

2018-05-15

# Radiographic bone loss in a Scottish non-smoking Type 1 Diabetes mellitus population; a Bitewing Radiographic Study.

Plessas, Anastasios

<http://hdl.handle.net/10026.1/11562>

---

10.1002/JPER.16-0788

Journal of Periodontology

American Academy of Periodontology

---

*All content in PEARL is protected by copyright law. Author manuscripts are made available in accordance with publisher policies. Please cite only the published version using the details provided on the item record or document. In the absence of an open licence (e.g. Creative Commons), permissions for further reuse of content should be sought from the publisher or author.*

**Title Page**

Radiographic bone loss in a Scottish non-smoking Type 1 Diabetes mellitus population; a Bitewing Radiographic Study

Anastasios Plessas, MSc,<sup>\*</sup> Douglas P Robertson PhD<sup>†</sup>, Penny J Hodge PhD<sup>†</sup>

Disclaimer: There are no conflicts of interest.

Corresponding author: A. Plessas, C507, Portland Square, Peninsula School of Dentistry, Plymouth University, Plymouth, PL4 8AA, 01752 586841

anastasios.plessas@plymouth.ac.uk

Word Count: 4,012

Figures: 1. Boxplot of average bone loss

Tables: 1. Demographic data, 2. Oral health data, 3. Bone loss data

---

<sup>\*</sup> Peninsula School of Dentistry, Peninsula Schools of Medicine and Dentistry, Plymouth University, Plymouth, UK

<sup>†</sup> Oral Science Research Group, Glasgow Dental School, School of Medicine, Dentistry and Nursing, College of Medical, Veterinary and Life Sciences, University of Glasgow, Glasgow, UK

This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the [Version of Record](#). Please cite this article as [doi: 10.1002/JPER.16-0788](https://doi.org/10.1002/JPER.16-0788).

This article is protected by copyright. All rights reserved.

Short Running title: Radiographic Bone Loss in Type 1 Diabetes Adults

One Sentence Summary: Patients with type 1 diabetes mellitus have been shown to exhibit greater average periodontal bone loss than their non-diabetes peers ( $P < 0.001$ ).

### **Abstract**

**BACKGROUND:** The dental complications of uncontrolled diabetes include reduced salivary flow rate, candidiasis and periodontal manifestations. A recent meta-analysis concluded that diabetes patients have a significantly higher severity, but not extent, of destructive periodontal disease than non-diabetes people. The authors reported that most type-1 diabetes studies using dental radiographic data have not controlled for confounding factors such as smoking. The aim of this cross-sectional study was to compare radiographic alveolar bone loss between type 1 diabetes (T1DM) and non-diabetes (NDM) participants in a Scottish non-smoking population.

**METHODS:** Digital bitewing radiographs for 174 Scottish adult never or ex-smoker (>5 years) participants (108 T1DM, 66 NDS), recruited from outpatient clinics throughout Greater Glasgow and Clyde, were included in the analysis. A single blinded, trained and calibrated examiner recorded the radiographic bone loss seen on bitewing radiographs using the digital screen caliper<sup>‡</sup>. The bone loss was measured as the distance between the cemento-enamel junction (CEJ) and the deepest radiographic alveolar bone margin interproximally of each tooth.

---

<sup>‡</sup> Screen Calliper ICONICO version 4.0 (Copyright (C) 2001-6 Iconico), New York, USA

RESULTS: T1DM participants had more radiographic alveolar bone loss throughout the all teeth measured (median:1.27mm vs 1.06mm,  $P<0.001$ ) and more than a two fold increase in the risk of having sites with  $\geq 2$ mm periodontal destruction (OR=2.297, 95%CI 1.058-4.986,  $P=0.036$ ) compared with non-diabetes subjects.

CONCLUSIONS: Patients suffering from type 1 diabetes are at higher risk of periodontitis even when controlling for multiple possible confounding factors and this difference can be detected on routine dental radiographs at an early stage. These data confirm radiographically the previously reported association between T1DM and periodontal bone loss.

Key Words: Diabetes Mellitus, Type 1; Alveolar Bone Loss; Radiography, Bitewing

### **INTRODUCTION:**

Diabetes mellitus is associated with a number of oral complications including gingivitis and periodontitis.<sup>1</sup> In a meta-analysis comparing the periodontal status between diabetes and non-diabetes individuals, the authors concluded that patients suffering from type 1 diabetes have a significantly higher severity but not extent of destructive periodontal disease than non-diabetes people.<sup>2</sup> A recent systematic review also cast doubt on the level of evidence supporting the assumption that Type 1 diabetes is a risk factor for periodontitis.<sup>3</sup> The authors cited the inappropriate design of the studies for type 1 diabetes by including type 1 and 2 diabetes and failing to exclude smokers and adjust for other confounding factors.<sup>3</sup>

Human studies, examining clinical parameters along with panoramic radiographs, have shown a correlation between diabetes status and bone loss with those suffering from uncontrolled diabetes being worst affected.<sup>4-7</sup>

The present authors have published data from a well-controlled study using measures of clinical probing depth and clinical attachment loss to confirm that T1DM is associated with periodontitis.<sup>8</sup> There is, however, a paucity of data using radiographs to study alveolar bone loss in T1DM patients. Bitewing radiographs have been suggested as a reliable tool for assessing alveolar bone loss in periodontal epidemiological studies.<sup>9</sup> It has been shown that distortion in bitewing radiographs is minimal and that there is no significant difference between standardized and non-standardised bitewing radiographs.<sup>9</sup> However, since the most recent systematic review<sup>3</sup> was published in 2009 by Chavarry et al., no studies have been published comparing the radiographic bone loss between T1DM adult patients and healthy controls. The aim of this cross-sectional study is to compare the degree of marginal alveolar bone loss in a Scottish non-smoking population of adult participants with Type 1 diabetes mellitus (T1DM) and age-matched non-diabetes controls, addressing the shortfalls of previous studies.

