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# Study of the Relationship between the Condition of Periodontal Tissues and Bone Mineral Density in People with Newly Diagnosed Type 2 Diabetes

## ABSTRACT

**Objective:** The aim of the study was to assess the relationship between the condition of periodontal tissues and reduced bone mineral density (BMD) in patients with newly diagnosed type 2 diabetes (T2D).

**Materials and methods:** A group of 108 patients with newly diagnosed T2D, up to 3 months after diagnosis, were included in the study. Smoking patients were excluded from the study. The patients underwent a periodontal examination, a blood test, and densitometry on the same day. The results were then subjected to statistical analysis by the PQStat v. 1.6.8. program using the Spearman test, as well as multivariate analysis by logistic regression. The threshold of significance was  $p < 0.05$ .

**Results:** A group of 103 patients with newly diagnosed T2D were qualified for the study, including 38 women (36.9%) and 65 men (63.1%). The mean age of the

patients was 56.5 years ( $SD = 13.0$  years). In the group of women, the relationship between bone density and clinical attachment loss (CAL) was statistically significant also after taking age into account. The correlation between CAL and femoral neck density was so strong that, when taking it into account, age did not show a statistically significant relationship. The density of the femoral neck showed a strong relationship with the number of missing teeth, completely dominating the importance of age.

**Conclusions:** It was shown that the degree of periodontal disease in the group of women with newly diagnosed T2D was affected by reduced BMD, regardless of age.

**Keywords:** periodontitis, bone mineral density, newly diagnosed type 2 diabetes

## Introduction

Due to bone loss in both periodontitis and osteoporosis, it was considered highly likely that systemic bone loss could contribute to periodontal tissue destruction. In a meta-analysis of studies on the relationship between periodontal disease and osteoporosis, it was shown that patients suffering from osteoporosis are significantly exposed to periodontitis (the risk of periodontitis increased by 70%), and this risk is higher in women [1]. The patho-

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Clinical Diabetology 2024

DOI: 10.5603/cd.99682

Received: 6.03.2024 Accepted: 3.10.2024

Early publication date: 18.11.2024

genesis of this relationship is believed to be a decrease in jaw bone density [2], which is the result of systemic, simultaneous bone resorption, due to inflammatory mediators (IL-1, TNF- $\alpha$ , RANKL), stimulating osteoclastogenesis, genetic conditions, and susceptibility to bone resorption associated with inflammation [3]. However, the exact pathomechanism has not been proven. The correlation between type 2 diabetes (T2D) and osteoporosis has been a subject of research for many years. People with T2D have increased risk of bone fractures compared to people without diabetes. This higher risk of fractures may occur with normal or even increased bone mineral density (BMD) because of poorer bone quality in patients with T2D [4, 5]. The pathophysiological mechanisms underlying increased risk of osteoporotic fractures in the population of patients with T2D are complex. The main ones include chronic hyperglycemia and accumulation of collagen glycation end products (AGEs), insulin resistance, bone marrow adiposity, numerous cytokines, adipokines, oxidative stress, and reduced concentration of hydrogen sulfide [6, 7]. Disease duration, glycemic control, and the presence of chronic complications (retinopathy, nephropathy, macroangiopathy) are predictors of osteoporotic fractures. Antidiabetic drugs are also of significance for bone tissue metabolism [4].

The primary outcome of this study was to analyze the relationship between periodontal disease severity, as represented by clinical attachment loss (CAL), and neck-femur BMD, including patients' age and gender as potential confounders.

The secondary outcomes included the relationship between other indices of periodontal state [plaque index (PI), bleeding index (BI), pocket depth (PD), number of deep pockets with bleeding, and tooth loss as a general indication of poor oral health] and 3 indices describing BMD: neck-femur BMD, femur total BMD, and L1–L4 BMD, as well as biochemical parameters related to the BMD [calcium (Ca), phosphorus (P), parathyroid hormone (PTH), and vitamin D3 levels].

