

# The Frequency of Periodontitis in A population with Cardiovascular disease:A clinical Cross-sectional Study

Muna S. Elburki

Department of Periodontics, Faculty of Dentistry, University of Benghazi, Libya

**Correspondence:** Muna S. Elburki, BDS, MPhil, PhD, Department of Periodontics, Faculty of Dentistry, University of Benghazi, Benghazi, Libya, Email [muna.elburki@uob.edu.ly](mailto:muna.elburki@uob.edu.ly)

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## Abstract

**Background:** Periodontal disease in addition to being the most prevalent chronic inflammatory illness known to mankind and the main reason for adult tooth loss, it has also been related to a number of other medical conditions, including Cardiovascular disease (CVD).

CVD and periodontitis are closely related. Periodontitis increases the systemic inflammatory burden, which worsens CVD and the CVD can affect the progression of periodontal disease. We don't fully understand how one disease can affect another disease. The purpose of this study was to determine the prevalence and severity of periodontitis in patients with CVD according to the new 2017 classification of periodontal and peri-implant diseases.

**Methods:** This cross-sectional study included 137 participants with CVD. Patients' data was collected as face-to-face interviews, followed by clinical examination for each participant. Aproximal plaque index and bleeding on

probing were recorded. Probing depth and clinical attachment level were measured. The subjects were categorized into three groups: periodontally healthy individuals, gingivitis and periodontitis. The severity of periodontitis has been identified.

**Results:** Out of 137 subjects who participated in the study, 57 were male and 80 were female, with a mean age of 54.5 years. Poor oral hygiene and periodontitis were found to be much higher among CVD patients. 97.0% of them have periodontitis and 90.5% have severe forms (stage III and IV).

**Conclusions:** Periodontitis is relatively common in patients with CVD. Further research is necessary to determine whether the association is fundamental and if the management of periodontal disease could be beneficial for the CVD patient.

**Keywords:** Periodontitis, Cardiovascular disease, Systemic inflammation, C-reactive protein

**Abbreviations:** CVD: Cardiovascular disease, MMPs: Matrix metalloproteinases, HsCRP: High sensitivity C-reactive protein, LPS: Lipopolysaccharide, IL-6: Interleukin 6, BOP: Bleeding on probing, PD: Probing depth, CAL: Clinical attachment level.

## Introduction

Periodontitis is a chronic inflammatory illness that affects millions of people worldwide and is one of the most common long-term infections. 10-15% of people have severe forms of the illness, which places a significant inflammatory load on the population. According to reports, those with advanced periodontitis are far more likely to experience cardiovascular disease (CVD), which includes atherosclerosis, myocardial infarction, and stroke. It is well-recognized that coronary heart disease and premature death in males are closely associated. A growing body of evidence suggests a connection between periodontal disease and an elevated risk of CVD.<sup>1-4</sup>

Periodontal disease is initiated by bacteria predominantly anaerobic gram-negative microorganisms for instance, Porphyromonas gingivalis (*P. gingivalis*), Prevotella intermedia, Tannerella forsythia and others in the subgingival plaque or biofilm, or their microbial products particularly lipopolysaccharide (LPS) or endotoxin (a constituent of the cell wall of these gram-negative bacteria), inducing inflammation in the adjacent gingival and periodontal tissues. However, it is now generally acknowledged that the host response

plays a significant role in mediating the degradation of collagen and connective tissue in the gingiva and periodontal ligament as well as the loss of alveolar bone.<sup>5-7</sup>

When LPS and other chemicals reach the gingival tissues, they trigger and spread immuno-inflammation, which results in the production of more proinflammatory cytokines than normal. they, along with other inflammatory mediators, trigger the formation of matrix metalloproteinases (MMPs), which break down the connective tissues of the gingiva and periodontal ligament; they, along with prostaglandins, promote the resorption of alveolar bone.<sup>8,9</sup>