## **MATERIALS AND METHODS**

### **Participants**

The radiographs available for analysis were retrieved by one of the authors (DR) as part of an earlier clinical study, approved by the Glasgow Royal Infirmary Local Research Ethics Committee (Ref: 05/S0705/70). The study was conducted in

accordance with the Helsinki Declaration of 1975, as revised, in 2013. The methodology, recruitment process, inclusion and exclusion criteria have been published elsewhere.<sup>8</sup> Briefly, the T1DM participants, aged 20–55 years, were recruited from outpatient clinics at five hospitals in Glasgow, UK. The control group participants were recruited from physiotherapy clinics, using the buddy system and through an advertisement in a free newspaper.<sup>8</sup> The buddy system involves each diabetes participant asking a friend of the same gender and similar age to consent to joining the study as a healthy control.<sup>8</sup> All participants provided informed written consent before they were enrolled in the study. The general dental practitioners (GDP) of participants registered with a dentist, were contacted requesting the latest radiographs. The radiographs sent by the GDP, unless digital, were digitized using the Microtek ScanMAKER 9800XL TMA 1600 scanner (1600 dpi by 3200 dpi optical resolution and 16-bit grayscale). For participants not registered with a GDP, or those who reported they did not have any radiographs taken within the past year, a pair of digital bitewing radiographs was taken by DR using the DenOpix System (Gendex). Radiographic images for a hundred and eighty-four (184) participants of those enrolled in the earlier clinical study were available. Participants with a bilateral pair of bitewing radiographs of excellent or acceptable diagnostic quality were deemed eligible for the present radiographic study. The exclusion criteria included a) participants who had only periapical or unilateral bitewing images available and b) participants whose bitewing radiographs were of poor non-diagnostic quality.

The eligibility of each participant was assessed based on the type and diagnostic quality of the available radiographic images by consensus between AP and DR. Any

disagreement was resolved with discussion. Participants with a) only periapical radiographs (3 participants), b) unilateral bitewing radiographs (3 participants) and c) bitewings of poor quality which were not diagnostic (3 participants) were excluded from the study. A participant who had crowns on all the posterior teeth was also excluded. A total of 174 participants therefore were included in the radiographic study. From those, 108 were type 1 diabetes patients (T1DM) and 66 were healthy controls (NDM). The principal investigator (AP) was blind to the diabetic status of the patients.

### **Training and Calibration**

A single blinded trained examiner (AP) performed all the radiographic measurements. Training was provided by an experienced periodontal specialist researcher (DR). Training included a consensus session where the radiographic position of the cemento-enamel junction (CEJ) and bone crest was discussed. As measurements were carried out using a screen caliper software<sup>§</sup>, the training session also included training on the use of the caliper and its logger. The caliper was calibrated to measure mm of radiographic bone loss in a size 2 intraoral standard adult dental radiograph film (31x41mm). Following the training session, AP and DR independently carried out bone loss measurements on 30 pairs of bitewings, using the screen calliper. Reproducibility was assessed by calculating the intraclass correlation coefficient (ICC). A high intraclass correlation coefficient (inter-examiner agreement) of 0.858 ([0.782-0.908],  $P < 0.001$ ) confirmed that the principal investigator (AP) was adequately trained.

---

<sup>§</sup> Screen Calliper ICONICO version 4.0 (Copyright (C) 2001-6 Iconico), New York, USA

As there was to be only one examiner, intra-examiner reproducibility was the most important factor in training and calibration. Two calibration sessions took place to ensure that recordings were reproducible; one prior to the commencement of the study and one shortly after the radiographic measurements had started. The principal investigator AP repeated the measurements in the same bitewing radiographs as above, a week after the initial training. The intra-examiner reproducibility was judged as excellent {0.958 ([0.949-0.965],  $P < 0.001$ )} and allowed the commencement of the data collection. During the radiographic assessment, the measurements were repeated for every tenth patient (10% of the dataset), ensuring that the principal investigator (AP) maintained the ability to offer reliable measurements {0.980 ([0.968-0.987],  $P < 0.001$ )}.

### **Radiographic Data**

The marginal bone loss was measured as the distance between the cemento-enamel junction and the bone crest shown radiographically for the mesial and distal surfaces of every visible tooth. Only premolar and molar sites were included. Third molars were excluded. Sites, in which the CEJ was not visible either because of image distortion and teeth overlapping or the presence of a restoration with margins extended to or over the CEJ, were excluded.

The median and interquartile range of bone loss for each pair of bitewing radiographs was calculated. Also, for each participant, the number of sites with bone loss greater than 2, 3 and 4mm were calculated. These cut-off points of bone loss were selected based on previous bitewing radiographic studies. A distance greater

than 2mm between cemento-enamel junction and alveolar bone crest has been designated as alveolar bone loss in a number of studies<sup>10-12</sup>, whilst other studies have used the cut-off point of 3mm to classify periodontal damage.<sup>13, 14</sup> The cut-off point of 4mm was used to investigate the association between severe periodontal destruction and diabetes status.

### **Diabetes, Smoking and demographic data**

To ensure that the examiner remained blinded until after the completion of the radiographic measurements, data describing diabetes status, age, gender, social class, oral health behavior, smoking history and body mass index were withheld until after the measurements had been carried out.