## Materials and methods

### Subjects

The study group consisted of patients hospitalized at the Department of Internal Medicine, Endocrinology, and Diabetology of the Central Clinical Hospital of the Ministry of Interior and Administration in Warsaw and patients of the Diabetes Clinic of this hospital. The maximum time since diagnosis of T2D was 3 months. A group of 103 patients with newly diagnosed T2D was qualified for the study, including 38 women (36.9%) and 65 men (63.1%). The mean age of the patients was 56.5 years (SD = 13.0 years). Smoking patients were excluded from the study. The mean body mass index (BMI) was 29.1 kg/m<sup>2</sup> (SD = 4.3). The percentage of

overweight (BMI 25.0–29.99 kg/m<sup>2</sup>) and obese (BMI  $\geq$  30 kg/m<sup>2</sup>) patients was 43% and 40.5%, respectively, among newly diagnosed ones. All tests were carried out in accordance with the provisions of the Helsinki Declaration of 1973 (updated in 2002). A positive opinion was obtained from the Ethics and Supervision Committee for Research on Humans and Animals of the Central Clinical Hospital of the Ministry of Interior and Administration in Warsaw (10/2012). All patients were presented with a study information form, and their written consent for the study was obtained.

### Study design

The patients underwent a detailed periodontal examination. It was performed in artificial light, using a dental mirror and a Hu-Friedy PCP-15 UNC probe, calibrated every 1 mm, each time with force not exceeding 0.25 N (25 g). The patients also underwent a blood test and densitometry on the same day.

### Data collection

The following parameters were rated in periodontal examination: number of teeth, presence or absence of plaque on 4 tooth surfaces - mesial, distal, buccal, and palatal, simplified PI according to O' Leary [8] was calculated, presence or absence of bleeding during probing at 4 points around the tooth — mesially, centrally, and distally from the buccal side and centrally from the oral cavity, and then the bleeding rate was calculated — bleeding on probing (BOP) (%), according to Ainamo and Bay [9], PD at 6 points around the tooth — mesially, centrally, distally from the buccal side and mesially, centrally, and distally from the oral cavity. Pocket depth was defined as the distance from the bottom of the pocket, assessed by probing, to the gingival margin. The location of the connective tissue attachment — CAL at 6 points around teeth — 3 measurement points on the buccal surface (mesial, central, distal) and similarly 3 points on the palatal/lingual surface (mesial, central, distal). Measurement of connective tissue attachment was defined as the distance from the bottom of the pocket, assessed by probing, to the cemento-enamel junction [10].

In the general blood test, basic morphological and biochemical parameters were determined, as well as the level of glycemia (mg/dL) and concentration of glycosylated hemoglobin (HbA1c). The following values were considered the norm: fasting glucose < 100 mg/dL; HbA1c  $\leq$  6.5%. Additionally, the following were determined: the level of acute phase protein — C-reactive protein (normal 0–5 mg/L); Ca (norm 2.1–2.6 mmol/L); P (normal 0.8–1.4 mmol/L); PTH (normal 10–60 pg/mL); and vitamin D3 (norm 31–50 ng/mL).

In densitometric examination, the following parameters of measurable BMD were determined: neck-femur

**Table 1. Comparison of Age, BMI, and Laboratory Parameters Depending on Gender (Mann-Whitney Test) and Age (Spearman Test)**

