Journal of Clinical Periodontology
Official Journal of The European Federation of Periodontology
Founded by the British, Dutch, French, German, Scandinavian, and Swiss Societies of Periodontology

J Clin Periodontol 2009; 36: 765–774 doi: 10.1111/j.1600-051X.2009.01445.x

Journal of Clinical Periodontology

Association between type 1 and type 2 diabetes with periodontal disease and tooth loss

Gaganpreet Kaur[1], Birte Holtfreter[1], Wolfgan G. Rathmann[2], Christian Schwahn[1], Henry Wallaschofski[3], Sabine Schipf[4], Matthias Nauck[3] and Thomas Kocher[1]

[1]Unit of Periodontology, Department of Restorative Dentistry, Periodontology, and Endodontology, Dental school, University of Greifswald, Greifswald, Germany; [2]German Diabetes Center, Institute of Biometrics and Epidemiology, Leibniz Center for Diabetes Research at Heinrich Heine University, Düsseldorf, Germany; [3]Institute for Clinical Chemistry and Laboratory Medicine, University of Greifswald, Greifswald, Germany; [4]Department of Community Medicine, University of Greifswald, Greifswald, Germany

Kaur G, Holtfreter B, Rathmann W, Schwahn C, Wallaschofski H, Schipf S, Nauck M, Kocher T. Association between type 1 and type 2 diabetes with periodontal disease and tooth loss. J Clin Periodontol 2009; 36: 765–774. doi: 10.1111/j.1600-051X.2009.01445.x.

Abstract

Aim: The aim of this study was to determine whether both type 1 (T1DM) and type 2 diabetes mellitus (T2DM) are associated with increased prevalence and extent of periodontal disease and tooth loss compared with non-diabetic subjects within a homogeneous adult study population.

Material and Methods: T1DM, T2DM and non-diabetic subjects were recruited from the population-based Study of Health in Pomerania. Additionally, T1DM subjects were retrieved from a Diabetes Centre. The total study population comprised 145 T1DM and 2647 non-diabetic subjects aged 20–59 years, and 182 T2DM and 1314 non-diabetic subjects aged 50–81 years. Periodontal disease was assessed by attachment loss (AL) and the number of missing teeth.

Results: Multivariable regression revealed an association between T1DM ($p < 0.001$) and T2DM ($p < 0.01$) with mean AL after full adjustment. After age stratification ($p = 0.04$ for interaction), the effect of T2DM was only statistically significant in the 60–69-year-old subjects (B = 0.90 (95% confidence intervals [95% CI]; 0.49, 1.31). T1DM was positively associated with tooth loss (adjusted, $p < 0.001$). The association between T2DM and tooth loss was statistically significant only for females (odds ratios = 1.60 [95% CI: 1.10, 2.33]).

Conclusions: Our study confirmed an association between both T1DM and T2DM with periodontitis and tooth loss. Therefore, oral health education should be promoted in diabetic subjects.

Key words: attachment loss; epidemiology; periodontal disease; study of health in Pomerania; tooth loss; type 1 diabetes; type 2 diabetes

Accepted for publication 31 May 2009

Conflict of interest and source of funding statement

There are no conflicts of interest associated with this work.
This research is supported by SHIP, which is part of the Community Medicine Research net (http://www.medizin.uni-greifswald.de/cm) of the University of Greifswald, Germany, which is funded by the German Federal Ministry of Education and Research (BMBF-01-ZZ-9603/0), the Ministry for Education, Research and Cultural Affairs as well as the Ministry of Social Affairs of the Federal State of Mecklenburg-West Pomerania. G. Kaur was supported by an educational grant by Gaba, Switzerland.

Diabetes mellitus comprises a group of metabolic diseases characterized by hyperglycaemia resulting from defects in insulin secretion, insulin action or both (American Diabetes Association 2007). It is an evolving disease with changing patterns in both type 1 diabetes mellitus (T1DM) and type 2 diabetes mellitus (T2DM). Unlike T2DM, T1DM is well defined, usually diagnosed at a young age, has a rapid onset of symptoms and is rarely undiagnosed (American Diabetes Association 2007).

Periodontal disease is an inflammatory disease caused by infection of the supporting tissue around the teeth and may subsequently lead to tooth loss if left untreated (Listgarten 1986, Burt 2005). Different studies have supported the existence, strength and effect of both type 1 and type 2 diabetes on periodontal disease (Emrich et al. 1991, American Academy of Periodontology 2000, Ryan et al. 2003, Borrell & Papapanou 2005, Lalla et al. 2006a). Differences in the reported prevalence of periodontal disease in T1DM and T2DM subjects may relate to the specific pathogenesis of the two types of diabetes, as well as utilization of dental care, ethnic disparities in study populations, disparities in confounder distributions and differences in

the study design and methodology. Further, most studies were too small to adjust for confounders, resulting in possibly biased results.

Some studies evaluating the relationship between diabetes mellitus and periodontal disease failed to distinguish between both types of diabetes (Sznajder et al. 1978, Tervonen & Knuuttila 1986, Bridges et al. 1996), while others included T1DM or T2DM subjects only (Hugoson et al. 1989, Emrich et al. 1991, Mattout et al. 2006, Lalla et al. 2006a, b). A few studies were even conducted without a reference group (Furukawa et al. 2007, Lalla et al. 2007a). Moreover, studies on periodontal disease in T1DM and T2DM subjects did not use comparable definition criteria.

Our knowledge of the relationship between T1DM and periodontal disease has emerged from studies in young individuals (< 18 years) (Lalla et al. 2007a, b). The role of T1DM as a risk factor for periodontal disease has not yet been investigated systematically in a large homogeneous adult cohort. In addition, a limited number of population-based studies have investigated the association between both types of diabetes and tooth loss (Kapp et al. 2007). Thus, our understanding of the evolving role of T1DM as a risk factor for periodontal disease is limited.

The aim of this study was to determine whether both T1DM and T2DM are associated with increased prevalence and extent of periodontal disease and tooth loss compared with non-diabetic subjects in a homogeneous adult study population.

Material and Methods

Study population

The Study of Health in Pomerania (SHIP) is a population-based survey, including a medical and dental examination of the adult population in a northeast region of Germany. Details about the study population, recruitment and examinations have been published elsewhere (John et al. 2001). From the entire regional population of 212,157 inhabitants, a representative sample of 7008 subjects with German citizenship aged 20–79 years was selected from the population registration offices. A two-stage cluster sampling method was adopted from the World Health Organization Monitoring Trends and Determinants in Cardiovascular Disease (MONICA) Study, yielding 12 5-year age strata (20–79 years) for both genders, each including 292 individuals. Between October 1997 and May 2001, a total of 4310 individuals (response 68.8%) participated in this study.