Area based social deprivation was assessed by using the Scottish Index of Multiple Deprivation (SIMD) which is the Scottish Government's official tool for quantifying the level of deprivation in a given area.<sup>15</sup> The SIMD is based on small areas known as datazones. The Index provides a relative ranking for each datazone, from 1 (most deprived) to 5 (least deprived). The seven domains in SIMD used to measure the multiple aspects of deprivation are employment, income, health, education, skills, training, geographic access to services, crime and housing.<sup>15</sup>

This study was designed to account for the common confounding factor of smoking and so subjects had to either be never smokers or stopped for more than five years. Pack years were calculated for those who had smoked in the past and are a measure of past smoking experience over a period of time. Pack years are calculated by multiplying the number of packs of cigarettes smoked per day by the

number of years the person has smoked and dividing the total by 20. Never smokers were defined as those individuals who had a pack year score of less than 0.25 during their lifetime. Data of patients' registration with a dentist, frequency of dental attendance, oral hygiene habits (tooth brushing frequency, use of adjunctive interdental cleaning aids) and dental anxiety were available.

The glycaemic control for the T1DM participants had been calculated using the average of all available HbA1c measurements over the previous 2 years and the cut-off point used was 7.5%. Since June 2011, the method of reporting of HbA1c values has switched from a percentage to a measurement in mmols/mol. The equivalent of the DCCT (Diabetes Control and Complications Trial) HbA1c targets of 6.5% and 7.5% are 47.5 and 58.5 respectively in the new IFCC HbA1c units (International Federation of Clinical Chemistry and Laboratory Medicine).<sup>16</sup> The non-diabetes reference range of 4.0% to 6.0% is equivalent to 20 mmol/mol to 42 mmol/mol.<sup>17</sup> The available DCCT HbA1c measurements were converted to the equivalent IFCC HbA1c measurements by using the diabetes.co.uk HbA1c Units Converter.<sup>18</sup>

All data were handled confidentially and were stored on a password protected computer.

### **Statistical analysis**

Statistical analysis was undertaken using the IBM® SPSS® v21 statistical package. Demographic and other characteristics of the study sample were described using the five number summary (median, inter-quartile range, and range) for skewed data and

means (95% confidence intervals) for symmetrically distributed data. Categorical variables were expressed as percentages. The  $\chi^2$  or Fisher's exact test for small numbers was used to check for associations between categorical variables. Non-parametric Mann–Whitney U-test was applied to examine differences in continuous variables between the two groups.

Odds ratios were calculated using binary logistic regression and the difference in mean radiographic bone loss was tested using a general linear model. Both models were adjusted for age, gender, previous smoking, deprivation (SIMD), education and BMI.

## **RESULTS**

### ***Demographic characteristics for diabetes and non-diabetes participants***

Table (1) describes the demographic characteristics of the 2 groups: T1DM (n = 108) and NDM participants (n = 66). Demographic characteristics were analyzed for differences between the two groups. There were no significant differences in age, socioeconomic status (SIMD), alcohol consumption, smoking status and body mass index (BMI).

The BMI median of both groups was similar (T1DM 26.88 vs. NDM 25.43) demonstrating that the majority of the participants were classified as overweight. More specifically, 66.7% (n=72) of the T1DM participants and 57.6% (n=38) of the NDM participants were overweight with BMI  $\geq 25$ , and almost one-third of each group was obese with BMI  $\geq 30$  (32.4% (n=35) T1DM vs. 25.8% (n=17) NDM). None of these differences reached statistical significance. There was, however, a significant

difference in gender ( $P = 0.04$ ). In the NDM group there were significantly fewer males than females (21 vs. 45); in the diabetes group, the proportion of males to females was more or less equal (52 vs. 56).

### **Oral health behaviors of diabetes and non-diabetes participants**

Table (2) describes the oral health behaviors of the study participants. The majority of the participants were registered with a dentist (T1DM: 85.2% and NDM: 74.2%) and were regular attenders (T1DM: 67.6% and NDM: 63.6%). 61.1% of T1DM participants and 71.2% of NDM participants were brushing twice a day and around half of them were flossing on a regular basis (47.2% and 47.0%). No statistical differences were found for dental registration, dental attendance, dental anxiety and oral hygiene habits apart from the use of interdental brushes. Overall, only a minority of the participants were performing daily interdental cleaning using interdental brushes. However, the number of NDM participants using interdental brushes was significantly higher (15.2% and 3.7%,  $P = 0.009$ ).

### **Diabetes status**

The vast majority of the T1DM participants were poorly controlled; 97 (89.8%) had a mean HbA1c measurement as high as 74.81 ( $\pm 11.71$ ) mmol/mol. Only 11 (10.2%) of the T1DM participants were well controlled with a mean HbA1c 52.84 ( $\pm 5.47$ ) mmol/mol. All the NDM participants were confirmed as being non-diabetes with an HbA1c of  $< 42$  mmol/mol.

### **Average bone loss**

The sample was not normally distributed. The data for the mean bone loss was positively skewed and therefore a non-parametric test was used for the statistical analysis (Mann-Whitney U-test). The level of significance was set at  $P=0.05$ . The median value of the mean bone loss for T1DM patients was statistically significantly higher (1.23mm, (IQR:0.96,1.5) [95% CI:0.56-2.69]) than for NDM participants (1.01mm (IQR:0.8,1.27), [95% CI:0.5-2.2]) ( $P =0.001$ ). The median of the average bone loss difference between the two groups is depicted in the box plot in Fig (2). After adjusting for age, gender, previous smoking, deprivation, education and BMI, the difference remained statistically significant (mean: 1.323mm vs 1.109mm,  $p<0.001$ ).

