

RESEARCH ON THE BIDIRECTIONAL RELATIONSHIP BETWEEN PERIODONTAL DISEASE AND HIGH BLOOD PRESSURE

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RESEARCH ON THE BIDIRECTIONAL RELATIONSHIP BETWEEN PERIODONTAL DISEASE AND HIGH BLOOD PRESSURE (Abstract): As the importance of the connection between periodontal disease and cardiovascular disease becomes increasingly prominent in medical practice, it is essential to explore this relationship and its implications for patients. The **aim** of this research was to investigate the impact of periodontal disease on the development and progression of cardiovascular disease and to establish that periodontal disease represents a relevant risk factor for the occurrence of cardiac pathologies. **Materials and methods:** A retrospective study was carried out, including 138 consecutive patients who addressed the Dental Education Clinical Base, between November 2021 and November 2023. The patients included in the study were divided into two groups, a group composed of 74 patients (group I: n=74) with periodontitis and a group of 64 patients without periodontitis (group II: n=64). **Results:** Research has revealed that the prevalence and severity of periodontal disease are higher in individuals with hypertension compared to those with normal blood pressure levels. **Conclusions:** our results argue once again for the assessment of the bidirectional correlation between periodontal disease and hypertension. **Keywords:** PERIODONTAL DISEASE, PERIODONTITIS, HIGH BLOOD PRESSURE, HYPERTENSION, BIOFILM, ORAL MICROBIOTA.

Periodontal disease is considered a chronic bacterial infection characterized by persistent inflammation, degradation of connective tissue, and destruction of alveolar bone (1). It includes gingivitis (where inflammation is limited to the gums and is reversible if the patient maintains good oral

hygiene) and periodontitis (a bacterial infection characterized by a destructive inflammatory process due to the action of bacteria and their products, which extends and leads to tissue destruction and alveolar bone resorption) (2, 3).

This condition is primarily induced by

bacteria that form biofilms in the periodontium, leading to inflammatory changes in the tissues that support dental units (3, 4). Diagnosing it is complex and is based on clinical examination, the patient's age at the time of diagnosis, the rate of disease progression, as well as systemic and local factors (5). The global prevalence of periodontal diseases is substantial, affecting a significant portion of the population (6). It is considered a public health issue due to its high prevalence worldwide (7).

From a clinician's perspective, defining periodontal disease is fundamental for understanding and addressing this complex pathology. Periodontitis is a slowly progressive disease and tissue destruction is largely irreversible. In the early stages, the disease is usually asymptomatic, but many patients become aware of it when the condition has progressed far enough to result in tooth mobility. Deep pockets occur as a result of further destruction of the fibers of the periodontal ligament (called loss of attachment) and resorption of the alveolar bone that occurs in parallel with the loss of attachment progress.

These diseases are set up by a chronic inflammatory process, starting with bacterial biofilm forming on tooth surfaces, followed by an inflammatory reaction of the host tissues. The complex interplay between pathogenic microorganisms, host immune response and environmental factors leads to progressive tissue and bone changes and damage that can affect oral and general health (8).

Advanced periodontal inflammation is characterized by gingival erythema and edema, gingival bleeding and recession, tooth mobility, pathological malpositioning of teeth, suppuration of periodontal pockets and tooth loss. The condition is very com-

mon, with a frequency of 10-15% in adults in most populations studied (9). Moderate periodontitis is even more common, affecting 40-60% of adults, and severe periodontitis has been identified with the sixth highest prevalence of the disease worldwide (10).

In the detailed evaluation of periodontal disease, it is essential to investigate the typologies and stages of this condition for a proper understanding of the mechanisms involved and the development of appropriate therapeutic strategies (11).

Studies show that periodontitis is a chronic inflammatory condition of the periodontal tissue with a multifactorial etiology, caused, among other factors, by the disruption of the oral biofilm. Key pathogens such as *Aggregatibacter actinomycetemcomitans*, *Porphyromonas gingivalis*, *Fusobacterium nucleatum*, *Prevotella intermedia* and *Tannerella forsythia* (12, 13) can disrupt the oral microbiota, inducing dysbiosis and chronic inflammation of the periodontium. These elements are essential in understanding the complex interactions involved in periodontal disease.