The T1DM cohort (233 subjects aged 20–81 years) was recruited from the Centre of Cardiology and Diabetes, Karlsburg, and the surrounding practicing diabetologists. These subjects lived in the same geographical region as the subjects recruited for SHIP. Data collection for T1DM subjects was performed between December 1997 and December 2000 from the diabetic registries of the Centre of Cardiology and Diabetes, Karlsburg. The study methods for these subjects were identical to the SHIP methods. All participants gave informed written consent. Both the studies were approved by the local ethics committee *a priori*.

Periodontal measurements

Data collection comprised oral and medical examinations, health-related interviews and risk-related questionnaires. Periodontal status was registered according to the half-mouth method on the right or the left side in alternate subjects using a periodontal probe (PCP 11, Hu-Friedy, Chicago, IL, USA) at four sites per tooth (mesiobuccal, midbuccal, distobuccal and midlingual) (Hensel et al. 2003). Periodontal assessment included attachment loss (AL) and probing depth (PD) measurements. AL represents the distance from the cemento-enamel junction to the bottom of the periodontal pocket. PD represents the distance from the gingival margin to the base of the periodontal pocket. All fully erupted teeth, except the third molars, were assessed, resulting in a maximum of 14 teeth per subject. The number of teeth was determined full mouth on a maximum of 28 teeth. The frequency of dental visits in the last 12 months was also recorded. Similar periodontal examinations were performed in T1DM subjects recruited from the Centre of Cardiology and Diabetes.

Calibrated licensed dentists performed all the examinations. Every 6–12 months, calibration exercises were performed on a subset of persons not connected to the study, yielding an intra-class correlation of 0.82–0.91 per examiner, and an inter-rater correlation of 0.84 relative to AL (Hensel et al. 2003).

Definition of diabetes

The T1DM cohort (233 subjects aged 20–81 years) was recruited from the Centre of Cardiology and Diabetes. The diagnosis of T1DM in these subjects was confirmed by the physician.

In SHIP, diabetes was assessed by self-reported physician diagnosis as well as use of anti-diabetic drugs. To ascertain the use of anti-diabetic drugs, prescriptions or medications brought during health-related interviews were categorized according to the Anatomical Therapeutic Chemical (ATC) classification system. Diabetes duration, and duration and mode of anti-diabetic therapy were assessed by self-reports.

In SHIP, subjects were defined as having T1DM if the onset of disease was before the age of 30 years or if administration of insulin started less than one year after the onset of the disease. Eight subjects (prevalence 0.2%) were identified as having T1DM. In SHIP, subjects were defined as having T2DM if the onset of disease was after the age of 29 or if the administration of insulin started > 1 year after disease onset in subjects younger than 30 years. In addition, subjects with T2DM were identified via a self-administered questionnaire, diet recommendations or oral anti-diabetic drugs according to the ATC codes. In SHIP, 339 subjects (prevalence 7.9%) were identified as having T2DM. A total of 241 T1DM (eight from SHIP and 233 from the Centre of Cardiology and Diabetes) and 339 T2DM subjects were examined (Fig. 1). Non-diabetic subjects from SHIP served as the reference group.

Assessment of confounders

A computer-aided personal interview was used to gain information on medical and dental history, behavioural and socio-demographic characteristics. School education level was categorized based on the eastern German three-level school system as low (< 10 years), medium (10 years) and high (> 10 years). Height and weight were determined using calibrated scales. The measurement of waist circumference (WC) (in centimetres) was based on the narrowest place between the last rib and the highest part of the abdomen and was categorized into normal ($WC \leqslant 102$ cm in males, $WC \leqslant 88$ cm in females) and increased ($WC > 102$ cm in males, $WC > 88$ cm in females). Cigarette smoking was categorized as never, former and current smoking. Non-fasting venous

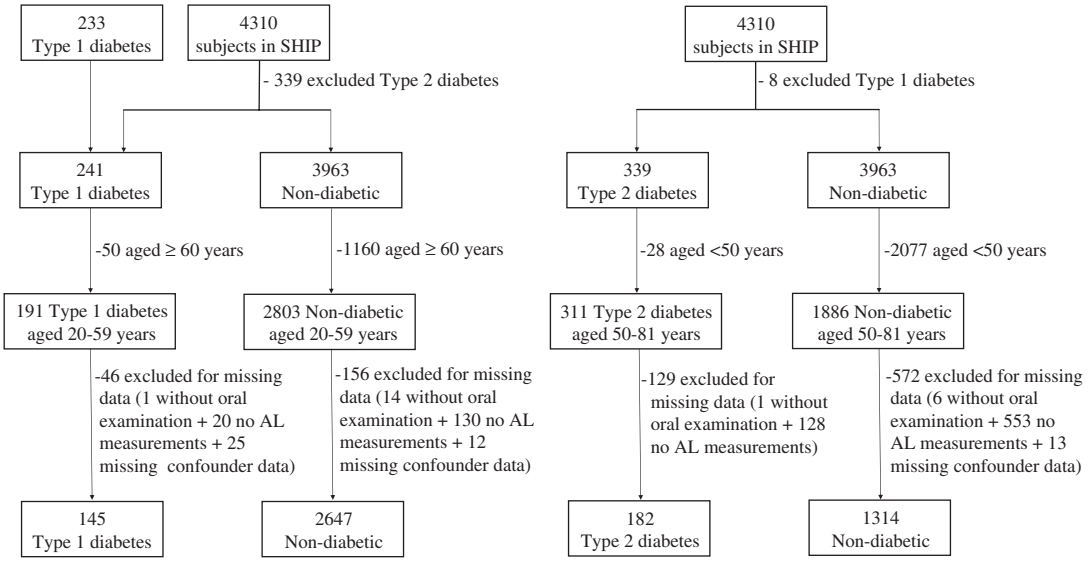

Fig. 1. Description of the study population. AL, attachment loss.

blood samples were collected. Glycosylated haemoglobin (HbA1c) was measured by high-performance liquid chromatography (HPLC) (ClinRep HbA1c, Recipe chemicals and Instruments GmbH, Munich, Germany). HbA1c was categorized into three levels (<6.0 and 6.0–6.9, ⩾7.0%). White blood cell (WBC) count was measured using the impedance measurement method (Coulter®MaxM™, Coulter Electronics, Miami, FL, USA).

