

## CARDIOVASCULAR DISEASE AND DIABETES, POTENTIAL RISK FACTORS FOR PERIODONTAL DISEASE

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### ABSTRACT

**Introduction and aim:** The investigation of potential systemic risk factors, such as cardiovascular disease and diabetes, for periodontal disease.

**Materials and methods:** A cross-sectional sample consisting of 395 dentate adults (mean age  $54 \pm 13$ ), 55.7% female and 44.3% male, were enrolled in the study. Subjects attended periodontal care between 2016-2017 in Constanța, Romania (participation rate was 82%). The self-reported CVD and diabetes were recorded for the study. Clinical parameters such as periodontal probing depth (PPD) and bleeding on probing (BOP) were measured in order to assess the periodontal status. For the purpose of this study and in order to correlate the systemic status to the periodontal status, all patients were categorized according to their maximum PPD: either PPD <4 mm (no periodontitis) or PPD  $\geq 4$  (periodontitis). The data was analyzed using IBM SPSS statistics software version 20.

**Results:** Patients with known CVD are more likely to have pockets deeper than 4 mm (periodontitis) OR = 5; 95% confidence interval (CI): 2.41-10.34. Self-reported diabetes was positively associated with the risk for periodontal disease with pockets deeper than 4 mm OR = 3.12; 95% CI: 1.18-8.25. No statistically significant relation was found between BOP and the presence of CVD ( $p=0.09$ ), as well as between BOP and diabetes ( $p=0.161$ ).

**Conclusion:** Cardiovascular disease and diabetes act as potential risk factors for periodontal disease, but gingival inflammation assessed by bleeding on probing was not proven to be influenced by CVD or diabetes.

**Keywords:** periodontal disease, diabetes, cardiovascular disease, periodontal pockets, risk factor.

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### Introduction

Periodontal disease is a chronic inflammatory-infectious disease, initiated by the presence of a bacterial biofilm, which affects both the periodontal ligaments and the alveolar bone, with the occurrence of periodontal pockets. As the disease progresses, the periodontal pockets deepen, and the untreated disease leads to tooth loss. Many systemic conditions are proved to interfere with the onset of the periodontal disease and aggravate its evolution. Some of these conditions, such as diabetes and cardiovascular diseases (CVD) could be included among risk factors for periodontal disease, according to recent findings. Some literature studies suggest that periodontal disease (PD) itself can be involved in the etiology of some systemic pathology, especially CVD, due to periodontopathogen bacteria residing in periodontal

pockets, bacteria which can enter in systemic blood circulation<sup>(1)</sup>.

On the other hand, periodontitis is a very common oral pathology in developed and developing countries<sup>(2,3)</sup>. The identification of risk factors for periodontitis is essential to improve the understanding of the disease pathogenesis and to establish effective health preventive strategies. It has become very important to identify the risk factors that make patients susceptible to PD. Some studies recognize smoking, diabetes and some pathogen bacteria as true risk factors, whereas some background factors have been regarded as risk indicators<sup>(4,5)</sup>.

Other studies demonstrate a significant association between periodontal disease and future cardiovascular events. Common risk factors such as diabetes and smoking are shared between cardiovascular and periodontal diseases<sup>(6)</sup>.

In diabetic patients, the uncontrolled periodontal infection can make the glycemic level difficult to control. The less diabetes is controlled, the more severe the periodontal destruction becomes<sup>(7)</sup>. From this point of view, a collaboration between the clinician and the periodontist might help control these pathologies. However, it is important to underline that several recent studies failed to show an association between diabetes and periodontal disease<sup>(8)</sup>. For this main reason, further investigation is needed to confirm the potential link between these two highly prevalent disorders.

Many epidemiological studies have identified statistically significant associations between periodontitis and cardiovascular diseases<sup>(9)</sup>. Also, this association is not without dispute<sup>(10, 11)</sup>. Some previous studies investigated the role of infection in CVD<sup>(12)</sup>. In fact, periodontal disease has an infectious etiology, which can lead to the assumption that these pathologies can be somehow connected. Pro-inflammatory mediators involved in hyperglycemia have also been associated in some studies with periodontitis, also indicating increased cardiovascular disease risks<sup>(13)</sup>. The prevalence of coronary heart disease in some cross-sectional studies was greater among individuals with periodontitis than in subjects without periodontitis<sup>(14)</sup>.

In any case, different prevalence rates of periodontitis in populations with different age groups, ethnicity, geographic location, can make it difficult to assess the association between periodontitis, diabetes and cardiovascular disease. There are not many studies on this topic to refer at the Romanian population. Thus, the aim of this paper was to investigate the potential systemic risk factors, such as cardiovascular disease and diabetes, for periodontal disease in a cross-sectional group from Constanta city, Romania.

