes may have a positive effect on the level of metabolic control in these individuals (Grossi et al. 1997, Rodrigues et al. 2003, Faria-Almeida et al. 2006). Therefore, and in consideration of the present findings, oral screenings and periodontal prevention/treatment programs should be considered as a standard of care for young patients with diabetes.

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Clinical Relevance

Scientific rationale for the study: Multiple studies have demonstrated increased prevalence and severity of periodontitis in diabetic adults. Our objective was to explore the periodontal status of a large cohort of

children and adolescents with diabetes.

Principal findings: In a cohort of 700 6–18 year old children, diabetes was found to be significantly associated with increased odds of both gingival bleeding and attachment loss.

Practical implications: The findings of the present study support the notion that periodontal screening, prevention, and treatment programmes should be the standard of care for children and adolescents with diabetes.