There is evidence of systemic inflammation in individuals with chronic destructive periodontitis, as shown by elevations in C-reactive protein (CRP), fibrinogen, interleukin 6 (IL-6), and other circulating indicators, such as higher cholesterol levels.<sup>10,11</sup> Inflammation throughout the body has been linked to CVD and periodontitis. Additionally, the risk factors for both periodontitis and several systemic disorders, notably cardiovascular disease, include smoking, being a man, being of a certain race or ethnicity, stress, age, and, in particular, diabetes.<sup>5</sup>

The American Academy of Periodontology reports that although the research isn't conclusive yet, those with periodontal disease are almost twice as likely to have coronary artery disease. In this regard, one study discovered that the prevalence of common oral health issues

including gingivitis, cavities, and tooth loss were just as effective at predicting CVD illness as high cholesterol levels.<sup>12</sup>

Given the high prevalence of both periodontal disease and CVD in industrialized cultures, a relationship between the two conditions may have significant public health implications. The potential effects on public health and the possibility that this research will help develop periodontal disease treatment plans that can break this link make it worthwhile to look into the relationship between periodontal disease and CVD. Additionally, when combined with other risk profile characteristics, periodontal parameters such as bleeding on probing, probing depth (PD), and clinical attachment level (CAL) may help determine CVD risk.<sup>13,14</sup>

The current study aimed to estimate the prevalence and severity of periodontitis in patients with CVD according to the new 2017 classification of periodontal and peri-implant diseases,<sup>15</sup> as well as to develop an effective risk assessment criteria for CVD.

## Subjects and methods

A cross-sectional study was carried out at the largest heart center in Benghazi /Libya (National Heart Center). The *Research Ethics Committee of the Faculty of Dentistry/University of Benghazi* reviewed and approved the study protocol. All participants received an explanation of the procedure and provided informed consent. A total of 137 patients, both male and female, were included in the study (sample size calculation was based on the number of patients who visited the National Heart Center by statistic).

### Inclusion criteria

Patients with CVD for at least 6 months and aged  $\geq 20$  years were included in the study. Patients with a known history of congenital heart disease and patients with a risk of infective endocarditis were excluded from the study. Patients with a history of malignancy and patients who had received periodontal therapy within six months before the examination were also excluded from the study.

### Data Collection Method:

Patients' data included the patient's age, sex, smoking status, frequency of brushing, history of heart disease and heart surgery, medications, and any systemic diseases other than CVD. All cases were diagnosed based on the patient's medical history, which was reviewed by a certified physician, as well as some laboratory tests.

### Clinical Periodontal Examination:

The clinical examination was performed by one examiner who calibrated the exact diagnostic procedure for the patients. The

aproximal plaque index (API) by Lange<sup>16</sup> and the bleeding on probing (BOP) by Ainamo and Bay<sup>17</sup> were used to assess the periodontal and oral hygiene status.

With a periodontal Michigan O probe, a full mouth periodontal examination and periodontal charts were done for all the participants. Probing depth (PD) and clinical attachment level (CAL) were measured on six locations of the teeth (mesio-facial, mid-facial, disto-facial, mesio-lingual, mid-lingual, disto-lingual) excluding third molars. Tooth loss due to periodontitis will be addressed through history taking from the patient.

Based on the clinical examination and periodontal status according to the new 2017 classification of periodontal and peri-implant diseases,<sup>18</sup> subjects were categorized into three groups: periodontally healthy individuals, gingivitis and periodontitis. The severity of periodontitis was determined as (stage I, stage II, stage III and stage IV).

## Statistical Analysis

Version 28 of the Statistical Package for Social Science (SPSS) was employed in the investigation.

The findings were summarized using descriptive statistics, such as means, standard deviations, and percentages. Spearman's correlation coefficient was used to assess numerical correlations.

