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Pre-diabetes and diabetes: Medical risk factors and periodontal conditions

MURAD ALTAMASH[1,2], SOPHIA ARLEDAL[3], BJÖRN KLINGE[1] & PER-ERIK ENGSTRÖM[1]

[1]*Karolinska Institutet, Department of Dental Medicine, Division of Periodontology, Huddinge, Sweden,* [2]*Altamash Institute of Dental Medicine, Karachi, Pakistan, and* [3]*Karolinska Institutet, Department of Dental Medicine, Division of Image and Functional Odontology, Huddinge, Sweden*

Abstract

Objective. The aim of this study was to evaluate the difference between subjects with pre-diabetes, well or poorly controlled diabetes mellitus type 2 (T2D) and non-diabetes concerning such medical risk factors as hemoglobin A1c, body mass index (BMI) and waist circumference (WC) with periodontal conditions. ***Materials and methods.*** BMI, WC, PI, BOP, PD and marginal bone level (MBL) were recorded. Hemoglobin A1c (HbA1c) level and random blood glucose level (RBGL) were analyzed. ***Results.*** Forty-five subjects were pre-diabetics, 64 subjects had poorly controlled T2D, 28 subjects had well controlled T2D and 76 subjects were non-diabetics. Non-diabetics, pre-diabetics as well as subjects with T2D were overweight. Females in all groups had increased mean levels of WC. Number of PD ≥ 6 mm were increased in subjects with poorly controlled T2D compared to non-diabetics and pre-diabetics ($p < 0.05$). ***Conclusions.*** Pre-diabetic subjects showed the same periodontal conditions as non-diabetic subjects. Forty-five of the subjects reporting to have no diabetes were pre-diabetics. Non-diabetic, pre-diabetic and diabetic subjects were overweight. Subjects with poorly controlled T2D had severe periodontal conditions.

Key Words: *alveolar bone loss, body mass index, HbA1c, type2 diabetes, waist circumference*

Introduction

Pre-diabetes is a condition with an increase in blood glucose levels above normal range but does not fulfill the standard for determination of diabetes mellitus type 2 (T2D) [1].

Pre-diabetic individuals have impaired fasting glucose (IFG) with fasting plasma glucose (FPG) levels from 100 mg/dl (5.6 mmol/l) to 125 mg/dl (6.9 mmol/l) and in the oral glucose tolerance test (OGTT), the levels are from 140 mg/dl (7.8 mmol/l) to 199 mg/dl (11.0 mmol/l) [2]. Therefore, these pre-diabetic individuals have a relatively high risk for development of T2D [3].

Diabetes mellitus type 2 has been classified as fasting plasma glucose (FPG), with high levels from 126 mg/dl (7.0 mmol/l) or according to the oral glucose tolerance test (OGTT) with glucose levels from 200 mg/dl (11.1 mmol/l) [4].

Overweight (body-mass index (BMI) ≥ 25 kg/m^2) and obese (BMI ≥ 30 kg/m^2) individuals are at risk to develop T2D. Furthermore, low education and increased waist circumference (WC) have been associated with a high prevalence of T2D [5]. Studies conclude that smoking cigarettes has been associated to diabetes T2D, mostly as an effect to nicotine which elevates blood glucose levels, HbA1c and is also associated with considerable weight gain [6,7].

Periodontal disease is a major cause of tooth loss in adults and is the most common chronic oral infection and has also been considered as the sixth complication of diabetes mellitus [8]. Marginal bone loss is 4-times higher in individuals with T2D compared to subjects with no diabetes [9].

The aim of the study was to compare the risk factors, HbA1c, BMI and WC with periodontal conditions, to further evaluate the difference between subjects with pre-diabetes, T2D and non-diabetes. Hypothesis is that increased blood sugar levels in pre-diabetic and diabetic subjects will give rise to severe periodontal conditions.

Correspondence: Dr Murad Altamash, Department of Dental Medicine, Division of Periodontology, Karolinska Institutet, Box 4064, SE 141 04 Huddinge, Sweden. Fax: +46 8 711 83 43. E-mail: murad.altamash@ki.se

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Materials and methods

Interview questionnaire

A questionnaire was made for adult patients, aged 25 years and above, who were coming into Altamash Institute Hospital, Karachi, Pakistan, for dental treatment. Patients were selected as per their presenting complaints regarding periodontal conditions. In the period of January–November 2010 subjects were examined and provided written consent, which was translated into Urdu (being the native language of Pakistan). The questionnaire was filled in with the patient and examiner. Level of education, age, gender, smoking and general health including T2D were recorded. Individuals were questioned if they had T2D and had been asked to present their medical records for confirmation of T2D. Subjects that had been smoking one or above cigarette daily were considered as smokers and those subjects who did not smoke were considered as non-smokers.