### **Number of sites with bone loss**

The difference in the extent of bone loss between the two groups was investigated. Table 3 demonstrates the differences in the prevalence of bone loss between T1DM and NDM participants for different cut-off points of bone loss ( $\geq 2$ mm,  $\geq 3$ mm and  $\geq 4$ mm). For every cut-off point T1DM participants had consistently more sites with bone loss.  $\geq 2$ mm T1DM 65.70% vs NDM 53.0%,  $\geq 3$ mm, T1DM 29.6% vs NDM 22.7% and  $\geq 4$ mm T1DM 13.0% vs NDM 3.0%.

The unadjusted and adjusted odd ratio (OR) values and 95%CI for each cut-off point are reported in Table 3. Odds ratios were higher in T1DM compared with NDM in both adjusted (1.587-3.633) and unadjusted (1.432-4.766) models. Unadjusted

binary logistic regression identified that T1DM participants are almost 5 times more likely to exhibit severe bone loss ( $\geq 4$  mm) than their non-diabetes peers (OR=4.766, 95%CI: 1.047-21.688, P=0.043). In the fully adjusted regression analysis, accounting for age, gender, previous smoking, deprivation, education and BMI, T1DM was associated with periodontal bone loss ( $\geq 2$  mm) (OR=2.297, 95%CI: 1.058-4.986, P=0.036), but not statistically significantly with more severe bone loss.

## DISCUSSION

The aim of the present study was to compare the degree of bone loss shown in bitewing radiographs between T1DM and NDM participants in an adult population of white non-smoking Europeans from the same geographic area, thereby reducing any demographic, socio-economic and genetic variation.

According to Chavarry et al.<sup>3</sup> the main drawbacks in design of previously published studies looking at the relationship between T1DM and periodontal destruction include: small sample size, lack of training and calibration, unblinded examiners, a mixture of type 1 and type 2 diabetes patients, inclusion of solely or mostly paediatric and adolescent participants, inadequate consideration of confounding factors such as smoking and not confirming the glycaemic status of the control group.<sup>3</sup> The design of the original study<sup>8</sup> and method of the present radiographic study address most of the above limitations. Briefly, the study design focused purely on patients with type 1 diabetes and only included non-smokers; the age range was between 20 and 55 years; the demographic characteristics of the two groups were as closely matched as possible. The examiner (AP) received training before and soon after the

commencement of the radiographic study and two calibration exercises followed. The level of agreement was found to be high. The examiner remained blinded to the diabetes status of the participants during the radiographic assessment.

The smoking history of the participants was taken into consideration in this study. Our sample consisted of never smokers and smokers who had quit for at least five years. Smoking has a detrimental effect on the host-immune response, both cell-mediated and humoral, in the periodontium. It suppresses neutrophil function, chemokinesis, chemotaxis, and phagocytosis.<sup>19</sup> Moreover, lymphocyte, epithelial cell, fibroblast, and osteoclast function is impeded.<sup>19</sup> A plethora of studies has shown a clear association between smoking and periodontitis.<sup>20, 21</sup> Smoking is a well-established risk factor for periodontitis.<sup>20, 21</sup> It has been reported that smokers have an increased prevalence and severity of periodontal disease, as well as a higher prevalence of tooth loss and edentulism.<sup>21</sup> The effect of smoking has been shown to be dose dependent.<sup>22</sup> Smoking-attributable periodontitis has been found to be prevalent within the Australian (32%, equivalent to 700,000 adults: The National Survey of Adult Oral Health)<sup>23</sup> and American populations (41.9%, equivalent to 6.4 million cases for current smokers and 10.9%, equivalent to 1.7 million cases for former smokers; Third National Health and Nutrition Examination Survey)<sup>24</sup>. In this study, the vast majority of the participants had never smoked (88.5%). Only ten participants of each group were former smokers. Therefore, the impact of former smoking in the interpretation of the results of the present study was deemed to be insignificant.

A longitudinal study by Machtei et al.<sup>25</sup> aiming to evaluate the correlation between changes in clinical attachment level (CAL) and radiographic alveolar bone loss concluded that although changes in CAL and crestal bone height seem to progress somewhat independently over a short period, these differences seem to level off in the long term. Thus, in cross-sectional and long-term prospective studies either variable may be used alone.<sup>25</sup> In addition, Merchant et al. compared the diagnostic accuracy in assessing bone loss between standardized and non-standardised bitewing radiographs and concluded that measurements retrieved by non-standardised bitewing radiographs are reasonably accurate and valid.<sup>9</sup> For these reasons in the present study, only data retrieved from non-standardised radiographs were used and analyzed. No clinical data, although available and already published elsewhere<sup>8</sup>, were taken into consideration.

This study demonstrated that Type 1 diabetes mellitus results in an increase in the prevalence, extent and severity of periodontal destruction. T1DM patients exhibited greater average bone loss than their non-diabetes peers and a more than twofold increase in the risk in having sites with bone loss. T1DM and periodontitis share a number of common risk factors and so binary logistic regression and a general liner model were used in order to adjust the analysis for confounding factors. The association between T1DM and periodontal bone loss remained significant in the number of sites greater than or equal to 2mm even after adjusting for possible confounders. The findings of the current radiographic study are consistent with the clinical probing depths and attachment loss reported in an earlier cross-sectional

study in the same population where mean clinical attachment loss (CAL) was found to be higher in the T1DM than the control group ( $P \leq 0.001$ )<sup>8</sup>.