	Total (n = 103)	Men (n = 65)	Women (n = 38)
	Mean ± SD	Mean ± SD	Mean ± SD
Age	56.5 ± 13.0	56.6 ± 12.6	56.4 ± 13.8
BMI	29.1 ± 4.3	28.3 ± 3.9	30.7 ± 4.7
WBC	6.9 ± 1.7	7.1 ± 1.7	6.5 ± 1.6
Fasting blood glucose	163.7 ± 85.8 **	177.1.2 ± 94.0*	142.6 ± 67.0
HbA1c	8.3 ± 2.6 **	8.6 ± 2.5 *	7.7 ± 2.7
Cholesterol	187.2 ± 57.5 **	185.9 ± 63.7	189.2 ± 46.2
HDL	47.0 ± 15.4 **	44.3 ± 13.3*	51.5 ± 17.5
LDL	106.4 ± 50.3**	105.9 ± 56.7	107.2 ± 38.4
Triglycerides	187.0 ± 218.8**	203.1 ± 256.1	160.4 ± 136.1
Ca	2.3 ± 0.2	2.3 ± 0.2	2.4 ± 0.1
P	3.4 ± 0.6 **	3.3 ± 0.6	3.6 ± 0.5*
PTH	38.0 ± 21.9	35.6 ± 18.9	41.8 ± 25.8
Vit. D3	14.4 ± 7.0	14.3 ± 6.9	14.5 ± 7.4
CRP	9.6 ± 19.5	6.9 ± 12.5	15.4 ± 29.1
ALT	46.6 ± 50.0**	52.4 ± 60.7	36.8 ± 20.3
AST	37.1 ± 41.6	41.8 ± 51.1	29.3 ± 13.0
Neck-Femur BMD	0.99 ± 0.14**	1.01 ± 0.13	0.96 ± 0.14
Femur total BMD	1.08 ± 0.15**	1.12 ± 0.13	1.02 ± 0.15*
L1–L4 BMD	1.21 ± 0.18	1.24 ± 0.17	1.15 ± 0.18*

\*p-value < 0.05 comparison depending on gender (Mann-Whitney test); \*\*p-value < 0.05 comparison depending on age (Spearman test) — relationships were statistically inverse with the exception of the HDL parameter

ALT — alanine transaminase; AST — aspartate transaminase; BMD — bone mineral density; BMI — body mass index; Ca — calcium; CRP — C-reactive protein; HbA1c — glycated hemoglobin; HDL — high-density lipoprotein; LDL — low-density lipoprotein; P — phosphorus; PTH — parathyroid hormone; SD — standard deviation; WBC — white blood cells

BMD — mineral density of the femur neck, femur total BMD — femur mineral density, and L1–L4 BMD — bone mineral density of lumbar spine.

## Statistical analysis

The results obtained from the periodontal examination, blood test, and densitometric examination were then subjected to statistical analysis by PQStat v. 1.6.8. software using the Mann-Whitney U test, Spearman test, and multivariate analysis by logistic regression. The threshold of significance was  $p < 0.05$ . The minimum sample size calculated using G\*Power software (power 0.80, alpha 0.05) for correlation analysis was 67 participants.

## Results

The study group was characterized by an unsatisfactory condition of periodontal tissues, in particular the large number of lost teeth (median of 9 lost teeth), number of pockets  $\geq 4$  and  $\geq 4$  with associated bleeding (median of 10 and 4 pockets per person, respectively), as well as CAL (median 3 mm) and BOP (average 27.1%). These parameters mostly correlated significantly with the age of patients in the

study group but did not differ depending on gender. In the study group, women had significantly higher BMI, high-density lipoproteins (HDL), and values of P concentration. The level of phosphorus also decreased with the age of patients. Men, however, had higher glycemia and HbA1c levels (Tab. 1).

Mineral density of the femoral neck, femur, and lumbar spine (L1–L4) decreased with age. In addition, the densities of the femur and lumbar spine (L1–L4) were significantly lower in women than in men (Tab. 1).

An inverse correlation was found between bone density and clinical attachment loss and the number of lost teeth (for neck-femur BMD also with median PD) (Tab. 2).

All these parameters are age-dependent; therefore, multi-factor models have been developed that also take age into account. Due to the differences in the results of the densitometric examination between men and women, the analysis was carried out separately for each sex (Tab. 2–4).

After adjusting for age, bone density was not independently correlated with loss of attachment position in the male group.

**Table 2. Correlation of Periodontal Parameters with Biochemical and Densitometric Parameters (Spearman Correlation Analysis)**