HbA1c and RBGL

HbA1c were examined for all individuals in which subjects were categorized as non-diabetics with HbA1c $\leq$ 5.6% and as pre-diabetics with HbA1c between 5.7–6.4%. Diabetics were determined with HbA1c levels $\geq$ 6.5% [10]. Diabetes status was obtained by taking the history of the patient in the form of a questionnaire and blood glucose tests. Blood samples were drawn for determination of HbA1c and analyzed in the Karachi Laboratory Diagnostic Center, Karachi, Pakistan (Roche Tinaquant® Hemoglobin A1C II method was performed on the Hitachi Modular P analyzer). For determination of random blood glucose level (RBGL) the finger-prick method was applied for recording with the (Accu Check Active System Roche Diagnostics, Mannheim, Germany) hand-held glucometer with a measuring range of 10–600 mg/dl and a sample size of 1 μL on a sensor comfort strips with a measuring time of 5 s.

Body mass index and waist circumference

Body mass index was measured for all individual along with waist circumference in centimeters. The formula for BMI was calculated according to the international system of units of BMI with the formula: mass (kg)/(height(m))^2. Weight was measured in kilograms, whereas the height was measured in meters [11,12].

Periodontal examination

The dental hygienist and the author (M.A) recorded periodontal measurements of pocket depth (PD) in 15 subjects and compared there results. The periodontal measurements of plaque PI [13] and bleeding on probing BOP [14] were also analyzed. In the study measurements of PD, BOP and PI were recorded by the dental hygienist. Full mouth was recorded which included maxillary teeth and mandibular teeth excluding third molars. Plaque index (PI) [13], bleeding on probing (BOP) [14] and pocket depth (PD) were registered at four sites (mesial, distal, buccal and lingual/palatal). A graded probe (Hu-Friedy Manufacturing, Chicago, IL) was used to measure PD to the nearest millimeter. Periodontal pocket depths were recorded between $4 < 6$ mm and ≥ 6 mm and teeth being considered missing when roots remnants are embedded. All missing teeth were also recorded.

Radiographs

An analog panoramic tomography machine (Villa Sistemi Medicali, MR05, Buccinasco (MI), Italy and Yoshida Panovra, 10-C, Tokyo, Japan) was used to take extra-oral panoramic radiographs (Kodak T-Mat, Eastman Kodak, Rochester, NY and Konica Minolta MG-SR PLUS NIF, finished in Mexico for Konica), which were used and the radiographs were further scanned by a scanner (Epson Perfection V700 PHOTO (Dual Lens System) Tokyo, Japan) for investigation. A computer monitor (Eizo S1910 Tokyo, Japan) was used to view the radiographs and the distance vertically commencing from the assumed cement enamel junction (CEJ) to the most apical portion of the marginal bone level (MBL) was measured. Surfaces of those teeth at which the CEJ and bone crest were not clear because of technical issues such as overlapping restorations, dental caries and poor quality of radiograph were not measured. If the bony landmarks on the mesial or distal aspect were not identifiable the tooth surface was exempted.

Marginal bone loss was analyzed in pixels (ImageJ Tool 1.43, National Institutes of Health, Bethesda, Maryland, USA) and calibration of one pixel was equal to 0.025 mm in the radiographs that were scanned. MBL for premolars and molars (excluding third molars) in both arches were measured. The radiographs were analyzed by the main author after being trained and calibrated by a dentist working in radiology. Marginal bone level in radiographs was measured as the vertical distance from the cemento-enamel junction to the most apical part of the marginal bone.