Analyses were conducted separately for T1DM and T2DM. As the prevalence of T1DM and T2DM differs considerably with age (American Diabetes Association 2007), analyses on T1DM *versus* non-diabetic subjects were restricted to subjects aged 20–59 years. Analyses on T2DM *versus* non-diabetic subjects were limited to subjects aged 50–81 years. Subjects without oral examinations, missing AL measurements or missing data for potential confounders (age, gender, school education, smoking, WC and the frequency of dental visits in the last 12 months) were excluded (see Fig. 1). Finally, 145 T1DM (seven from SHIP and 138 from the Centre of Cardiology and Diabetes) and 2647 non-diabetic subjects aged 20–59 years, and 182 T2DM and 1314 non-diabetic subjects aged 50–81 years were available for analyses.

Statistical analysis

Continuous data were expressed as mean and standard deviation. Nominal data were presented as absolute numbers and per cent values. For continuous data, comparisons between groups were performed using the Mann–Whitney *U*-test. For nominal data, the χ^2 test was applied.

Linear regression models were fitted to assess the association between T1DM as well as T2DM and mean AL as the dependent variable. The final model was adjusted for age, gender, school education, smoking, WC and the frequency of dental visits (in the last 12 months). Linear regression coefficients (B) with their 95% confidence intervals (95% CI) and *p* values were reported.

To evaluate the association between T1DM or T2DM and the number of missing teeth multivariable logistic regression analyses were performed. Because of a bimodal and skewed distribution of number of missing teeth, the variable was dichotomized. Cases with a high number of missing teeth were assessed in relation to their age and gender. Thus, 25% of females and males (separately) with the highest number of missing teeth in each 5-year age group were considered as cases. The reference group included the remaining 75% of females and males (separately) within each 5-year age group. This dichotomous variable was used to estimate the association between both types of diabetes and a high number of missing teeth. The final model was adjusted for age, gender, school education, smoking, WC and the frequency of dental visits. Odds ratios (OR) with 95% CI and *p* values are listed in the tables.

Effect modifications were assessed including interaction terms between confounders and the exposure variable in the multivariable models. The statistical significance of interactions was assessed using likelihood ratio tests. In case of a statistically significant interaction ($p<0.1$ for interaction), stratified analyses were run, and the results are presented in Tables 2–4 and Fig. 2.

Sensitivity analyses were run to assess the association between T1DM, T2DM and periodontal disease by changing disease definition to verify the stability of findings regarding the association between both diabetes types and periodontitis. We replaced the mean AL by the square-rooted mean AL as it better fulfils the model assumptions, the mean PD (log-transformed to fulfil the model assumptions) and different extent measures (AL⩾4 mm and PD⩾4 mm, dichotomized). Additionally, analyses were restricted to subjects with at least 12 sites with valid AL measurements.

A value of $p<0.05$ was considered to be statistically significant for all analyses. Analyses were performed using STATA 10.0 (Stata Corporation LP, College Station, TX, USA) and R 2.7.1 (free statistical shareware).

Results

General characteristics

T1DM subjects were younger, but did not differ considerably with regard to education and smoking habits compared with non-diabetic subjects (Table 1). No differences were observed between T1DM and non-diabetic subjects with respect to periodontal variables. The mean age of

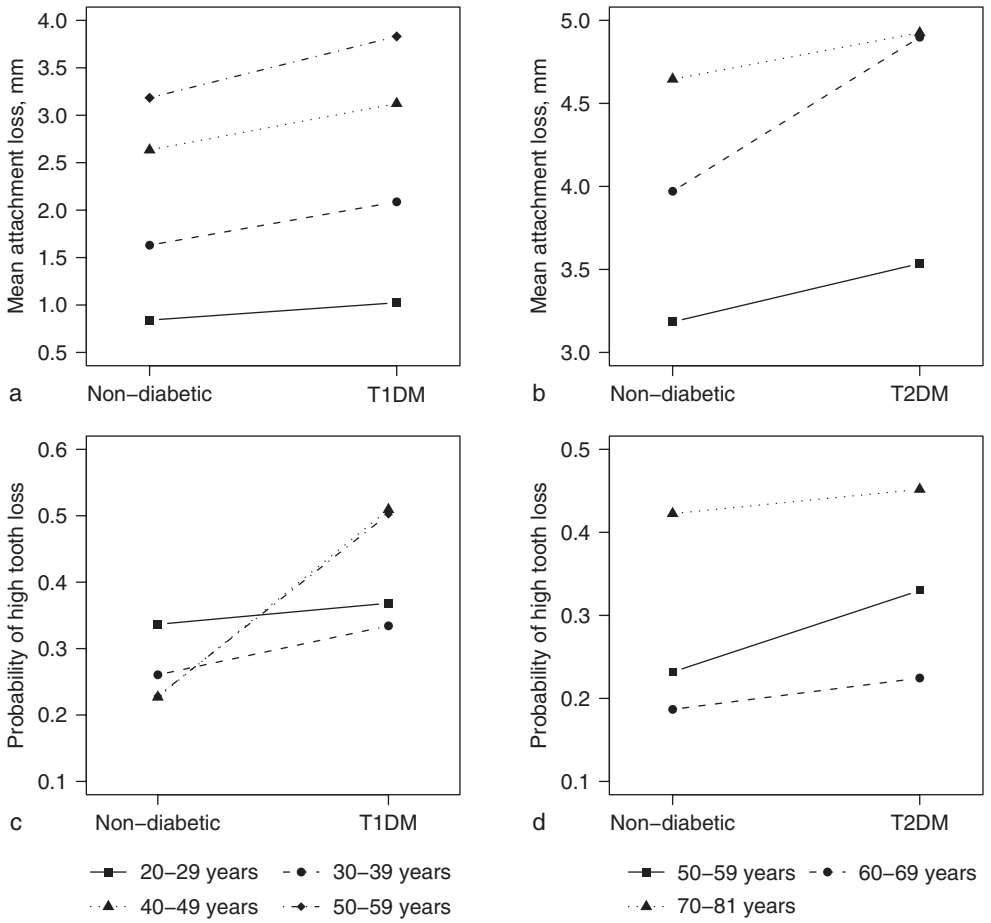

Fig. 2. Mean attachment loss across age groups: (a) among type 1 diabetes mellitus (T1DM) and non-diabetic subjects ($p = 0.55$ for age interaction) and (b) among type 2 diabetes mellitus (T2DM) and non-diabetic subjects ($p = 0.04$ for age interaction). Probability of high tooth loss (dependent variable: age- and gender-specific highest quartile *versus* three lower quartiles for the number of missing teeth) by age groups: (c) among T1DM and non-diabetic subjects ($p = 0.02$ for age interaction) and (d) among T2DM and non-diabetic subjects ($p = 0.69$ for age interaction). All models were adjusted for age, gender, school education, smoking, waist circumference and frequency of dental visits.

diagnosis and the mean duration of T1DM was 20.5 ± 11.6 and 17 ± 11.0 years, respectively. Sixty-three per cent of T1DM subjects had HbA1c levels above 7%.