Interestingly, a significant association was observed between T1DM and prevalence of bone loss  $\geq 2$  mm. No statistically significant association, however, was found when using other thresholds of bone loss after accounting for confounders although there was a trend in this direction. This may be due to the fact that more T1DM patients exhibited more generalised mild periodontitis but not an increase in the prevalence of more severe disease. It is more likely that with the low number of patients with more severe disease and the high prevalence of periodontal disease in the control group as described in the clinical paper<sup>8</sup> this study was inadequately powered to detect a statistical difference between the groups.

In contrast to the present study, Barnett et al. and De Pommereau et al. found no signs of radiographic bone loss in bitewing radiographs of patients with type 1 diabetes.<sup>10, 26</sup> However, the participants of those studies did not exceed 18 years of age. Similarly, in a study by Rylander et al. the young participants aged 18-26 years old demonstrated similar marginal bone levels in the diabetes and control groups, and only an equal minority of the two groups exhibited bone loss greater than 2mm.<sup>12</sup> Seppala et al. in a longitudinal study examining orthopantomographs of adult T1DM participants aged 35-56 years of age found that those with long term poorly controlled diabetes lost more proximal bone than their well-controlled peers.<sup>27</sup> Ternoven et al. likewise found that patients with complicated diabetes demonstrated more marginal bone loss, whereas well-controlled patients seem to be no more susceptible than non-diabetes controls of the same age.<sup>28</sup> Both later studies<sup>27, 28</sup>

included a very small number of participants, making the extrapolation of the results difficult. The results of the present study are in agreement with those published by Thorstensson et al. using bitewing and periapical radiographs<sup>29</sup> and Seppala et al. using panoramic radiographs<sup>27</sup>, which demonstrated that patients with diabetes exhibit significantly more proximal alveolar bone loss.

The use of interdental aids was not common among our participants. Less than half of the participants in each group used floss on a regular basis (47.2% T1DM, 47% NDM,  $p=1.00$ ) and only a small proportion of participants used toothpicks (10.6% T1DM, 11.1% NDM  $p=1$ ) and interdental brushes (T1DM 4%, NDM 10%,  $p=0.009$ ). The poor compliance with recommended preventative measures would fit with the high level of mild to moderate periodontal bone loss; the lower level of usage of interdental brushes in T1DM patients may represent reduced access to dental care or a reluctance to comply. Although the difference between the two groups for using interdental brushes was found to be highly significant, it is questionable whether this would affect the primary outcomes of the study (mean bone loss and prevalence of severe bone loss) due to the small numbers of subjects in both groups adhering to this habit (T1DM 4% and NDM 10%).

A limitation of the present study is that only partial mouth measurements were used (posterior teeth), resulting in possible underestimation of the marginal bone loss<sup>30</sup>. This study used a single blinded trained and calibrated examiner where we could have used multiple examiners to double count. Resources meant that this approach was not followed but thorough training and calibration and analysis of inter and intra-examiner reproducibility ensured confidence in the data. This study was not able to

draw conclusions about the effect of glycaemic control as there was only a very small number of well-controlled diabetes patients (n=11) in this sample population. No comparison between the well and poorly-controlled diabetes patients was therefore attempted. Finally, due to the cross-sectional nature of the study design, no causality can be inferred.

The present study, has attempted to address the shortfalls of previous studies as identified by Chavarry et al.<sup>3</sup>. The sample under investigation consisted of adult never or former smokers. Current smokers were excluded from this study, at the recruitment stage.<sup>8</sup> In addition, the potential confounding effects by other factors, such as age, gender and obesity were thoroughly evaluated and accounted for, in the statistical analysis. Therefore, this study showed that patients who are confirmed to have Type 1 diabetes exhibit greater extent and severity of periodontal destruction than their non-diabetes peers even in absence of smoking and after controlling for known confounders. Many previous studies have been affected by poor study design as described by Chavarry et al but this study adds to the compiling evidence of an association between Type 1 diabetes mellitus and periodontal disease.

Early diagnosis of bone loss and destructive periodontal disease is of paramount importance. Late diagnosis can lead to more extensive and complicated treatment and jeopardize the survival of the dentition where in some cases multiple extractions may be required. This has major implications for the patient's quality of life. Bitewings used for routine dental examination have the potential to augment clinical examination in the diagnosis of early marginal bone loss.

Patients living with diabetes should be made aware of the above link and the bidirectional relationship between diabetes and periodontitis. Patient's education of their role in maintaining effective daily plaque removal in the prevention of periodontitis is key to the successful management and maintenance of periodontal health. This becomes even more significant when risk factors (such as diabetes) coexist. Therefore, medical, nursing and dental practitioners should be aware of and educate patients about this link. General dental practitioners should monitor carefully the periodontal health of Type 1 diabetes patients as they appear to be at higher risk of periodontal destruction.

### **CONCLUSIONS**

Within the limitations of the present study, the following conclusions can be drawn: Adult non-smoking T1DM patients presented with greater radiographic bone loss than their NDM peers ( $P < 0.001$ ). This study supports the findings of previous studies that T1DM patients experience more severe periodontal destruction regardless of smoking history and this is measurable on routine bite wing radiographs.

### **ACKNOWLEDGMENTS AND CONFLICTS OF INTEREST**

We acknowledge Jenny Young, dental research nurse at the University of Glasgow for project administration and for assisting DR during the clinical study, and Sheena Mitchell, research nurse, for recruitment of the participants. We acknowledge Professor Philip Preshaw of the University of Newcastle for training and calibrating

DR. We thank the consultants, staff and patients of the following hospitals who kindly took part in the study: Glasgow Royal Infirmary, Stobhill Hospital, Southern General Hospital, Victoria Infirmary, and Royal Alexandra Hospital, Paisley. We acknowledge the Chief Scientists Office of Scotland for providing the necessary funding. Finally, we would like to thank Dr Andrea Sherriff (Senior Lecturer in Statistics at the University of Glasgow) for her valuable advice on the statistical analysis. The corresponding author (AP) is an NIHR (National Institute for Health Research, UK) funded Academic Clinical Fellow.