Statistics

A software program SPSS 17.0 software (SPSS Inc., Chicago, IL) was used to perform all statistical analyses for MBL of molars and premolars concerning mesial and distal aspects. Independent variables were considered for the mean of mandibular and maxillary arches along with 95% confidence interval, whereas

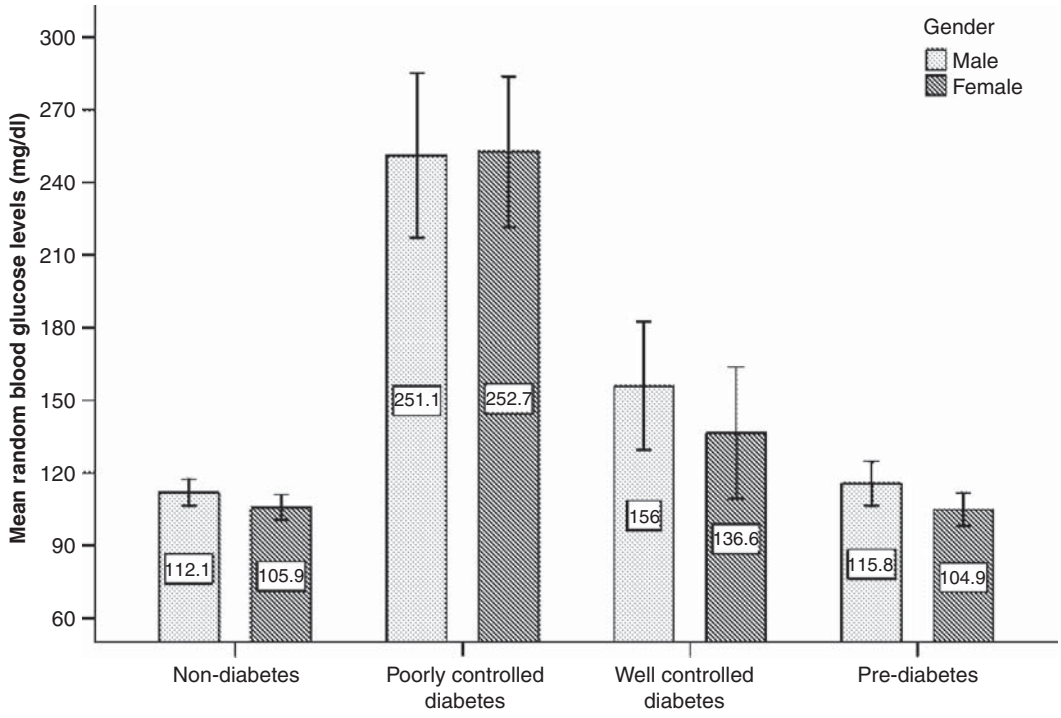

Figure 1. Mean values of random blood glucose levels in male and female subjects with non-diabetes, poorly controlled T2D, well controlled T2D and pre-diabetes. Error bars with SD ±2 and 95% confidence interval which give the graphical representation of the data variability among the groups (shown as vertical line in the graph).

dependent variables were considered for the mean of MBL in comparison to variables of pre-diabetes, well controlled T2D, poorly controlled T2D and non-diabetes. Age, gender, BMI, WC and PI, BOP, PD were analyzed by one-way analysis of variance (ANOVA). Bonferroni and post-hoc tests were performed for multiple comparisons.

Results

Interview questionnaire

Out of 213 subjects, 96 were females and 117 were males, where 92 individuals (43.2%) were medically diagnosed with T2D (47 females and 45 male). Sixty-eight out of 92 individuals reported diabetes in the questionnaire for the time period of 8 years as a mean value (range = 1–35 years). Mean age for debut of T2D was 50 years of age (range = 27–72 years).

HbA1c and RBGL

Out of 92 subjects, 64 individuals (30%) were diabetics having poorly controlled T2D (36 females and 28 males), whereas 28 individuals (13.1%) had diabetes which was well under control (11 females and 17 males). Out of the remaining 112 individuals, 76 subjects (35.7%) were non-diabetic subjects (42 males and 34 females) and 45 subjects (21.1%) were pre-diabetics (16 females and 29 male). Subjects with poorly controlled T2D had a mean value of HbA1c at 9.8% for males and at 9.7% for females (range = 7–13.8% for males and range 7–19.4% for females) and subjects with well controlled diabetes had a mean value of HbA1c at 6.5% (range = 6.5–6.9% for males and 5.3–6.9% for females).

Pre-diabetic subjects had a mean value of HbA1c at 5.9% (range = 5.7–6.4% for both males and females) and non-diabetic subjects had a mean value of HbA1c at 5.1% (range = 4.3–5.6% for males and 4.4–5.6% for females).