T2DM subjects were less educated, more obese and more frequently former smokers than non-diabetic subjects (Table 1). Also, T2DM subjects had a substantially higher mean AL, mean PD and a higher number of missing teeth than non-diabetic subjects ($p < 0.01$). Furthermore, the percentage of sites with AL $\geqslant$ 4 mm was significantly higher in T2DM (59.3 *versus* 46.4%, $p < 0.001$). As expected, T2DM subjects were older at the age of diagnosis (54.6 ± 9.5 years) and had a shorter duration of diabetes (10.0 ± 7.6 years) compared with T1DM subjects. Forty-eight per cent of T2DM subjects had HbA1c levels above 7%. Moreover, T2DM and non-diabetic subjects differed significantly in the WBC count ($p < 0.001$).

Multivariate analyses

T1DM and mean attachment loss

A statistically significant association was observed between T1DM and mean AL after adjusting for confounders (B = 0.40 [95% CI: 0.19, 0.61]) compared with non-diabetic subjects (Table 2). To check whether HbA1c or WBC may act as an intermediator between diabetes and periodontal disease, we stepwise included both variables in the fully adjusted linear models. For T1DM, inclusion of HbA1c considerably reduced the coefficient for T1DM from 0.40 to 0.08 ($p = 0.55$). Inclusion of the WBC count did not materially affect the regression coefficient for T1DM.

Considering interactions between T1DM with age group (Fig. 2a), gender, smoking status or high WC, none of them revealed statistical significance.

T2DM and mean attachment loss

Subjects with T2DM had a significantly higher mean AL compared with non-diabetic subjects after adjusting for confounders (B = 0.47 [95% CI: 0.21, 0.73]). As for the T1DM model, inclusion of HbA1c reduced the coefficient for the fully adjusted T2DM model from 0.47 to 0.27 ($p = 0.09$). Inclusion of the WBC count did not relevantly affect the regression coefficient for T2DM.

Examination of interaction terms with T2DM in the fully adjusted model revealed an effect modification by age group ($p = 0.04$ for interaction). According to age-stratified analyses, the statistically significant effect of T2DM on the mean AL was observed in the 60–69-year-old age group (B = 0.90 [95% CI: 0.49, 1.31], see Table 2 and Fig. 2b). The effect of T2DM on the mean AL was not statistically significant in subjects aged 50–

Table 1. Demographic, medical, and dental characteristics of the study population in T1DM *versus* non-diabetic subjects aged 20–59 years and T2DM *versus* non-diabetic subjects aged 50–81 years

	T1DM ($N = 145$)	Non-diabetic ($N = 2647$)	p value*	T2DM ($N = 182$)	Non-diabetic ($N = 1314$)	p value*
Age (years)	37.4 ± 10.1	39.8 ± 11.1	0.01	64.5 ± 8.1	61.0 ± 7.6	<0.001
Male gender	76 (52.4%)	1213 (46.5%)	NS	104 (57.1%)	662 (50.4%)	NS
School education						
<10 years	25 (17.2%)	528 (19.9%)		134 (73.6%)	758 (57.7%)	
10 years	90 (62.1%)	1580 (59.7%)		34 (18.7%)	352 (26.8%)	
>10 years	30 (20.7%)	539 (20.4%)	NS	14 (7.7%)	204 (15.5%)	<0.001
Waist circumference (cm)	83.9 ± 13.4	85.9 ± 13.7	NS	99.6 ± 13.1	92.8 ± 12.6	<0.001
Smoking status						
Never smoker	49 (33.8%)	878 (33.2%)		78 (42.9%)	583 (44.4%)	
Former smoker	37 (25.5%)	748 (28.3%)		87 (47.8%)	495 (37.7%)	
Current smoker	59 (40.7%)	1021 (38.6%)	NS	17 (19.3%)	236 (18.0%)	<0.01
HbA1c (%)						
<6	13 (9.0%)	2437 (92.6%)		45 (24.7%)	1040 (79.4%)	
6–6.9	41 (28.3%)	176 (6.7%)		50 (27.5%)	247 (18.9%)	
⩾7	91 (62.8%)	19 (0.7%)	<0.001	87 (47.8%)	22 (1.7%)	<0.001
White blood cell count (Gpt/l)	7.0 ± 2.2	6.8 ± 2.0	NS	7.0 ± 1.9	6.4 ± 1.9	<0.001
Duration of diabetes (years)	17 ± 11.0	–		10.0 ± 7.6	–	
Age at diabetes diagnosis (years)	20.5 ± 11.6	–		54.6 ± 9.5	–	
Mean AL (mm)	2.3 ± 1.7	2.1 ± 1.6	NS	4.5 ± 2.0	3.7 ± 1.8	<0.001
Mean PD (mm)	2.4 ± 0.7	2.4 ± 0.7	NS	2.9 ± 0.9	2.7 ± 0.8	<0.01
Percentage of sites with AL⩾4 mm (%)	24.3 ± 31.8	19.0 ± 26.4	NS	59.3 ± 32.9	46.4 ± 32.4	<0.001
Percentage of sites with PD⩾4 mm (%)	12.1 ± 16.7	10.5 ± 15.3	NS	22.0 ± 23.5	16.5 ± 18.9	<0.01
Number of missing teeth	6.1 ± 6.3	5.2 ± 5.3	NS	13.9 ± 7.5	11.0 ± 7.2	<0.001
Frequency of dental visits	3.9 ± 4.2	2.8 ± 2.9	<0.001	2.5 ± 2.9	2.7 ± 2.7	<0.05

Data shown as mean ± SD or number (percentages).
*χ^2 test (nominal data); Mann–Whitney U-test (continuous data).
T1DM, type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus; N, number of subjects; HbA1c, glycosylated haemoglobin; AL, attachment loss; PD, probing depth; NS, not significant; SD, standard deviation.

59 years (B = 0.20 [95% CI: −0.24, 0.64]) and subjects aged 70–81 years (B = 0.13 [95% CI: −0.45, 0.72]). There was no statistically significant interaction of T2DM with gender, smoking status or high WC.

T1DM and the number of missing teeth

In agreement with the results for AL, logistic regression analyses revealed twofold higher odds for increased number of missing teeth for T1DM subjects compared with non-diabetic subjects after adjustment for confounders (OR = 1.93 [95% CI: 1.37, 2.71]).