Conflict of Interest: None to be declared.

## REFERENCES

1. Glavind L, Lund B, Loe H. The relationship between periodontal state and diabetes duration, insulin dosage and retinal changes. *J Periodontol* 1968;39:341-347.
2. Khader YS, Dauod AS, El-Qaderi SS, Alkafajei A, Batayha WQ. Periodontal status of diabetics compared with nondiabetics: a meta-analysis. *J Diabetes Complications* 2006;20:59-68.
3. Chavarry NG, Vettore MV, Sansone C, Sheiham A. The relationship between diabetes mellitus and destructive periodontal disease: a meta-analysis. *Oral Health Prev Dent* 2009;7:107-127.
4. Al-Zahrani MS, Kayal RA. Alveolar bone loss and reported medical status among a sample of patients at a Saudi dental school. *Oral Health Prev Dent* 2006;4:113-118.
5. Taylor GW, Burt BA, Becker MP, Genco RJ, Shlossman M. Glycemic control and alveolar bone loss progression in type 2 diabetes. *Ann Periodontol* 1998;3:30-39.
6. Taylor GW, Burt BA, Becker MP, et al. Non-insulin dependent diabetes mellitus and alveolar bone loss progression over 2 years. *J Periodontol* 1998;69:76-83.
7. Emrich LJ, Shlossman M, Genco RJ. Periodontal-disease in non-insulin-dependent diabetes-mellitus. *J Periodontol* 1991;62:123-131.
8. Hodge PJ, Robertson D, Paterson K, Smith GL, Creanor S, Sherriff A. Periodontitis in non-smoking type 1 diabetic adults: a cross-sectional study. *J Clin Periodontol* 2012;39:20-29.
9. Merchant AT, Pitiphat W, Parker J, Joshipura K, Kellerman M, Douglass CW. Can nonstandardized bitewing radiographs be used to assess the presence of alveolar bone loss in epidemiologic studies? *Community Dent Oral Epidemiol* 2004;32:271-276.
10. Depommereau V, Dargentpare C, Robert JJ, Brion M. Periodontal status in insulin-dependent diabetic adolescents. *J Clin Periodontol* 1992;19:628-632.

11. Kallestal C, Matsson L. Criteria for assessment of interproximal bone loss on bite-wiring radiographs in adolescents. *J Clin Periodontol* 1989;16:300-304.
12. Rylander H, Ramberg P, Blohme G, Lindhe J. Prevalence of periodontal disease in young diabetics. *J Clin Periodontol* 1987;14:38-43.
13. Lalla E, Cheng B, Lal S, et al. Diabetes-related parameters and periodontal conditions in children. *J Periodontal Res* 2007;42:345-349.
14. Merchant AT, Jethwani M, Choi Y-H, Morrato EH, Liese AD, Mayer-Davis E. Associations between periodontal disease and selected risk factors of early complications among youth with type 1 and type 2 diabetes: a pilot study. *Pediatr Diabetes* 2011;12:529-535.
15. The Scottish Government. Scottish index of multiple deprivation 2012. A National Statistics Publication for Scotland Available at: [http://22fa0f74501b902c9f11-8b3fbddfa1e1fab453a8e75cb14f3396.r26.cf3.rackcdn.com/simd\\_448749\\_v7\\_201212\\_17.pdf](http://22fa0f74501b902c9f11-8b3fbddfa1e1fab453a8e75cb14f3396.r26.cf3.rackcdn.com/simd_448749_v7_201212_17.pdf). Accessed: 08.10.16.
16. Marshall SM. Standardization of HbA1c: good or bad? *Nat Rev Endocrinol* 2010;6:408-411.
17. Scottish Diabetes Group. HbA1c Standardization for Clinical Health Care Professionals. 2009. Available at: [http://www.diabetesinscotland.org.uk/publications/hba1c\\_hcp\\_leaflet\\_0509print.pdf](http://www.diabetesinscotland.org.uk/publications/hba1c_hcp_leaflet_0509print.pdf). Accessed: 08.10.16.
18. Diabetes.co.uk. HbA1c Units Converter - DCCT to IFCC. Available at: <http://www.diabetes.co.uk/hba1c-units-converter.html> Accessed: 17.10.2016.
19. Palmer RM, Wilson RF, Hasan AS, Scott DA. Mechanisms of action of environmental factors--tobacco smoking. *J Clin Periodontol* 2005;32 Suppl 6:180-195.
20. Genco RJ, Borgnakke WS. Risk factors for periodontal disease. *Periodontol 2000* 2013;62:59-94.
21. Johnson GK, Guthmiller JM. The impact of cigarette smoking on periodontal disease and treatment. *Periodontol 2000* 2007;44:178-194.
22. Stabholz A, Soskolne WA, Shapira L. Genetic and environmental risk factors for chronic periodontitis and aggressive periodontitis. *Periodontol 2000* 2010;53:138-153.
23. Do LG, Slade GD, Roberts-Thomson KF, Sanders AE. Smoking-attributable periodontal disease in the Australian adult population. *J Clin Periodontol* 2008;35:398-404.
24. Tomar SL, Asma S. Smoking-attributable periodontitis in the United States: findings from NHANES III. National Health and Nutrition Examination Survey. *J Periodontol* 2000;71:743-751.
25. Machtei EE, Hausmann E, Grossi SG, Dunford R, Genco RJ. The relationship between radiographic and clinical changes in the periodontium. *J Periodontal Res* 1997;32:661-666.
26. Barnett ML, Baker RL, Yancey JM, MacMillan DR, Kotoyan M. Absence of periodontitis in a population of insulin-dependent diabetes mellitus (IDDM) patients. *J Periodontol* 1984;55:402-405.
27. Seppala B, Seppala M, Ainamo J. A longitudinal study on insulin-dependent diabetes mellitus and periodontal disease. *J Clin Periodontol* 1993;20:161-165.
28. Tervonen T, Karjalainen K, Knuuttila M, Huuonen S. Alveolar bone loss in type 1 diabetic subjects. *J Clin Periodontol* 2000;27:567-571.
29. Thorstensson H, Hugoson A. Periodontal disease experience in adult long-duration insulin-dependent diabetics. *J Clin Periodontol* 1993;20:352-358.