Subjects with poorly controlled T2D, according to HbA1c, had a mean of RBGL at 252 mg/dl (14.2 mmol/l) (range = 86–460 mg/dl [4.8–25.6 mmol/l]) and individuals with well controlled T2D had a mean value of RBGL at 148 mg/dl (8.2 mmol/l) (range = 84–268 mg/dl [4.7–14.9 mmol/l]). Non-diabetic subjects had a mean value of RBGL at 109 mg/dl (6.07 mmol/l) (range = 77–162 mg/dl [4.3–9 mmol/l]) and pre-diabetic subjects had a mean value of RBGL at 112 mg/dl (6.2 mmol/l) (range = 81–202 mg/dl [4.5–11.2 mmol/l]). Mean value of random blood glucose levels for males and females according to HbA1c are shown in Figure 1 with the following different groups, non-diabetic subjects, poorly controlled T2D, well controlled T2D and pre-diabetic subjects.

Age, BMI and WC

All 213 subjects had a mean value of BMI at 26 kg/m^2. Poorly controlled T2D was recorded with a mean

Table I. Age, WC and BMI in subjects with non-diabetes, poorly controlled T2D, well controlled T2D and pre-diabetes.

	Non-diabetes (n = 76)		Poorly controlled T2D (n = 64)		Well controlled T2D (n = 28)		Pre-diabetes (n = 45)	
	Males (42) Mean/Range	Females (34) Mean/Range	Males (28) Mean/Range	Females (36) Mean/Range	Males (17) Mean/Range	Females (11) Mean/Range	Males (29) Mean/Range	Females (16) Mean/Range
Age years	37/25–73	36/25–53	48/25–73	48/25–72	47/25–70	49/35–64	41/25–65	41/25–65
WC/cm	89/64–112	88/84–135	99/81–125	99/71–147	95/81–117	95/71–107	97/74–122	97/71–133
BMI	25/15–60	25/15–38*	28/14–32	28/14–47*	27/22–30	27/21–34	26/12–36	26/18–42

Differentiations between non-diabetics, poorly controlled T2D, well controlled T2D and pre-diabetes were tested with one-way ANOVA. For multiple comparisons, the Bonferroni *post-hoc* test was performed.
* $p < 0.005$.

value of BMI at 28 kg/m^2 (range = 14–47 kg/m^2) and well controlled T2D with a mean at 27 kg/m^2 (range = 21–38 kg/m^2). BMI for non-diabetic individuals had a mean value at 25 kg/m^2 (range = 15–60 kg/m^2) and pre-diabetic subjects had a mean value at 26 kg/m^2 (range = 12–42 kg/m^2). Data for both males and females are shown in Table I.

Waist circumferences of poorly controlled T2D were found to be between 71–147 cm (mean value = 98 cm) and for well controlled T2D between 71–127 cm (mean value = 88 cm). Non-diabetic subjects had a waist circumference between 64–134 cm (mean value = 97 cm) and pre-diabetics between 71–132 cm (mean value = 97 cm). In Table I data for females and males are shown. Individuals with poorly controlled T2D had a mean value of 48 years of age (range = 25–72 years) and subjects with well controlled diabetes had a mean value of 48 years of age (range = 25–70 years). Non-diabetic subjects had a mean age of 36 years (range = 25–73 years) and pre-diabetics had a mean age of 41 years (range = 25–65 years). Data for males and females are shown in Table I.

Education

Sixty-seven per cent of subjects having poorly controlled T2D and 64% of subjects with well controlled T2D were found not to be educated. Sixty-four per cent of individuals with no T2D and 58% of subjects with pre-diabetes were also without any education.

MBL

Marginal bone level and number of individuals with poorly controlled T2D (n = 51) were recorded for molars with a mean value at 3.9 mm (range = 1.3–11.2 mm), for premolars with a mean value at 3.8 mm (range = 1.5–10.7 mm), for well controlled T2D (n = 28), molars with a mean value at 3.5 mm (range = 1.8–5.3 mm) and for premolars with a mean value at 3.5 mm (range = 2.4–6.5 mm). Marginal bone level for non-diabetic subjects (n = 64) showed for molars a mean value at 3.1 mm (range = 1.5–5.9 mm) and for premolars with a mean value at 2.9 mm (range = 1.6–7 mm). Pre-diabetic subjects (n = 38) showed MBL in molars with a mean value at 2.9 mm (range = 1.3–10.1 mm) and in premolars with a mean value at 3.0 mm (range = 1.3–5.5 mm). Marginal bone level for molars and premolars for each individual group are shown in Table II.