The interaction between T1DM and age groups was statistically significant when it was added to the fully adjusted model (Table 3). Stratifying according to age groups revealed that the association between T1DM and tooth loss was statistically significant in subjects aged 40–49 years (OR = 3.49 [95% CI: 1.92, 6.36]) and 50–59 years (OR = 4.54 [95% CI: 1.70, 12.10]), while it was not statistically significant in subjects aged 20–29 years (OR = 0.86 [95% CI: 0.41, 1.82]) or 30–39 years (OR = 1.28 [95% CI: 0.67, 2.46]); see Table 3 and Fig. 2c. No statistically significant interaction was observed between T1DM and gender, smoking status or high WC.

T2DM and the number of missing teeth

For T2DM, a statistically significant association between T2DM and the number of missing teeth was only observed in the crude model (OR = 1.38 [95% CI: 1.07, 1.77]), but not in the fully adjusted model (OR = 1.17 [95% CI: 0.90, 1.52]).

A statistically significant effect modification was found for gender ($p = 0.01$ for interaction, Table 4). In gender-stratified analyses, the association between T2DM and tooth loss was statistically significant only in females (OR = 1.60 [95% CI: 1.10, 2.33], Table 4). There was no effect modification by age group, smoking status or high WC.

Sensitivity analyses

The statistically significant association between T1DM and periodontal disease was confirmed for the square-root transformed mean AL, the extent of AL⩾4 mm and the extent of PD⩾4 mm. For T2DM the association with periodontal disease was confirmed by replacing the mean AL by the square-rooted mean AL, mean PD (log transformed) and the extent of PD⩾4 mm. For a more precise definition of the periodontal status, the main and sensitivity analyses with mean AL as the dependent variable were restricted to subjects with a minimum of 12 sites with valid AL measurements. Restrictions did not alter the statistically significant association between both diabetes types and mean AL.

Further, to increase the homogeneity of non-diabetic subjects, additional analyses were run excluding non-diabetic subjects with HbA1c levels⩾7%. Overall, sensitivity analyses confirmed the association between both diabetes types and periodontal disease. None of the restrictions substantially changed the effect estimates for T1DM or T2DM on periodontal disease.

Discussion

This population-based study confirmed an association between both T1DM and T2DM with periodontal disease and tooth loss within a homogeneous study population. This association was persistent using various definitions for

Table 2. Linear regression models for mean attachment loss in T1DM ($N = 145$) *versus* non-diabetic subjects ($N = 2647$) aged 20–59 years, and regression model in T2DM ($N = 182$) *versus* non-diabetic subjects ($N = 1314$) aged 50–81 years including the statistically significant interaction term for age group

Model	T1DM *versus* non-diabetic	Overall	T2DM *versus* non-diabetic age categories[‡]		
	overall		50–59 years	60–69 years	70–81 years
Unadjusted					
Diabetes mellitus	0.03 (0.05, 0.54)*	0.79 (0.50, 1.07)**			
Adjusted					
Diabetes mellitus	0.40 (0.19, 0.61)**	0.19 (– 0.28, 0.65)	0.20 (– 0.24, 0.64)	0.90 (0.49, 1.31)**	0.13 (– 0.45, 0.72)
Age (years)					
20–29	0				
30–39	0.79 (0.66, 0.92)**				
40–49	1.80 (1.66, 1.93)**				
50–59	2.32 (2.17, 2.46)**	0			
60–69		0.70 (0.49, 0.91)**			
70–81		1.38 (1.11, 1.65)**			
60–69 years × T2DM		0.69 (0.07, 1.30)†			
70–81 years × T2DM		0.01 (– 0.68, 0.69)			
Gender (reference: females)	0.27 (0.16, 0.37)**	0.67 (0.46, 0.89)**	0.55 (0.27, 0.83)**	0.68 (0.31, 1.06)**	1.10 (0.47, 1.73)**
School education (reference: <10 years)					
10 years	– 0.43 (– 0.56, – 0.30)**	– 0.43 (– 0.64, – 0.22)**	– 0.50 (– 0.75, – 0.24)**	– 0.50 (– 0.90, – 0.10)†	0.14 (– 0.52, 0.80)
>10 years	– 0.63 (– 0.79, – 0.48)**	– 0.82 (– 1.07, – 0.57)**	– 0.65 (– 0.99, – 0.31)**	– 1.02 (– 1.43, – 0.60)**	– 0.99 (– 1.77, – 0.22)†
Smoking (reference: never smokers)					
Former smokers	0.14 (0.02, 0.26)†	0.23 (0.03, 0.44)†	0.31 (0.02, 0.60)†	0.22 (– 0.13, 0.57)	0.09 (– 0.48, 0.66)
Current smokers	0.63 (0.51, 0.74)**	1.02 (0.77, 1.27)**	1.01 (0.70, 1.31)**	1.25 (0.78, 1.73)**	0.52 (– 0.52, 1.55)
High WC (reference: low WC)	0.10 (– 0.05, 0.25)	0.22 (– 0.01, 0.46)	0.15 (– 0.18, 0.47)	0.004 (– 0.38, 0.39)	0.97 (0.30, 1.64)*
Frequency of dental visits	0.01 (– 0.01, 0.02)	– 0.03 (– 0.07, – 0.002)†	– 0.004 (– 0.05, 0.04)	– 0.05 (– 0.10, 0.004)	– 0.15 (– 0.26, – 0.03)†

Models for T2DM and mean attachment loss stratified by age group are presented.

Linear regression coefficients with their 95% confidence intervals are presented.

**$p \leqslant 0.001$, *$p \leqslant 0.01$, †$p \leqslant 0.05$.

‡Adjusted for gender, school education, smoking, WC and frequency of dental visits (in last 12 months).

T1DM, type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus; *N*, number of subjects; WC, waist circumference.

Table 3. Overall and age stratified logistic regression models in increased tooth loss (dependent variable: age- and gender-specific highest quartile *versus* three lower quartiles for the number of missing teeth) in T1DM ($N = 161$) *versus* non-diabetic subjects ($N = 2777$) aged 20–59 years