30. Shroot MK, Hildebolt CF, Vannier MW, Province M, Vahey EP. Periodontal disease morbidity quantification. I. Optimal selection of teeth for periodontal bone loss surveys. *J Periodontol* 1990;61:618-622.

**Legends for figures and tables:**

Figure 1:

Boxplot showing median, 25th and 75th percentile values of mean bone loss between diabetes and non-diabetes participants. Testing for differences between the two groups was carried out using the Wilcoxon rank sum test. A highly statistically significant difference is denoted by \*\*.

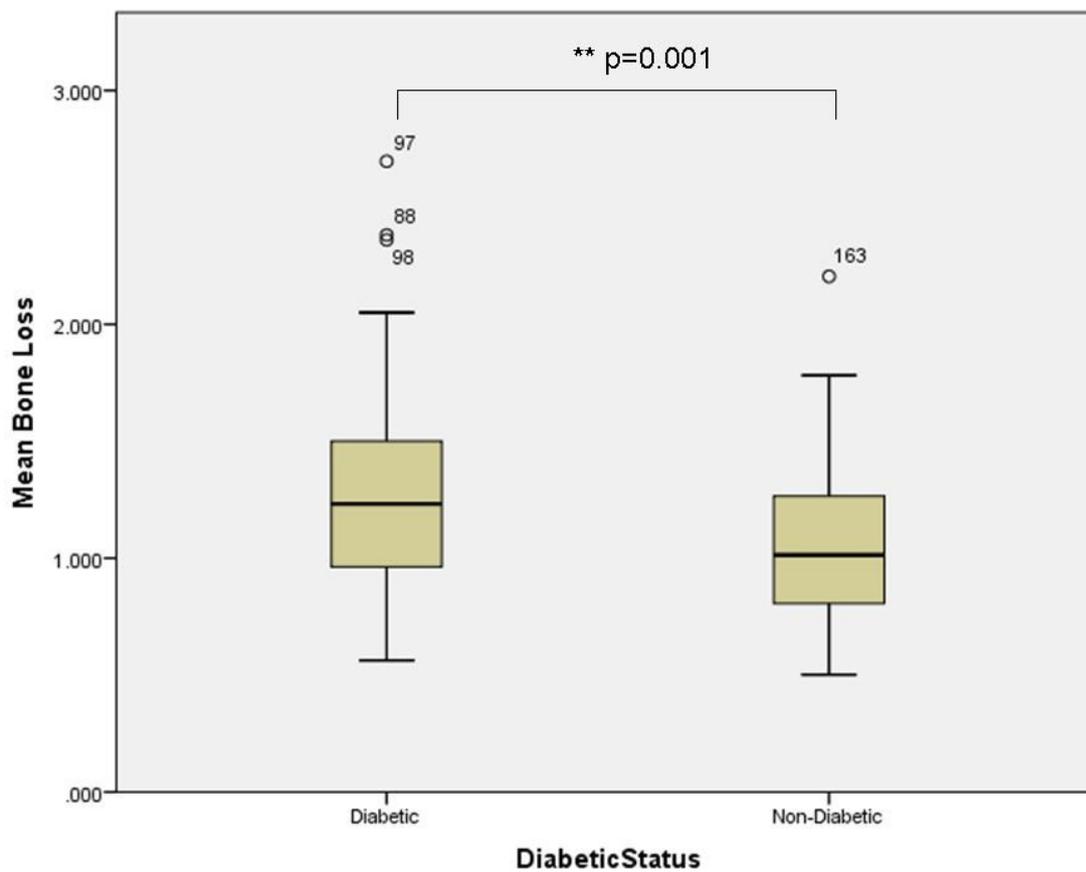


Table 1.

Demographic data for diabetes and non-diabetes participants

Data shown is the percentage of the group (n). Intergroup comparison was carried out using the Fisher's Exact Test †, Pearson Chi-Square ‡, or Mann-Whitney U Test §. Statistically significant differences between groups are in bold ( $P \leq 0.05$ ).

Table 2.

Oral health behaviours of diabetes and non-diabetes participants

Data shown is the percentage of the group (n). Intergroup comparison was carried out using the Fisher's Exact Test † or Pearson Chi-Square ‡. Statistically significant differences between groups are in bold ( $P \leq 0.05$ ).

Table 3.

Bone loss between diabetic and non-diabetic participants \*

Data shows percentage (n) of patients with bone loss  $\geq 2\text{mm}$ ,  $3\text{mm}$  and  $4\text{mm}$ .

Adjusted odds ratios were calculated using binary logistic regression with 95% confidence intervals.

† Unadjusted: Separate logistic regression analysis was performed.