## Materials and methods

A cross-sectional sample consisting of 395 dentate adults, age >30 years (mean 54±13), 55.7% female, 44.3% male, was used in order to assess the link between periodontitis and CVD, or periodontitis and diabetes. The self-reported systemic condition was used in evaluation. In addition, periodontal probing depth (PPD) and bleeding on probing (BOP) were used in order to assess the periodontal status and inflammation. For the purpose of this study and in order to relate systemic status to existence of periodontal disease, all patients were categorized ac-

ording to their maximum PPD: either PPD of <4 mm (no periodontitis), or PPD of ≥4 (periodontitis).

The data was analyzed using IBM SPSS statistics software version 20.

**Study design.** Subjects were selected from patients attending dental care in the Faculty of Dentistry Constanta and Clinical Infectious Diseases Hospital Constanta, Romania. The study was conducted during 2016-2017.

**Data collection.** All subjects have undergone periodontal examination and have filled in a questionnaire regarding their demographic features, daily oral hygiene, frequency of tooth brushing, lifestyle, cardiovascular pathology, known diabetes condition, as well as smoking habits. An informed consent was obtained both to collect data using a structured questionnaire, and for the dental examination. In order to assess the reliability of the self-reported data, 15 subjects of the study sample were asked to fill in the questionnaire again. This was made 14-20 days after the first appointment. The history of cardiovascular disease (CVD) and diabetes of the participants were established by direct inquiry.

### *Screening procedure for PD*

A previously standardized dentist performed the oral examinations with a periodontal probe, a flat dental mirror, while the patient was sitting on a dental chair. Periodontal probing depth (PPD), bleeding on probing (BOP) and Community Periodontal Index (CPI) were used to assess the periodontal condition. The BOP was recorded for each patient immediately after the pocket depth measurements.

For the purpose of the study the results were dichotomized as follows: (1) no bleeding on gentle probing; (0) bleeding on gentle probing. All permanent fully erupted teeth, excluding third molars and radices, were examined with the manual CPI periodontal probe with a 0.5mm ball tip, black bands at 3.5–5.5 mm, and rings at 8.5 and 11.5 mm from the ball tip. Six sites per tooth were assessed in the mesiobuccal, midbuccal, distobuccal, distolingual, midlingual and mesiolingual sites, in order to determine the maximum PPD per each tooth. Only the depth of the deepest pocket for each tooth was recorded for the study in the chart of the patient. The detailed procedure has been described by Lai and coll.<sup>(15)</sup>.

The maximum CPI score for each patient was recorded according to the following scale: (0) periodontal health; (1) gingival bleeding; (2) calculus detected during probing; (3) pocket 4 to 5mm deep; and (4) pocket 6mm deep and over. The Simplified

Oral Hygiene Index (OHI-S) was used to assess the oral hygiene level. The OHI-S has two components, the Plaque Index (PI) and the Calculus Index (CI). For a proper periodontal health, PI and CI should be under 1 value, if possible close to 0<sup>(16)</sup>.

### Ethics

Ethical approval for the study was obtained from the local ethics committee. In addition, each patient signed an informed consent for the use of their data in this study, prior to the admission the study. The identity of all subjects was kept anonymous.

### Subject eligibility

Subjects qualifying for the study met the following inclusion criteria:

- over 30 years of age;
- more than 10 natural teeth in the mouth;
- regular manual or electric toothbrush users.

Patients were excluded for one of the following conditions:

- severe systemic pathology such as malignancies, leukemia, genetic syndromes.
- pregnancy
- if any antibiotic was taken 4 weeks before the examination (antibiotic intake can improve short-term the level of gingival inflammation assessed by bleeding on probing)
- chronic drugs or alcohol consumers

### Statistical analysis

The statistical analysis was performed using IBM SPSS statistics software version 20. Descriptive statistics were performed for all patients as well as within the subgroups of diabetics, non-diabetics, patients with CVD, patients with not known CVD and patients categorized with or without periodontitis (according to maximum PPD). The Odds ratios (OR) and relative risk (RR) were calculated in order to assess the studied systemic diseases risk for the occurrence of periodontal disease.

### Results

From the total number 480 of patients invited to participate, 395 agreed to participate in the study, 220 (55.7%) were female and 175 (44.3%) male. The participation rate was 82%. The age interval of participants was 31-85 years old, (mean 54±13).

From the total sample of patients, 12.7% (n=50) reported the existence of cardiac pathology and 5.3% (n=21) are diabetics.

There are no patients with both CVD and diabetes (table 1).