Consequently, a detailed understanding of the various types and stages of periodontal disease is fundamental for clinical and therapeutic approaches, highlighting the complexity of this condition and the necessity for personalized interventions (14, 15). At the EuroPerio's eighth edition in 2019, the Congress of the European Federation of Periodontology, a new classification of periodontal pathology was developed (16).

This classification adopted a staging and grading system for the diagnosis of periodontitis, which, on one hand, records different degrees of disease severity, and on the other hand, the anticipated progression of the condition. Therefore, diagnos-

ing periodontal disease also requires a thorough clinical and radiological evaluation, with modern imaging unequivocally contributing to the correlation between periodontal and systemic status (17).

Recent studies highlight the links between periodontal diseases and systemic conditions, including cardiovascular diseases, showing possible common pathogenic mechanisms (18). Over the past two decades, a substantial number of epidemiological studies have been conducted to investigate the relationship between periodontitis and cardiovascular diseases, making this topic one of the major areas of interest in periodontal research (19, 20).

The etiology and microbiology of periodontal diseases have been extensively studied, shedding light on the complex pathogenesis of these conditions (21). The understanding of the molecular mechanisms underlying periodontal tissue diseases has evolved over the years, providing insights into the inflammatory processes, cytokines and matrix metalloproteinases involved in the progression of the disease (21). In addition, the association between periodontal disease and chronic systemic conditions such as hypertension, dyslipidemia, stroke, myocardial infarction, angina pectoris and diabetes has been explored, revealing a higher prevalence of periodontal disease in individuals with these comorbidities (22, 23).

One third of all deaths worldwide are caused by cardiovascular disease, which is thus the leading cause of death worldwide. Moreover, globally, cardiovascular disease causes more deaths than cancer, chronic respiratory failure and diabetes combined (24).

In addition to their impact on the population as a factor increasing mortality, cardiovascular disease is also a major cause of

disability and chronic disease, placing a considerable burden on health systems and the economy.

The association between periodontal disease and cardiovascular disease has been intensively investigated and various theories have been proposed to explain this link. One theory suggests a direct invasion of endothelial cells by periodontal pathogens, while another proposes an indirect pathway by which periodontal disease triggers a systemic inflammatory response (25). In addition, a common genetic basis has been suggested as a possible link between these two conditions (25). These theories collectively emphasize the complex interaction between periodontal and cardiovascular status.

Studies emphasize the strong relationship between periodontal and cardiovascular diseases, focusing on two main directions of this association (26). The first direction suggests that bacteria in the oral cavity may directly exacerbate cardiovascular disease or modify systemic risk factors for cardiovascular disease (26). The second direction emphasizes how chronic periodontal inflammation, viewed as a focus of infection, may increase circulating levels of inflammatory molecules, exacerbating cardiovascular disease (26).

As the importance of the connection between periodontal disease and cardiovascular disease becomes increasingly prominent in medical practice, it is essential to explore this relationship and its implications for patients.

This study proposes to investigate the impact of periodontal disease on the development and progression of cardiovascular disease and to establish that periodontal disease represents a relevant risk factor for the occurrence of cardiac pathologies.

MATERIALS AND METHODS

A retrospective study was carried out, including 138 consecutive patients who addressed the Dental Education Clinical Base, between November 2021 and November 2023.

Inclusion criteria. Patients with gingival diseases not induced by dental biofilm, patients without signs of periodontal disease, patients with gingivitis induced by dental biofilm, patients with periodontitis and patients with periodontitis appearing as a manifestation of systemic diseases.

Exclusion criteria. Chronic alcohol users and patients with other cardiovascular diseases other than hypertension (HT) were excluded from the study. According to the World Health Organization (WHO), there is a significant variation in the prevalence of cases with severe forms of periodontitis in the population, which is approximately 10-15%.

Starting from this aspect, we considered an effect size of 11%, representing the reference prevalence for establishing the minimum sample size, which requires obtaining a minimum volume to ensure adequate representativeness of the patient category.

To achieve this prerequisite, we set a 95% confidence interval. The sample size was determined based on the condition of having a confidence interval smaller than the allowable level of error.