	Ca	P	PTH	Vit. D3	Neck-Femur BMD	Femur total BMD	L1–L4 BMD
Number of missing teeth	$r = -0.05$	$r = -0.07$	$r = -0.16$	$r = 0$	$r = -0.39^*$	$r = -0.27^*$	$r = -0.10$
PI	$r = -0.03$	$r = -0.08$	$r = -0.11$	$r = 0.11$	$r = -0.07$	$r = -0.02$	$r = -0.03$
BI	$r = -0.05$	$r = -0.17^*$	$r = -0.10$	$r = 0$	$r = -0.14$	$r = 0$	$r = -0.08$
PD mean	$r = -0.04$	$r = -0.07$	$r = -0.09$	$r = -0.03$	$r = -0.15$	$r = -0.08$	$r = -0.13$
PD median	$r = -0.07$	$r = -0.02$	$r = -0.15$	$r = -0.01$	$r = -0.24^*$	$r = -0.18$	$r = -0.19$
PD $\geq 4$ mm (number)	$r = 0.03$	$r = -0.08$	$r = 0.10$	$r = -0.08$	$r = 0$	$r = 0.06$	$r = -0.01$
PD $\geq 4$ mm (%)	$r = -0.02$	$r = -0.09$	$r = 0$	$r = -0.07$	$r = -0.18$	$r = -0.10$	$r = -0.08$
PD $\geq 4$ mm + BOP (number)	$r = 0$	$r = -0.10$	$r = 0.03$	$r = -0.03$	$r = 0.01$	$r = 0.11$	$r = 0.02$
PD $\geq 4$ mm + BOP (%)	$r = -0.04$	$r = -0.11$	$r = -0.03$	$r = -0.03$	$r = -0.10$	$r = 0$	$r = -0.02$
CAL mean	$r = -0.03$	$r = -0.10$	$r = -0.14$	$r = 0.02$	$r = -0.44^*$	$r = -0.29^*$	$r = -0.25^*$
CAL median	$r = -0.05$	$r = -0.08$	$r = -0.15$	$r = 0.07$	$r = -0.43^*$	$r = -0.32^*$	$r = -0.31^*$

\*p value < 0.05; Spearman correlation analysis

BI — bleeding index; BOP — bleeding on probing; BMD — bone mineral density; CAL — clinical attachment loss; PD — pocket depth; PI — plaque index; PTH — parathyroid hormone

**Table 3. Analysis of the Relationship between Median CAL, Age, and Bone Mineral Density Using Linear Regression, and between the Number of Missing Teeth, Age, and Bone Mineral Density Using Linear Regression in the Group of Women**

Women				
Missing teeth			Median CAL	
P-value for the model: < 0.0001			P-value for the model: 0.0001	
$R^2 = 0.56$			$R^2 = 0.46$	
	Standardized coefficient $\beta$	P-value		
Intercept		0.003	Intercept	0.0588
Age	0.2	0.1893	Age	0.31
Neck-Femur BMD	-0.62	0.0002	Neck-Femur BMD	-0.45
P-value for the model: < 0.0001			P-value for the model: 0.0003	
$R^2 = 0.48$			$R^2 = 0.42$	
	Standardized coefficient $\beta$	P-value		
Intercept		0.0427	Intercept	0.2012
Age	0.37	0.0156	Age	0.43
Femur total BMD	-0.46	0.0032	Femur total BMD	-0.34
P-value for the model: < 0.0001			P-value for the model: 0.0009	
$R^2 = 0.50$			$R^2 = 0.36$	
	Standardized coefficient $\beta$	P-value		
Intercept		0.053	Intercept	0.8566
Age	0.51	0.0004	Age	0.56
L1–L4 BMD	-0.46	0.0011	L1–L4 BMD	-0.19

BMD — bone mineral density; CAL — clinical attachment loss

In the group of women, however, the relationship between bone density and attachment loss remained statistically significant also after taking age into account. The correlation with the density of femoral neck was so strong that when age was taken into account, it did not show a statistically significant relationship (Tab. 3).

Similarly, the number of lost teeth in men did not depend on bone density, but only on age (Tab. 4).