Model	Overall	T1DM *versus* non-diabetic age group categories[‡]			
		20–29 years	30–39 years	40–49 years	50–59 years
Unadjusted					
Diabetes mellitus	1.88 (1.40, 2.54)**				
Adjusted					
Diabetes mellitus	0.97 (0.47, 2.00)	0.86 (0.41, 1.82)	1.28 (0.67, 2.46)	3.49 (1.92, 6.36)**	4.54 (1.70, 12.10)*
Age (years)					
20–29	0				
30–39	0.69 (0.54, 0.88)*				
40–49	0.55 (0.43, 0.71)**				
50–59	0.48 (0.37, 0.63)**				
30–39 years × T1DM	1.38 (0.53, 3.61)				
40–49 years × T1DM	3.38 (1.33, 8.61)†				
50–59 years × T1DM	4.19 (1.26, 13.95)†				
Gender (reference: females)	0.86 (0.72, 1.04)	0.68 (0.47, 0.98)†	1.00 (0.71, 1.42)	0.74 (0.50, 1.08)	1.27 (0.83, 1.94)
School education (reference: < 10 years)					
10 years	0.50 (0.40, 0.62)**	0.42 (0.24, 0.72)*	0.37 (0.21, 0.62)**	0.52 (0.35, 0.77)**	0.63 (0.43, 0.91)†
> 10 years	0.24 (0.18, 0.32)**	0.25 (0.13, 0.46)**	0.21 (0.11, 0.41)**	0.16 (0.08, 0.31)**	0.24 (0.13, 0.46)**
Smoking (reference: never smokers)					
Former smokers	1.31 (1.03, 1.65)†	1.22 (0.75, 1.99)	1.71 (1.03, 2.84)†	1.55 (0.95, 2.52)	0.94 (0.60, 1.48)
Current smokers	2.25 (1.83, 2.78)**	1.50 (1.0, 2.26)	3.31 (2.13, 5.15)**	2.80 (1.78, 4.41)**	1.93 (1.27, 2.95)*
High WC (reference: low WC)	1.24 (0.96, 1.61)	1.29 (0.65, 2.54)	1.28 (0.70, 2.32)	1.06 (0.66, 1.72)	1.63 (1.03, 2.58)†
Frequency of dental visits	1.04 (1.02, 1.07)**	1.08 (1.03, 1.14)*	1.09 (1.04, 1.15)**	1.02 (0.96, 1.07)	0.98 (0.93, 1.04)

Odds ratios with their 95% confidence intervals are presented.
**$p \leqslant 0.001$, *$p \leqslant 0.01$, †$p \leqslant 0.05$.
‡Age stratified models were adjusted for gender, school education, smoking, WC and frequency of dental visits (in the last 12 months).
T1DM, type 1 diabetes mellitus; *N*, number of subjects; WC, waist circumference.

severity and extent of AL and PD. Considering the fact that T1DM and T2DM occur predominantly at different ages, the present analyses were performed in different age groups. This enabled a valid evaluation of the association between periodontal disease and T1DM as well as T2DM compared with non-diabetic subjects. Moreover, analyses were performed excluding non-diabetic subjects with HbA1c levels $\geqslant 7\%$, because undiagnosed diabetes was found to be highly frequent in the general population (Rohlfing et al. 2000, Rathmann et al. 2003). None of the restrictions substantially changed the effect estimates.

Previous studies reported comparable results regarding the association between T1DM or T2DM and periodontal diseases (Ryan et al. 2003, Mealey & Oates 2006). Both types of diabetes mellitus were seldom reported together in a large adult population. A statistically significant association was found between T1DM and mean AL compared with non-diabetic subjects aged 20–59 years. However, most studies on periodontal health in T1DM subjects were carried out in children, reporting significantly more plaque (Lalla et al. 2006a) and increased clinical AL in T1DM subjects compared with non-diabetic subjects (Lalla et al. 2007b).

The results from the present study demonstrated a statistically significant association between T2DM and mean AL compared with non-diabetic subjects aged 50–81 years. Importantly, the effect of T2DM on the mean AL was significantly pronounced in 60–69-year-old subjects. An epidemiological study conducted among the Pima Indians reported significantly poorer periodontal health in T2DM subjects, with odds of destructive AL being about three times higher than among non-diabetic subjects (Emrich et al. 1991). Similarly, other studies confirmed the significant association between diabetes and extent of PD (Oliver & Tervonen 1993, Tervonen & Karjalainen 1997) and AL (Moore et al. 1999).

Tooth loss can be a consequence of severe periodontal disease. In the present study, a strong association was observed between T1DM and the number of missing teeth after adjusting for confounders. Stratified analyses revealed that the effect was restricted to 40–49- and 50–59-year-old subjects. The presence and severity of diabetes-related periodontal disease might have led to an increased number of missing teeth in T1DM subjects. However, in other studies an association between T1DM and tooth loss was not concordantly reported (Hugoson et al. 1989, Thorstensson & Hugoson 1993). A recent study comparing T1DM with non-diabetic subjects aged 18–70 years reported more severe periodontal disease in the younger age groups (Lalla et al. 2006b), supporting the findings of more pronounced tooth loss in T1DM subjects. These results concur with our results for T1DM subjects, suggesting poor oral health care among T1DM subjects. In the present study, T1DM subjects had fewer teeth although they more frequently visited the dentist compared with non-diabetic subjects. This finding may indicate a lack of skilled dental services.

The relationship between T2DM and tooth loss is also complicated by the fact that disease onset generally occurs in middle and late age, coinciding with the time point when periodontal disease becomes more prevalent. In this study, the association between T2DM and the number of missing teeth was not maintained after adjusting for age and other confounders. The dilution of the effect of T2DM on the number of teeth in older subjects could be explained by the presence of primary confounders

Table 4. Overall and gender-stratified multivariable logistic regression analyses for increased tooth loss (dependent variable: age- and gender-specific highest quartile *versus* three lower quartiles for the number of missing teeth) in T2DM ($N = 310$) *versus* non-diabetic subjects ($N = 1858$) aged 50–81

Model	Overall	T2DM *versus* non-diabetic gender‡	
		female	male
Unadjusted			
Diabetes mellitus	1.38 (1.07, 1.77)**		
Adjusted			
Diabetes mellitus	1.65 (1.13, 2.39)	1.60 (1.10, 2.33)†	0.84 (0.57, 1.24)
Age (years)			
50–59	0	0	0
60–69	0.89 (0.70, 1.14)	0.80 (0.56, 1.14)	0.96 (0.68, 1.36)
70–81	1.91 (1.48, 2.46)**	1.67 (1.16, 2.40)*	2.12 (1.48, 3.03)**
Gender (reference: females)	1.00 (0.76, 1.30)		
Male gender × T2DM	0.50 (0.29, 0.85)†		
School education (reference: < 10 years)			
10 years	0.63 (0.49, 0.82)**	0.53 (0.36, 0.76)**	0.77 (0.54, 1.09)
> 10 years	0.38 (0.26, 0.55)**	0.24 (0.12, 0.48)**	0.49 (0.31, 0.77)*
Smoking (reference: never smokers)			
Former smokers	1.41 (1.11, 1.81)*	1.33 (0.93, 1.89)	1.75 (1.18, 2.58)*
Current smokers	2.27 (1.71, 3.02)**	1.88 (1.26, 2.80)*	3.06 (1.95, 4.80)**
High WC (reference: low WC)	1.34 (1.03, 1.74)†	1.37 (1.04, 1.82)†	0.88 (0.40, 1.92)
Frequency of dental visits	0.83 (0.78, 0.87)**	0.84 (0.78, 0.90)**	0.82 (0.75, 0.89)**