	Frequency	Percent	Valid Percent	Cumulative Percent
Healthy	324	82.0	82.0	82.0
CVD	50	12.7	12.7	94.7
Diabetes	21	5.3	5.3	100.0
Total	395	100.0	100.0	

**Table 1:** Distribution of subjects according to systemic status.

The comparison of periodontal status in terms of oral hygiene and presence of pockets, according to systemic condition is shown in table 2

Systemic status		N	Min	Max	Mean	Std. Deviation
Healthy	PI	324	0.00	3.00	1.4442	.71715
	CI	324	0.00	3.00	1.2590	.77237
	CPI	324	0.00	4.00	2.5679	.85750
	PPDmax (mm)	324	0.00	13.00	3.5432	2.61479
CVD	PI	50	.33	3.00	1.9186	.61112
	CI	50	.33	3.00	1.7730	.71651
	CPI	50	2.00	4.00	3.2000	.72843
	PPDmax (mm)	50	1.00	11.00	5.0600	2.27596
Diabetes	PI	21	.20	3.00	1.4029	.66210
	CI	21	.15	3.00	1.5548	1.01758
	CPI	21	2.00	4.00	3.3333	.85635
	PPDmax (mm)	21	1.00	11.00	5.4048	2.90525

**Table 2:** Periodontal and systemic status.

The mean of PI and CI are increased in patients with cardiac pathology, as compared to healthy subjects. The CPI scores are higher in patients with diabetes and CVD, as compared to healthy subjects, values of 3 and 4 of CPI suggesting periodontal involvement, with existence of periodontal pockets (table 2).

Also, the medium values for CPI scores calculated (One-Way Anova) for groups of healthy, CVD and diabetic subjects differ significantly ( $F = 18.69$ ;  $p < 0.001 < \alpha = 0.05$ ). The Post-Hoc Multiple Comparisons – Tamhane (Leven = 2.534,  $df1 = 2$ ,  $df2 = 392$ ,  $p = 0.048 < \alpha = 0.05$ ) shows significant differences between medium values of CPI for groups with no systemic pathology (CPI=2,56) and CVD (CPI=3,20),  $p < 0.001 < \alpha = 0.05$ , as well as groups of no systemic pathology (CPI=2,56) and diabetes (CPI=3,33),  $p = 0.002 < \alpha = 0.05$ .

Regarding the oral hygiene status, assessed by plaque index (PI) and calculus index (CI), the medium PI scores calculated (One-Way Anova) separately for groups of healthy, CVD and diabetic subjects differ significantly

( $F = 10.11$ ;  $p = 0.011 < \alpha = 0.05$ ). The Post-Hoc Multiple Comparisons - Tamhane (Leven = 4.558,  $df_1 = 2$ ,  $df_2 = 392$ ,  $p = 0.011 < \alpha = 0.05$ ) show significant differences between healthy (PI=1,44) and CVD (PI=1,91) groups,  $p < 0.001 < \alpha = 0.05$ , but between healthy (PI=1,44) and diabetes (PI=1,40) groups there is no significant difference ( $p = 0.990 > \alpha = 0.05$ ).

The medium CI scores calculated (One-Way Anova) separately for groups of healthy, CVD and diabetic subjects differ significantly ( $F = 10.24$ ;  $p < 0.001 < \alpha = 0.05$ ) and the Post-Hoc Multiple Comparisons - Tamhane (Leven = 4.299,  $df_1 = 2$ ,  $df_2 = 392$ ,  $p = 0.014 < \alpha = 0.05$ ) show significant differences between healthy (CI=1,25) and CVD (CI=1,77) groups,  $p < 0.001 < \alpha = 0.05$ , but between healthy (CI=1,25) and diabetes (CI=1,55) groups there are no statistically significant differences ( $p = 0.497 > \alpha = 0.05$ ).

The maximum periodontal pocket depth (PPD) assessed by probing for every patient was compared within the three subgroups: healthy patients, patients with CVD, and diabetics. The differences between the median values of PPD maxim are statistically significant ( $F = 11.49$ ;  $p < 0.001 < \alpha = 0.05$ ). The Post-Hoc Multiple Comparisons - Tamhane (Leven = 2.505,  $df_1 = 2$ ,  $df_2 = 392$ ,  $p = 0.043 < \alpha = 0.05$ ) show differences between healthy (PPD=3,54) and CVD (PPD=5,06),  $p < 0.001 < \alpha = 0.05$ , and also between healthy (PPD=3,54) and diabetes (PPD=5,40),  $p = 0.027 < \alpha = 0.05$ .