In the group of women, the results were not so clear. The density of the femoral neck showed a strong relationship with the number of lost teeth, completely dominating the importance of age. Examination of the proximal femur as a whole correlated with the number

**Table 4. Analysis of the Relationship between the Number of Missing Teeth, Age, and Bone Mineral Density Using the Linear Regression Method, and between Median CAL, Age, and Bone Mineral Density Using Linear Regression in the Group of Men**

Men				
Missing teeth		Median CAL		
P-value for the model: 0.0002				
R <sup>2</sup> = 0.30				
	Standardized coefficient $\beta$	P-value	Standardized coefficient $\beta$	P-value
Intercept		0.4116		0.4116
Age	0.54	0.0002	0.54	0.0002
Neck-Femur BMD	−0.02	0.9008	−0.02	0.9008
P-value for the model: 0.0002				
R <sup>2</sup> = 0.30				
	Standardized coefficient $\beta$	P-value	Standardized coefficient $\beta$	P-value
Intercept		0.2629		0.2629
Age	0.55	< 0.0001	0.55	< 0.0001
Femur total BMD	0.02	0.9022	0.02	0.9022
P-value for the model: < 0.0001				
R <sup>2</sup> = 0.33				
	Standardized coefficient $\beta$	P-value	Standardized coefficient $\beta$	P-value
Intercept		0.9156		0.9156
Age	0.52	< 0.0001	0.52	< 0.0001
L1–L4 BMD	−0.19	0.1229	−0.19	0.1229

BMD — bone mineral density; CAL — clinical attachment loss

of missing teeth, with age also being a significant risk factor. The result of the bone density test in the lumbar spine did not significantly modify the relationship between the number of lost teeth and age (Tab. 3).

There was no relationship between BMD and selected biochemical parameters related to bone tissue, as well as glucose and HbA1c levels (Tab. 1).

Among the biochemical parameters, a statistically significant correlation was observed only for the bleeding index and phosphorus — higher values of the bleeding index were accompanied by lower levels of phosphorus in the patients' blood (Tab. 1).

## Discussion

The relationship between BMD reduction and periodontal tissue condition, and between bone density and diabetes, has been extensively reported [2–6]. However, there are few studies describing reduced bone density in patients with T2D and periodontitis. Numerous studies [11–15] show a positive correlation between systemic BMD and oral bone loss. Given these results, this study hypothesizes that decreased systemic BMD associated with osteopenia or osteoporosis may affect alveolar bone microarchitecture, possibly af-

fecting the rate of periodontal tissue destruction in periodontitis.

Studies examining the relationship between BMD and periodontitis have used different sites to assess systemic mineral density, namely the metacarpals [16], femoral neck [17, 18], and lumbar spine [19]. Iki E et al. [20] reported faster loss of BMD in lumbar spine compared to BMD in femoral neck in 4550 Japanese women. Singh et al. [21] chose the lumbar spine as the preferred site for BMD measurement because the lumbar spine is mainly composed of trabecular bone. They believe that examination of the lumbar spine may be the most sensitive indicator of systemic deterioration of bone microarchitecture in osteoporosis.

In our study, results of BMD from the femoral neck, proximal femur, and lumbar spine (L1–L4) were used. It was observed that the mineral density of the femoral neck, femur, and lumbar spine decreased significantly with the age of the patients. In addition, the mineral density of femur and lumbar spine showed significantly lower values in women.

The number of lost teeth in the study group demonstrated significant inverse correlation with the mineral density of both the femoral neck and the

bone itself. On the other hand, clinical attachment loss showed a significant inverse correlation with bone density at all sites examined. Both tooth loss and clinical attachment loss are manifestations of periodontal disease progression, and progressive bone loss is critical in both cases. Age is a non-modifiable risk factor for both periodontitis and osteoporosis [22], and bone loss accelerates in women with onset of menopause [23]. In our own study, information about menopause was not included in anamnesis; however, the average age of the woman was  $56.4 \pm 13.8$  years, which may indicate a postmenopausal period. The age parameter was included in multivariate analyses. It was shown that loss of connective tissue attachment was affected by reduced bone mineral density, regardless of age. In the case of the number of lost teeth, the strongest correlation that was independent of age was noted for density of the femoral neck. For the proximal femur as a whole, age was a significant risk factor, while the lumbar spine mineral density score did not significantly modify the relationship between the number of lost teeth and age.