Accordingly, we used the equation:

$$n \geq \left(Z_{\left(1-\frac{\alpha}{2}\right)} \right)^2 \cdot \frac{p \cdot (1-p)}{d^2}$$

where $Z = 1.96$ for a 95% confidence interval and a minimum error of estimate of 5%.

We estimated a minimum sample size of 138 cases.

The patients included in the study were divided into two groups, a group composed of 74 patients (group I: $n=74$) with periodontitis and a group of 64 patients without periodontitis (group II: $n=64$).

The primary objective of the study was to assess the correlation between periodontitis and hypertension mediated by a number of risk factors.

Hypertension was considered as a dichotomous dependent variable defined by systolic blood pressure of 140 mmHg or more and/or diastolic blood pressure of 90 mmHg or more and/or current use of anti-hypertensives.

Data were processed in MS Excel and statistical analysis was performed with SPSS v. 29 program (IBM Ireland Product Distribution Limited, IBM House, Shelbourne Road, Ballsbridge, Dublin, Ireland) and STATA 16 software (StataCorp LLC, 4905 Lakeway Drive, College Station, TX, USA).

The existence of significant statistical differences was considered for a confidence interval of 95%, and parametric or non-parametric tests were applied depending on the characteristics of the variables. Student's t-test, Pearson- χ^2 , Fisher's test, Levene's test, ANOVA test, logistic regression and multivariate analysis tests were used.

The threshold of significance was $p = 0.05$ corresponding to a maximum acceptance error of 5%. Descriptive statistical indicators were calculated for continuous variables (mean, standard deviation, standard error, minimum, maximum and quartile intervals).

Within the descriptive statistics, the values of the location indicators (mean,

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median, mode), scattering (dispersion, amplitude) were calculated, we determined, as appropriate, the interval of variation with 95% confidence (for the study of proportions) and within the analysis statistics, we applied tests to determine the regression model, comparison of ANOVA means, the Chi square test (χ^2) for comparing proportions and we tested the sensitivities of the diagnostic methods. This allowed the highlighting of associations, relationships and interdependencies between variables of interest.

RESULTS

From the analyzed database, it has been observed that the prevalence and severity of periodontal disease are higher in individuals with hypertension compared to those with normal blood pressure levels.

Demographic characteristics. In the analyzed cohort, the prevalence of periodontal disease was 53.62% (74 cases). In the studied group, 48 patients with periodontitis manifested as a result of systemic diseases were included (tab. I).

TABLE I.
Study Group Structure Based on Periodontal Involvement

	Count	%
Periodontitis absent	64	46.38%
Without signs of periodontal disease	18	13.04%
Gingival diseases that are not induced by the dental biofilm	25	18.12%
Gingivitis induced by dental biofilm	21	15.22%
Periodontitis present	74	53.62%
Periodontitis	26	18.84%
Periodontitis appeared as a manifestation of systemic diseases	48	34.78%

High blood pressure was found in 67.39% of the cases included in the study (93 cases). The distribution of cases according to the degree of high blood pres-

sure showed a frequency of 18.84% for grade 1 high blood pressure, 28.99% for grade 2 high blood pressure, and 19.57% for grade 3 high blood pressure (tab. II).

TABLE II.
Frequency of high blood pressure in the study group

	Count	%
No high blood pressure	45	32.61%
High blood pressure	93	67.39%
High blood pressure grade 1	26	18.84%
High blood pressure grade 2	40	28.99%
High blood pressure grade 3	27	19.57%
Total	138	100%

The evaluation of the association of periodontitis with the presence of high blood pressure revealed a frequency of 89.19% of cases with periodontitis/periodontal disease that associates high blood pressure. The frequency of cases that associated periodontitis and hypertension (89.19%) was

significantly higher ($\chi^2=34.50$, $p < 0.001$) compared to the frequency of cases without periodontitis with hypertension (42.19%) (tab. III).

The analysis of the frequency of cases according to the degree of hypertension noted in table IV.