BOP, PD, PI and number of teeth

Subjects with poorly controlled T2D had the highest number of periodontal pockets and the highest BOP level. The lowest level of BOP was for subjects with well controlled T2D. Levels of PI were highest in subjects with poorly controlled T2D and the lowest level was found in subjects with well controlled T2D. Results for BOP, PD and PI in subjects with non-diabetes, well and poorly controlled diabetes and pre-diabetes are shown in Table III. Both poorly controlled and well controlled T2D had mean values of 24 teeth present (range 8–28 for poorly controlled T2D, range 12–28 for well controlled T2D) and non-diabetic subjects had a mean of 26 teeth present (range = 6–28). Subjects with pre-diabetes had a mean value of 25 teeth (range = 8–28).

Smoking

Out of 213 subjects 27 were smokers, out of which 26% were poorly controlled T2D, with a mean of 20 years since they have been smoking ranging from 6–30 years and a mean of 60 cigarettes per day (range = 20–120 cigarettes). Well controlled T2D individuals were 19% with a mean of 18 years since they have been smoking, range = 6–30 years, mean of 60 cigarettes per day and range = 20–140 cigarettes. Those subjects being non-diabetics T2D were 37% with a mean of 10 years, range = 3–20 years and had a mean of 52 cigarettes per day, range = 20–100 cigarettes. Pre-diabetics were 19%, with a mean of 10 years since they have been smoking, range = 4–20 years and a mean of 60 cigarettes, range = 20–100 cigarettes.

Table II. MBL (mean ± SD) in maxillary and mandibular premolars and molars in subjects with non-diabetes, poorly controlled diabetes, well controlled diabetes and pre-diabetes.

	Non-diabetes (n = 64) (mean ± SD)	Poorly controlled T2D (n = 51) (mean ± SD)	Well controlled T2D (n = 28) (mean ± SD)	Pre-diabetes (n = 38) (mean ± SD)
Maxilla				
Molars (#27 and #26)	3.33 ± 2.25	4.36 ± 2.73	3.60 ± 1.58	3.02 ± 2.16
Premolars (#25 and #24)	4.14 ± 2.38	5.63 ± 2.39	3.53 ± 0.36	3.54 ± 1.26
Molars (#16 and #17)	3.96 ± 3.15	4.69 ± 3.32	3.39 ± 1.70	3.44 ± 1.49
Premolars (#14 and #15)	2.61 ± 0.88	4.74 ± 1.82	4.08 ± 1.53	—
Mandible				
Molars (#46 and #47)	2.51 ± 2.03★	4.23 ± 3.33★†	2.65 ± 1.63†	2.96 ± 2.57
Premolars (#44 and #45)	3.41 ± 2.71	3.46 ± 1.78	2.99 ± 1.32	3.34 ± 1.49
Molars (#36 and #37)	2.70 ± 2.15	3.60 ± 2.69	2.72 ± 1.25	2.84 ± 1.94
Premolars (#34 and #35)	3.40 ± 1.95	4.19 ± 2.06†	2.62 ± 1.10	2.84 ± 1.94†

Differentiation in MBL between groups with non-diabetes, pre-diabetes and subjects with T2D were tested using one-way ANOVA. Differentiation in MBL between subjects with poorly controlled and well controlled T2D were tested using one-way ANOVA. For multiple comparisons, the Bonferroni adjustment post-hoc test was performed.
★ $p < 0.001$ compared poorly subjects to non-diabetes and well controlled T2D.
† $p < 0.05$ compared poorly subjects to pre-diabetes.

Discussion

Diabetes is a worldwide health problem and may increase the severity of periodontal disease. In the current study the subjects were asked to report the presence of medically diagnosed T2D and for the accuracy the diagnosis of diabetes was confirmed with HbA1c analyses from venous blood. In addition, we also analyzed blood sugar levels with RBGL measurement.

We found for the groups that RBGL values are in accordance with the diabetic condition for the subjects according to HbA1c determinations, and we detected that every fifth of the subjects who were non-diabetic had HbA1c level in the range for pre-diabetes. Of the two different methods, RBGL and HbA1c, only the HbA1c method was able to diagnose pre-diabetes.