Odds ratios with their 95% confidence intervals are presented.
**$p \leqslant 0.001$, *$p \leqslant 0.01$, †$p \leqslant 0.05$.
‡Gender-stratified models were adjusted for age (reference: 50–59 years), school education, smoking, WC and frequency of dental visits (in last 12 months).
T2DM, type 2 diabetes mellitus; *N*, number of subjects; WC, waist circumference.

such as age, smoking and co-morbidities. Moreover, in older subjects tooth loss is not only a consequence of periodontal disease, but occurs also due to endodontic infections, a lack of preventive methods or prosthetic treatment decisions. Previous studies have reported significantly more tooth loss in subjects with diabetes compared with non-diabetic subjects (Bridges et al. 1996), especially in younger age groups (Kapp et al. 2007). In contrast, Oliver & Tervonen (1994) reported that tooth loss was similar in Minnesota diabetic subjects and US employed adults. In this study, we investigated the effect of gender on the association between T2DM and the number of missing teeth. The association was stronger among females with T2DM possibly due to differences in health awareness between males and females.

The aetiopathogenesis of periodontal disease is complex. Several factors are probably responsible for the increased risk of periodontal disease in diabetic subjects. Systemic inflammation and hyperglycaemia are thought to play an important role in the pathogenesis of periodontal disease in diabetic subjects. Elevated numbers of WBC in diabetes and periodontal diseases have been reported previously (Loos et al. 2000, Vozarova et al. 2002). In the present study, no change in the coefficients for both diabetes types was observed when the WBC count was entered into the model. From these findings we may tentatively conclude that inflammation does not mediate the association between diabetes and periodontal disease, although it has been reported previously that elevated systemic inflammation plays an important role in the interaction between diabetes and periodontal disease (Lim et al. 2007). Further studies are needed to investigate the role of inflammation in diabetes-associated periodontitis.

The present data demonstrated that the association between T1DM or T2DM and periodontal disease may be mediated by HbA1c levels. Most previous studies favour a direct causal association, which would implicate that hyperglycaemia is directly involved in the aetiology of periodontal diseases (Tervonen & Knuuttila 1986, Seppala & Ainamo 1994, Engebretson et al. 2004). Several mechanisms explaining how diabetes leads to an alteration in different tissues and organs, including the periodontium, have been proposed (Soskolne & Klinger 2001, Mealey & Oates 2006). Earlier studies have demonstrated that Advanced Glycation Endproducts (AGE) formed by hyperglycaemia can transform macrophages into cells with a destructive phenotype producing high levels of interleukin (IL)-1, IL-6 and TNF-α (Hudson et al. 2003). Furthermore, AGE is able to render the endothelium hyperpermeable and to express high levels of adhesion molecule references. These changes cause an increased susceptibility to infections and an impaired healing process in diabetic patients. Therefore, achieving good glycaemic control appears to be a realistic approach to improve the periodontal condition in diabetic subjects.

The major strength of this study is the large sample size comprising a wide age range of social and medical data, permitting the estimation of the association between T1DM and T2DM with periodontal disease with good statistical precision. To reduce the misclassification of diabetes type, T1DM and T2DM subjects were clearly defined. One limitation may exist due to missing evaluation of the oral glucose tolerance test and non-fasting glucose values. Because of the cross-sectional design, there was no detailed information on the reasons for and the timing of tooth loss, previous periodontal treatment and previous glycaemic control. Furthermore, teeth with worse periodontal disease might have been extracted; hence the remaining teeth may not represent the long-term periodontal status. Thus, the association between periodontal disease and diabetes may be underestimated, especially for older T2DM subjects.

In conclusion, the present study demonstrated an association between both T1DM and T2DM and an increased severity of periodontal disease and tooth loss compared with non-diabetic subjects in a large homogeneous study population. However, T2DM was positively associated with mean AL in 60–69-year-old subjects. In T1DM, tooth loss was prominent in 40–49- and 50–59-year-old subjects, whereas in T2DM tooth loss was only significantly increased in female diabetic subjects compared with non-diabetic female subjects.

References

American Academy of Periodontology. (2000) Diabetes and periodontal diseases. Committee on Research, Science and Therapy. American

Academy of Periodontology. *J Periodontol* **71**, 664–678.

American Diabetes Association. (2007) Diagnosis and classification of diabetes mellitus. *Diabetes Care* **30** (Suppl. 1), S42–S47.

Borrell, L. N. & Papapanou, P. N. (2005) Analytical epidemiology of periodontitis. *Journal of Clinical Periodontology* **32** (Suppl. 6), 132–158.

Bridges, R. B., Anderson, J. W., Saxe, S. R., Gregory, K. & Bridges, S. R. (1996) Periodontal status of diabetic and non-diabetic men: effects of smoking, glycemic control, and socioeconomic factors. *Journal of Periodontology* **67**, 1185–1192.

Burt, B. (2005) Position paper: epidemiology of periodontal diseases. *Journal of Periodontology* **76**, 1406–1419.

Emrich, L. J., Shlossman, M. & Genco, R. J. (1991) Periodontal disease in non-insulin-dependent diabetes mellitus. *Journal of Periodontology* **62**, 123–131.

Engebretson, S. P., Hey-Hadavi, J., Ehrhardt, F. J., Hsu, D., Celenti, R. S., Grbic, J. T. & Lamster, I. B. (2004) Gingival crevicular fluid levels of interleukin-1beta and glycemic control in patients with chronic periodontitis and type 2 diabetes. *Journal of Periodontology* **75**, 1203–1208.

Furukawa, T., Wakai, K., Yamanouchi, K., Oshida, Y., Miyao, M., Watanabe, T. & Sato, Y. (2007) Associations of periodontal damage and tooth loss with atherogenic factors among patients with type 2 diabetes mellitus. *Internal Medicine* **46**, 1359–1364.

Hensel, E., Gesch, D., Biffar, R., Bernhardt, O., Kocher, T., Splieth, C., Born, G. & John, U. (2003) Study of Health in Pomerania (SHIP): a health survey in an East German region. Objectives and design of the oral health section. *Quintessence International* **34**, 370–378.

Hudson, B. I., Bucciarelli, L. G., Wendt, T., Sakaguchi, T., Lalla, E., Qu, W., Lu, Y., Lee, L., Stern, D. M., Naka, Y., Ramasamy, R., Yan, S. D., Yan, S. F., D'Agati, V. & Schmidt, A. M. (2003) Blockade of receptor for advanced glycation endproducts: a new target for therapeutic intervention in diabetic complications and inflammatory disorders. *Archives of Biochemistry and Biophysics* **419**, 80–88.