TABLE III.
Association of periodontitis with the presence of high blood pressure

		Periodontal disease		Total
		absent	present	
High blood pressure	absent	37	8	45
	%	57.81%	10.81%	
	present	27	66	93
	%	42.19%	89.19%	
	Total	64	74	138
Pearson's chi-squared test: $\chi^2=34.50$, $p < 0.001$ Spearman correlation: $r=0.5338$				

TABLE IV.
Evaluation of the presence of periodontal disease according to the degree of high blood pressure

		Periodontal disease		Total
		absent	present	
High blood pressure	absent	37	8	45
	%	57.81%	10.81%	
	grade 1	18	8	26
	%	28.13%	10.81%	
	grade 2	7	33	40
	%	10.94%	44.59%	
	grade 3	2	25	27
	%	3.13%	33.78%	
	Total	64	74	138
Pearson's chi-squared test: $\chi^2=58.61$, $p < 0.001$ Spearman correlation: $r=0.62649$				

In the context in which the specialized literature mentions a series of risk factors for both periodontitis and high blood pressure, demographic and clinical parameters were analyzed as possible associated risk

factors. Thus, they were analyzed as risk factors associated with periodontitis in increasing the chance of high blood pressure.

Gender. The gender of the patients did not present a significant association with

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periodontitis, an aspect that demonstrates the homogeneity of the group created by the consecutive introduction of cases according to the inclusion and exclusion cri-

teria in the group. In the analyzed group, the presence of periodontal disease showed a frequency of 54.05% in men and 45.95% in women (tab. V).

TABLE V.
Association of periodontal disease with gender of patients

		Periodontal disease		Total
		absent	present	
Patients gender	male	36	40	76
	%	56.25%	54.05%	
	female	28	34	62
	%	43.75%	45.95%	
	Total	64	74	138
Pearson's chi-squared test: $\chi^2=0.0668$, $p=0.7959$ Spearman correlation: $r=0.02201$				

The descriptive evaluation of the frequency of periodontal disease cases according to the gender of the patients and the association of high blood pressure revealed a significantly ($\chi^2 = 4.98$, $p = 0.03198$) higher proportion of male cases associating high blood pressure in the case of periodontal disease.

Age. The age of the patients included in the study group showed an average of 48.57 years (SD – standard deviation =

11.53). The minimum age values were 21 years, and the maximum values were 68 years. It was also noted that 50% of the analyzed patients were younger than 51 years old.

Comparing the values of the patients' age according to the presence of periodontitis, a non-normal distribution was noted. The very high frequency of cases with periodontal disease between the ages of 55 and 60 is noted (tab. VI).

TABLE VI.

Statistical indicators of patients' age according to the presence of periodontal disease

Periodontal disease	Average Age	Average		Dev. std	Min	Max	Q25	Median	Q75
		-95%	-95%						
Absent	42.19	39.58	44.79	10.44	21.00	58.00	32.50	45.00	49.50
Present	54.08	51.89	56.27	9.44	28.00	68.00	50.00	56.00	60.00
All Groups	48.57	46.62	50.51	11.53	21.00	68.00	38.00	51.00	57.00
Test statistic: Mann-Whitney U Test: $Z = -6.4193$, $p < 0.001$ Levene Test of Homogeneity of Variances: $F=5.5376$, $p=0.02004$									

Residence. Considering the fact that the literature presents socio-economic status as an important risk factor for periodontal disease, we evaluated the rural residential environment as a possible element that can

represent a risk for periodontal disease. This aspect can be explained by the limited access to dental care.

The results indicated an inhomogeneous sample in terms of resident environment (U:

R → 90:48). In order to eliminate this particular aspect of the two analyzed groups of patients, the frequency of periodontal disease was evaluated by referring to the number of patients in each group corresponding to the residence environment.

The analysis demonstrated a signifi-

cant association ($p = 0.0126$) of the rural environment of rural residence and the presence of periodontal disease in patients from the analysed group (62.5%). In the group of patients from the urban environment, the presence of periodontal disease was found at 48.89% (tab. VII).