An earlier study has also reported high prevalence of pre-diabetes, with 3.5% (7.4 million) of the population in the US [15]. Up to 50% of subjects with pre-diabetes may develop diabetes within 5 years and the increased serum glucose levels in addition with overweight assumes that the group of pre-diabetic subjects are a huge group of individuals both in the US and in Asia, which in the near future may develop diabetes and severe periodontal inflammatory conditions [10,15]. Prevalence of diabetes has been reported to be ~ 10% in both the US and in Pakistan [15,16]. It has been reported that the diabetes will increase dramatically with, in the US from year 2000, 17.7 million people to an estimated 30.3 million in 2030, and in Pakistan from 5.2 million people to 13.9 million during the same period [17].

In this study, 38.5% of the subjects had HbA1c values in the range for subjects with T2D. The high prevalence of subjects with elevated blood sugar levels is assigned to low education or may be of genetic origin [18,19]. Around two thirds of the subjects coming for dental treatment were pre-diabetics or diabetics according to HbA1c levels, consequently only one third of the subjects were without any diabetic condition. In addition, the unawareness of the pre-diabetic condition may worsen the periodontal

Table III. PI, BOP and PD (mean ± SD) in subjects with non-diabetes, poorly controlled T2D, well controlled T2D and pre-diabetes.

	Non-diabetes (n = 76)	Poorly controlled T2D (n = 64)	Well controlled T2D (n = 28)	Pre-diabetes (n = 45)
Pl (%)	76.1 ± 30.65	80.5 ± 24.86	65.7 ± 28.38	77.8 ± 28.65
BOP (%)	64.4 ± 30.65	65.7 ± 24.86	51.5 ± 28.38	53.2 ± 28.65
PD (4 < 6 mm)	11.9 ± 17.48	19.3 ± 21.1	13.1 ± 14.64	11.2 ± 16.1
PD (≥ 6 mm)	4.3 ± 9.87★	14 ± 23.82★§	6.4 ± 14.42	4.5 ± 11.55§

One-way ANOVA were used to test the differences between pre-diabetes, poorly controlled T2D, well controlled T2D and non-diabetes. Bonferroni adjustment post-hoc test was applied for multiple comparisons.
★ $p < 0.05$.
§ $p < 0.05$.

situation in the future when subjects may develop T2D.

It is well known that diabetes is connected to overweight and obesity [20]. In the US, 34.2% of the adult population is overweight and 33.8% of the population is obese and in Pakistan the figures are reported to be 25% for overweight individuals and 10.3% for obese subjects [20,21]. In our study, we found overweight in all three groups with diabetic conditions and also for the non-diabetes subjects. Furthermore, pre-diabetic, poorly and well controlled females showed increased mean levels of WC, whereas males in all groups showed mean levels under threshold. The reason for this gender difference is not investigated in this study, however it might be by genetic origin and/or lifestyle [22]. Another aspect of the risk to develop severe periodontal conditions is, along with obesity, due to that non-diabetic individuals being obese, also having periodontal disease is mostly caused by increase in oxidative stress and inflammatory factors [23]. In this study it was a high frequency of pre-diabetic subjects with BMI over 25 kg/m^2 and the overweight or obese have to be considered as a risk factor in itself for severe periodontal conditions and an additional risk factor will be T2D and particularly when the diabetes is uncontrolled [24,25].

It is well known that uneducated subjects are more often overweight or obese [26]. Our study consists of subjects with low education and it is therefore not surprising that individuals in all groups showed high BMI values.

Individuals with poorly controlled T2D had more marginal bone loss compared to subjects with pre-diabetes conditions and non-diabetics. We used extra oral panorama radiographs for measuring marginal bone levels, as has been performed by other researchers [27,28]. Subjects with poorly controlled diabetes have also increased numbers of PD ≥ 6 mm compared to subjects with non-diabetes, as has been shown earlier [28]. The parallelism with severe periodontal disease and poorly controlled T2D in overweight subjects with an increased value of WC supports a relationship between these two chronic diseases.

In conclusion, pre-diabetic subjects had the same periodontal conditions as non-diabetic subjects. Subjects with poorly controlled T2D showed increased MBL and more periodontal pockets with PD ≥ 6 mm as compared to non-diabetic subjects. Individuals with pre-diabetic conditions were overweight and pre-diabetic females had WC over the threshold. The same conditions, overweight and increased WC for females, were for subjects with poorly and well controlled T2D as well as non-diabetics.

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Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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