Tak et al. [24], in a study on the Korean population, observed an inverse correlation between mineral density of the lumbar spine and CAL in a group of women, but they did not report a similar relationship in the case of the femoral neck or the number of lost teeth in relation to BMD. The number of missing teeth, however, was correlated with the mineral density of the lumbar spine in men. Singh et al. studied women aged 46–54 years in the early postmenopausal period [21]. They conducted an analysis dividing the patients into 3 groups — normopenic, osteopenic, and osteoporotic. They showed an inverse correlation between mineral density and average CAL and average PD, and statistically significant differences between the groups. Regarding the number of missing teeth, the correlation with bone mineral density was not statistically significant.

Iwasaki et al. [25], examining the mineral density of the proximal femur and lumbar spine, also showed that the group of women with osteopenia/osteoporosis were more exposed to higher values of loss of connective tissue attachment; however, the number of lost teeth was not mentioned. Different results were obtained by Moeintaghavi et al. [26]; they did not observe a difference in either the number of lost teeth or loss of connective tissue attachment between the groups differing in mineral density, as in the previously mentioned publications. In our study, osteoporosis was diagnosed in one woman based on L1–L4 T-score. However, the normopenic and osteopenic groups were not homogeneous in terms of

size, which prevented a thorough analysis between the groups.

Regarding the number of lost teeth, Grocholewicz et al. [27] described a positive correlation with reduced mineral density, while Drozdowska et al. [28] observed a decrease in bone mineral density in edentulous women compared to women with partially missing teeth.

Similar results to our own observations regarding CAL and BMD of the femoral neck were published by Gondim et al. [29]. However, a significant correlation was observed only in the group of women with CAL > 5 mm, but the correlation with BMD was significant. Perhaps an additional factor influencing this correlation in our study was newly diagnosed diabetes.

In these scientific reports, the glycemic status of patients was not taken into account, or patients with diabetes were excluded from the study.

Although our study did not show a statistically significant relationship between parameters of mineral density and the level of HbA1c, a possible impact of glycemic disorders on bone tissue metabolism and indirectly on the condition of periodontal tissues should not be overlooked. Diabetes has a significant impact on intensification of osteoclastogenesis and increased apoptosis of osteoblasts. Interestingly, the effect of diabetes on bone loss is likely related to the effect of diabetes on both innate and adaptive immune responses [30]. There are also reports of normal or even increased BMD density in patients with T2D. However, bone microarchitecture is remodeled in this case, which in turn leads to increased predisposition to fractures in this group of patients [4, 5].

One of the few studies taking into account the impact of T2D on BMD density reduction and periodontitis was published by Ateeq et al. [31].

They studied BMD in patients with T2D with chronic periodontitis and in patients with T2D who were periodontally healthy, as well as in non-diabetic patients with periodontitis and in healthy patients. Importantly, the study excluded women in early menopause and those taking hormone replacement therapy.

The mean BMD density was lowest in the group of patients with T2D and periodontitis in comparison to those with diabetes and periodontitis only. However, there was no correlation between BMD and HbA1c in any of the groups of diabetic patients. The effect of diabetes on the condition of periodontal tissues and BMD density was concluded, emphasizing aggravation of this condition in patients with periodontitis. However, the cause of the relationship between a decrease in BMD and T2D and periodontitis has not been determined. The authors suggest that additional risk factors, such as BMI and other comorbidities, as well as duration of T2D, may play a role.



## Conclusions

In summary, low BMD may be associated with T2D and periodontitis. Early diagnosis of reduced BMD can significantly affect the condition of periodontal tissues. Therefore, it is advisable to refer patients with reduced BMD for a dental and periodontal examination. Similarly, patients with T2D should be assessed for osteoporosis risk to reduce the risk of bone loss and fractures.

## Article information

### Availability of data and materials

Original contributions presented in the study are included in the article. Further inquiries can be directed to the corresponding author.

### Ethical approval and consent to participate

A positive opinion was obtained from the Ethics and Supervision Committee for Research on Humans and Animals of the Central Clinical Hospital of the Ministry of Interior and Administration in Warsaw (10/2012). The patients gave their written informed consent to participate in this study.

### Author contributions

Conception and design of the study: Górska R., Franek E.

Acquisition of Data: Wysznińska-Pomian M.

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Drafting the manuscript: Wysznińska-Pomian M.

### Funding

This publication was prepared without any external source of funding.

### Competing interests

The authors declare no conflict of interest.

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