Hugoson, A., Thorstensson, H., Falk, H. & Kuylenstierna, J. (1989) Periodontal conditions in insulin-dependent diabetics. *Journal of Clinical Periodontology* **16**, 215–223.

John, U., Greiner, B., Hensel, E., Ludemann, J., Piek, M. & Sauer, S. (2001) Study of Health In Pomerania (SHIP): a health examination survey in an east German region: objectives and design. *Sozial- und Praventivmedizin* **46**, 186–194.

Kapp, J. M., Boren, S. A., Yun, S. & LeMaster, J. (2007) Diabetes and tooth loss in a national sample of dentate adults reporting annual dental visits. *Preventing Chronic Disease* **4**, A59.

Lalla, E., Cheng, B., Lal, S., Kaplan, S., Softness, B., Greenberg, E., Goland, R. S. & Lamster, I. B. (2007a) Diabetes-related parameters and periodontal conditions in children. *Journal of Periodontal Research* **42**, 345–349.

Lalla, E., Cheng, B., Lal, S., Kaplan, S., Softness, B., Greenberg, E., Goland, R. S. & Lamster, I. B. (2007b) Diabetes mellitus promotes periodontal destruction in children. *Journal of Clinical Periodontology* **34**, 294–298.

Lalla, E., Cheng, B., Lal, S., Tucker, S., Greenberg, E., Goland, R. & Lamster, I. B. (2006a) Periodontal changes in children and adolescents with diabetes: a case–control study. *Diabetes Care* **29**, 295–299.

Lalla, E., Kaplan, S., Chang, S. M., Roth, G. A., Celenti, R., Hinckley, K., Greenberg, E. & Papapanou, P. N. (2006b) Periodontal infection profiles in type 1 diabetes. *Journal of Clinical Periodontology* **33**, 855–862.

Lim, L. P., Tay, F. B., Sum, C. F. & Thai, A. C. (2007) Relationship between markers of metabolic control and inflammation on severity of periodontal disease in patients with diabetes mellitus. *Journal of Clinical Periodontology* **34**, 118–123.

Listgarten, M. A. (1986) Pathogenesis of periodontitis. *Journal of Clinical Periodontology* **13**, 418–430.

Loos, B. G., Craandijk, J., Hoek, F. J., Wertheim-van Dillen, P. M. & van der Velden, U. (2000) Elevation of systemic markers related to cardiovascular diseases in the peripheral blood of periodontitis patients. *Journal of Periodontology* **71**, 1528–1534.

Mattout, C., Bourgeois, D. & Bouchard, P. (2006) Type 2 diabetes and periodontal indicators: epidemiology in France 2002–2003. *Journal of Periodontal Research* **41**, 253–258.

Mealey, B. L. & Oates, T. W. (2006) Diabetes mellitus and periodontal diseases. *Journal of Periodontology* **77**, 1289–1303.

Moore, P. A., Weyant, R. J., Mongelluzzo, M. B., Myers, D. E., Rossie, K., Guggenheimer, J., Block, H. M., Huber, H. & Orchard, T. (1999) Type 1 diabetes mellitus and oral health: assessment of periodontal disease. *Journal of Periodontology* **70**, 409–417.

Oliver, R. C. & Tervonen, T. (1993) Periodontitis and tooth loss: comparing diabetics with the general population. *Journal of American Dental Association* **124**, 71–76.

Oliver, R. C. & Tervonen, T. (1994) Diabetes – a risk factor for periodontitis in adults? *Journal of Periodontology* **65**, 530–538.

Rathmann, W., Haastert, B., Icks, A., Lowel, H., Meisinger, C., Holle, R. & Giani, G. (2003) High prevalence of undiagnosed diabetes mellitus in Southern Germany: target populations for efficient screening. The KORA survey 2000. *Diabetologia* **46**, 182–189.

Rohlfing, C. L., Little, R. R., Wiedmeyer, H. M., England, J. D., Madsen, R., Harris, M. I., Flegal, K. M., Eberhardt, M. S. & Goldstein, D. E. (2000) Use of GHb (HbA1c) in screening for undiagnosed diabetes in the US population. *Diabetes Care* **23**, 187–191.

Ryan, M. E., Carnu, O. & Kamer, A. (2003) The influence of diabetes on the periodontal tissues. *Journal of American Dental Association* **134** (Spec. No.), 34S–40S.

Seppala, B. & Ainamo, J. (1994) A site-by-site follow-up study on the effect of controlled versus poorly controlled insulin-dependent diabetes mellitus. *Journal of Clinical Periodontology* **21**, 161–165.

Soskolne, W. A. & Klinger, A. (2001) The relationship between periodontal diseases and diabetes: an overview. *Annals of Periodontology* **6**, 91–98.

Sznajder, N., Carraro, J. J., Rugna, S. & Sereday, M. (1978) Periodontal findings in diabetic and nondiabetic patients. *Journal of Periodontology* **49**, 445–448.

Tervonen, T. & Karjalainen, K. (1997) Periodontal disease related to diabetic status. A pilot study of the response to periodontal therapy in type 1 diabetes. *Journal of Clinical Periodontology* **24**, 505–510.

Tervonen, T. & Knuuttila, M. (1986) Relation of diabetes control to periodontal pocketing and alveolar bone level. *Oral Surgery Oral Medicine Oral Pathology Oral Radiology and Endodontics* **61**, 346–349.

Thorstensson, H. & Hugoson, A. (1993) Periodontal disease experience in adult long-duration insulin-dependent diabetics. *Journal of Clinical Periodontology* **20**, 352–358.

Vozarova, B., Weyer, C., Lindsay, R. S., Pratley, R. E., Bogardus, C. & Tataranni, P. A. (2002) High white blood cell count is associated with a worsening of insulin sensitivity and predicts the development of type 2 diabetes. *Diabetes* **51**, 455–461.

Address:
Birte Holtfreter
Department of Restorative Dentistry, Periodontology, and Endodontology
Unit of Periodontology
Ernst-Moritz-Arndt-University Greifswald
Rotgerberstr 8
17487 Greifswald
Germany
E-mail: birte.holtfreter@uni-greifswald.de

Clinical Relevance

Scientific rationale for the study: The association between both types of diabetes with periodontal disease and tooth loss was assessed within a homogeneous adult study population in West Pomerania.

Principal findings: Subjects with type 1 and type 2 diabetes are at a high risk of having periodontal disease and tooth loss compared with non-diabetic subjects. The effect of T2DM on mean AL was only statistically significant within the 60–69-year-old age group.

Practical implications: The results highlight the need to increase the focus on maintaining good oral hygiene and metabolic control in subjects with diabetes.