TABLE VIII.
Association of periodontal disease with the domicile of the patients

		Periodontal disease		Total
		absent	present	
Residence	Urban	46	44	90
		51.11%	48.89%	
	Rural	18	30	48
		37.50%	62.50%	
		64	74	138
Pearson's chi-squared test: $\chi^2=12.332$, $p = 0.0126$ Spearman correlation: $r=0.3707$				

The analysis of the correlation between the presence of periodontal disease, high blood pressure and the gender of the patient demonstrated a significant association ex-

plained by the high frequency of cases with periodontal disease, high blood pressure coming from rural areas (62.5%) (tab. VIII).

TABLE VIII.
Association of periodontal disease with high blood pressure and gender of patients

	High blood pressure	Urban	Rural	Total
		Periodontal disease absent	HBP absent	26
	28.89%		22.92%	
Total	HBP present	20	7	27
		22.22%	14.58%	
Pearson's chi-squared test: $\chi^2 = 7.11272$, $p = 0.7381$ Spearman correlation: $r=-0.1823$				
Periodontal disease present	HBP absent	8	0	8
		8.89%	0.00%	
Total	HBP present	36	30	66
		40.00%	62.50%	
Column Total		44	30	74
		90	48	138
Pearson's chi-squared test: $\chi^2 = 8.9718$, $p = 0.00274$ Spearman correlation: $r = 0.6225$				

DISCUSSION

This result once again argues for the assessment of the bidirectional correlation between periodontal disease and hypertension. The approach in this study of a retrospective analysis will allow the analysis of this correlation only from the perspective of identifying to what extent periodontal disease increases the chance/risk of hypertension.

Over the past twenty years, multiple studies have demonstrated that persons with periodontitis have an increased susceptibility to cardiovascular events, such as myocardial infarction, peripheral artery disease, stroke, and heart failure (HF).

Crucially, pre-clinical research has also corroborated this association. For example, Akamatsu and colleagues showed that periodontal infections caused myocarditis and/or myocardial infarction in mice (17).

While a potential correlation between cardiovascular disease (CVD) and periodontitis has been seen in clinical settings, the specific mechanism that links these two conditions has not yet been fully understood. However, the primary mechanism that explains this association seems to be the spread of oral pathogens into the bloodstream.

For example, bacteremia, which is frequently produced by both non-surgical and surgical dental procedures, is a significant contributor to infective endocarditis in those who are prone to heart disease (18). Therefore, individuals with heart disease who are undergoing dental procedures are offered prophylaxis (18).

The underlying physiological processes responsible for oral health or periodontal disease and hypertension are not thoroughly comprehended. Several studies have indicat-

ed that individuals with primary arterial hypertension and poor dental health are more prone to experiencing oxidative stress. This can lead to higher levels of reactive oxygen metabolites, lipid peroxidation, and reduced total antioxidant capacity. This may lead to the deactivation of prostacyclin and nitric oxide (NO). Therefore, an increase in peripheral vascular resistance and hypertension is observed (19, 20).

The correlation between periodontitis and hypertension is crucial, as the advancement of cardiovascular disease is greatly influenced by the level of blood pressure management attained in individuals with hypertension. Fifteen Identifying modifiable risk factors for the advancement of hypertension-induced damage is a top goal worldwide, given its substantial impact on illness, death, and healthcare costs.

Additionally, our investigation was subject to many constraints. The design of our study precludes us from making causal inferences about our findings, as we lack information on the time sequence of the relationship between periodontal disease and blood pressure. Nevertheless, hypertension is unlikely to be a direct cause of periodontal disease.

Additionally, our study was constrained by a small sample size, which resulted in insufficient statistical power for conducting subgroup analyses on specific groups such as diabetics, individuals who have never smoked, and individuals who are former or present smokers.

Although our study has limitations, it clearly shows a potential significant connection between periodontal health and the control of blood pressure. This finding could have a significant influence on public health, particularly among the older popu-

lation. Due to the constraints of our study, additional research is required to validate this correlation in different populations.

CONCLUSIONS

The link between periodontal disease and cardiovascular disease is multifaceted, involving mechanisms such as inflammation, common genetic factors, and systemic responses to oral pathogens.

The results of the retrospective study, together with the findings from various studies, support a significant association between these two conditions, underscoring the importance of considering periodontal health in the management of cardiovascular

disease.

Understanding and addressing the interaction between periodontal disease and cardiovascular health is critical to comprehensive patient care and disease prevention strategies.

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