‡ Adjusted for age, gender, previous smoking, deprivation (SIMD), education and BMI

\*Statistical Significant,  $P < 0.05$

Table 1: Demographic data for diabetes and non-diabetes participants

Data shown is the percentage of the group (n). Intergroup comparison was carried out using the *Fisher's Exact Test* †, *Pearson Chi-Square* ‡, or *Mann-Whitney U Test* §. Statistically significant differences between groups are in bold ( $P \leq 0.05$ )

	<i>Non-diabetes participants</i> <b>66 (37.9%)</b>	<i>N</i>	<i>Diabetes participants</i> <b>108 (62.1%)</b>	<i>N</i>	<i>P value</i>
<i>N</i> (%)					
Age median. (IQR), [range]	37.81 (28.47,44.62) [20-55]		36.68 (27.20, 42.05) [20-55]		0.369§
Gender % (n)		66		108	<b>0.04†</b>
Female	68.2 (45)		51.9 (56)		
Male	31.8 (21)		48.1 (52)		
Socio-economic SIMD % (n)		66		108	0.62‡
1	25.8 (17)		20.4 (22)		
2	6.1 (4)		10.2 (11)		
3	19.7 (13)		22.2 (24)		
4	24.2 (16)		18.5 (20)		
5	21.2 (14)		26.9 (29)		
Missing	3.0 (2)		1.9 (2)		
Lifestyle Variables					
Alcohol Consumption Units/week median, (IQR), [range]	5 (1.15, 10) [0-40]	66	4 (1,10) [0-40]	108	0.394§
Excessive alcohol consumption (male $\geq 21$ units, female $\geq 14$ )	13.6 (9)		11.1 (12)		0.638†
Smoking status % (n)		66		108	0.327†
Never Smoked	84.8 (56)		90.7 (98)		
Smoked in past	15.2 (10)		9.3 (10)		
Pack years for previous smokers median, (IQR), [range]	4 (1,7.5) [0-15]	10	2 (1,7.5)[0-14]	10	0.232§
Body Mass Index median, (IQR), [range]	25.43 (23.12-29.61) [19.07-49.17]		26.88 (24.3, 31.2), [19.13-36.57]		0.286§
Obese participants (BMI $\geq 30$ )	25.8 (17)		32.4 (35)		0.396†

Table 2: Oral health behaviors of diabetes and non-diabetes participants

Data shown is the percentage of the group (n). Intergroup comparison was carried out using the *Fisher's Exact Test* † or *Pearson Chi-Square* ‡. Statistically significant differences between groups are in bold ( $P \leq 0.05$ )

<i>Participants oral health behaviour characteristics</i>	<i>Non-diabetes participants</i>	<i>N</i>	<i>Diabetes participants</i>	<i>N</i>	<i>P value</i>
<i>N (%)</i>	<b>66 (37.9%)</b>		<b>108 (62.1%)</b>		
Registered with dentist % (n)	74.2 (49)		85.2 (92)		0.102†
Missing	1.5 (1)		0.9 (1)		
Attendance at dentist % (n)		66		108	0.104 ‡
At least once a year	63.6 (42)		67.6 (73)		
Occasionally	4.5 (3)		13.0 (14)		
Only when in pain	6.1 (4)		7.4 (8)		
Never	24.2 (16)		11.1 (12)		
Missing % (n)	1.5 (1)		0.9 (1)		
Oral hygiene habits % (n)		66		108	
Tooth brushing					0.93 ‡
Never or less than once a day	0 (0)		1.9 (2)		
Once a day	10.6 (7)		24.1 (26)		
Twice a day	71.2 (47)		61.1 (66)		
More than twice	16.7 (11)		12.0 (13)		
Missing % (n)	1.5 (1)		0.9 (1)		
Use of floss	47.0 (31)		47.2 (51)		1.00†
Missing % (n)	1.5 (1)		0.9 (1)		
Use of interdental brushes	15.2 (10)		3.7 (4)		<b>0.009†</b>
Missing % (n)	1.5 (1)		0.9 (1)		
Toothpick use	10.6 (7)		11.1 (12)		1.00†
Missing % (n)	1.5 (1)		0.9 (1)		
Dental anxiety	31.8 (21)		20.4 (22)		0.103†
Missing % (n)	1.5 (1)		0.9 (1)		

**Table 3: Logistic regression of association between type 1 diabetes and alveolar bone loss.**

Bone Loss	Diabetes participants (N=108)	Non-diabetes participants (N=66)	Unadjusted†			Adjusted‡		
	%(n)	% (n)	OR	95% CI	P-value	OR	95% CI	P-value
≥2mm	65.70% (n=71)	53.0% (n=35)	1.700	0.909 – 3.178	0.097	2.297	1.058 – 4.986	0.036*
≥3mm	29.6% (n=32)	22.7% (n=15)	1.432	0.705 – 2.908	0.321	1.587	0.685 – 3.679	0.282
≥4mm	13.0% (n=14)	3.0% (n=2)	4.766	1.047 – 21.688	0.043*	3.622	0.730 – 17.967	0.115

Bone loss between diabetes and non-diabetes participants \*

Data shows percentage (n) of patients with bone loss ≥ 2mm, 3mm and 4mm. Adjusted odds ratios were calculated using binary logistic regression with 95% confidence intervals.

† Unadjusted: Separate logistic regression analysis was performed.

‡ Adjusted for age, gender, previous smoking, deprivation (SIMD), education and BMI

\*Statistical Significant, P<0.05

This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the [Version of Record](#). Please cite this article as [doi: 10.1002/JPER.16-0788](https://doi.org/10.1002/JPER.16-0788).

This article is protected by copyright. All rights reserved.