Risk analysis found dependent relation between periodontitis with pockets deeper than 4mm and cardiovascular disease (CVD) OR=5, 95% CI for OR: 2.41-10.34 ( $\chi^2_{calc} = 21.09$ ,  $df = 1$ ,  $p < 0.001 < \alpha = 0.05$ ). Those findings suggest that the risk to find pockets deeper than 4 mm in the group with CVD is 5 times higher than in the group of patients without systemic pathology. The bleeding on probing (BOP) was not associated with the CVD ( $p=0,09$ ). Self-reported diabetes was positively associated with the risk for periodontal disease OR = 3.12; 95% CI: 1.18-8.25, ( $\chi^2_{calc} = 5.77$ ,  $df = 1$ ,  $p = 0.016 < \alpha = 0.05$ ). The risk to find deep pockets in patients with diabetes is 3.12 times higher than in patients without systemic pathology. No statistically significant correlation was found between BOP and diabetes ( $p=0.161$ ). Sex was not found to be a risk indicator for CVD ( $p = 0.186 > \alpha = 0.05$ ), or for diabetes ( $p = 0.482 > \alpha = 0.05$ ).

## Discussion

Using a population-based study to assess periodontal status in adults aged 31-85 years old, we found that the risk of having deep periodontal pockets in subjects with diabetes was 3.12 times higher than in those without diabetes, in both men and women. However, PD is also a systemic disease and may also be affected by other etiological factors, as shown recently by Albandar et al<sup>(17)</sup>. The review of literature studies leads the researchers to the conclusion that diabetes is strongly associated with periodontal disease<sup>(18)</sup>. Tylor suggested a bi-directional relation between diabetes and PD, which means that each disease influences the other<sup>(18)</sup>. Also, their findings show a similar risk rate of 4,2 regarding the periodontal destruction in diabetics as compared to non-diabetics. Several limitations in the present study should be considered. First, the diabetes status was self-reported, we could not correlate the level of glycemia with periodontal status. Second, regarding any causal relationship between diabetes and PD, our study cannot account for the temporal relationship between diabetes and PD. Also, there is evidence that periodontal inflammation may itself contribute to the onset and persistence of hyperglycemia, because inflammation is associated with inadequate glycemic control in individuals with diabetes<sup>(19)</sup>. We could not find correlation between inflammation (expressed by bleeding on probing) and the diabetic status.

The results of our cross-sectional study showed that there was a link between the periodontal involvement (teeth with periodontal pockets >4 mm) and CVD, but bleeding on probing was not positively associated with cardiovascular pathology. The findings of our study agree with an earlier case-control study, where a link between the number of sites with a pocket depth > 4 mm and cardiac pathology was reported<sup>(20)</sup>.

Another study found an association between periodontitis and high systolic blood pressure<sup>(21)</sup>. Because we could not find correlation between BOP and CVD or diabetes, we could speculate that this result occurred since bleeding on probing is primarily influenced by the degree of plaque accumulation. Therefore, it is difficult to separate the local factors such as oral hygiene to the systemic influences when assessing the influence of systemic pathology on bleeding on probing.

Another recent study<sup>(22)</sup> shows no correlation between the number of teeth with deep periodontal pockets or the number of bleeding sextants and hypertension.

During the last decades, there has been a great interest in the impact of oral health, especially periodontitis, on cardiovascular diseases. The findings of one study resulted in the conclusion that periodontitis and poor oral health overall contribute to the pathogenesis of cardiovascular disease<sup>(23)</sup>. In our study we also found a poor oral hygiene in patients with CVD compared to healthy subjects. Other meta-analysis reports<sup>(24)</sup> show that periodontitis may contribute to CVD and stroke, due to systemic bacterial exposure from periodontitis, so the relation between periodontitis and CVD might also be dual.

Our study has some limitations. First, the term “cardiovascular diseases” is a broad term and it should be useful to specifically identified cardiovascular diseases (i.e. stroke, acute coronary syndrome, atherosclerosis) which can be linked to periodontitis. Secondly, the cardiovascular pathology was self-reported, which means that only patients diagnosed were included in statistical analysis. It could be possible that many patients with unknown cardiovascular pathology have been included in our healthy group. In any case, preventive care and proper lifestyle decisions may significantly reduce the risk of diabetes, cardiovascular disease, by maintaining healthy oral conditions.

## Conclusion

In conclusion, in this study group, cardiovascular disease and diabetes act as potential risk factors for periodontal disease, in terms of pocket formation, but bleeding on probing was not proven to be influenced by those two systemic pathologies. This data suggests that periodontitis may have overall systemic health consequences in cardiovascular and metabolic pathologies, and a good clinician-periodontist collaboration could prevent future complications of those diseases.

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