## Results

### Demographic Data and Personal Behavior:

To estimate the prevalence and severity of periodontitis in a sample of the Libyan population with CVD, a clinical cross-sectional study including 137 participants was conducted. Out of 137 subjects that took part in the study, the average age was  $54.5 \pm 13.2$  years; 57 (41.6%) men and 80 (58.4%) women made up the study's participant population.

Out of the 137 participants, 95 (69.3%) have hypertension and 57 (41.6%) have diabetes mellitus.

Smoking status was assessed as a smoker, former smoker and non-smoker. Out of the 137 participants, 21 (15.3%) were smokers, 21 (15.3%) of them were former smokers and 95 (69.4%) were non-smokers. All smokers were male (Table 1).

Examination of the oral cavity reveals poor oral hygiene in almost all of the participants (97.0%). The average aproximal plaque index (API) was 82.5% and the average bleeding on probing (BOP) was 46.1% (Table 2).

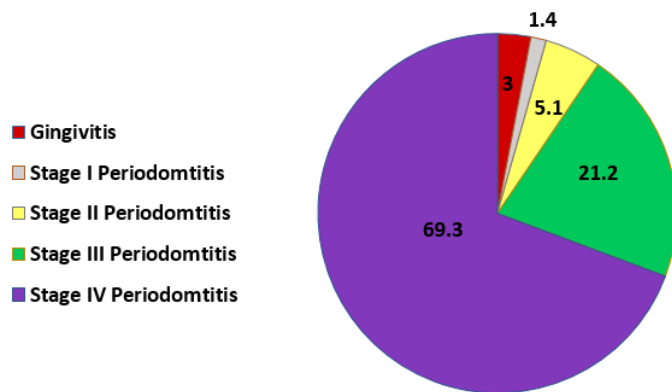
**Table 1** Descriptive data of CVD patients with different stages of periodontitis

Parameters	Total Sample	Periodontitis Stage			
	Mean $\pm$ SD	Stage I	Stage II	Stage III	Stage IV
Age	13.7 $\pm$ 50.45	12.0 $\pm$ 38.5	13.4 $\pm$ 50.2	5.7 $\pm$ 53.7	12.3 $\pm$ 61.5
Sex	Female n (%)	2 (2.6)	3 (3.9)	12 (15.5)	60 (78)
	Male n (%)	0 (0)	4 (7.1)	17 (30.4)	35 (62.5)
Smoking Status	Male n (%)	0 (0)	3 (14.3)	4 (19)	14 (66.7)
	Female n (%)	0	0	0	0
<b>Medical Condition</b>					
Hypertension	n (%)	1 (1.1)	6 (6.3)	20 (21.1)	68 (71.5)
Diabetes Mellitus	n (%)	0 (0)	2 (3.5)	9 (15.8)	46 (80.7)

**Table 2** Periodontal clinical parameters of CVD patients with different stages of periodontitis

Parameters	Total Sample	Periodontitis Stage			
	Mean ± SD	Stage I	Stage II	Stage III	Stage IV
<b>Clinical Parameters</b>					
Mean CAL (mm)	5.9±2.3	2.25±0.5	3.7±0.4	6.4±1.5	8.0±1.5
Aproximal plaque index (API)%	82.5±23.4	79±28.8	86.3±22.5	76.3±26.9	83.6±20.3
Bleeding on probing (BOP)%	46.1±39.3	39.5±47.2	55.3±40.1	30.8±32.2	47.7±40.6
Number of missing teeth	10.0±8.1	1.5±0.7	2.3±2.7	2.7±1.6	13.4±7.4

The majority of the 137 participants (97.0%) had some form of periodontitis, ranging from stage I to stage IV periodontitis and 3% of these cases have gingivitis (Figure 1).



**Figure 1** Pie chart showing the percentage of gingivitis and different stages of periodontitis in CVD patients.

### Periodontitis and Medical Status

With 95 (69.3%) patients, hypertension was the most common medical condition among patients with CVD, followed by 57 (41.6%) patients with diabetes mellitus. Table 1 shows the prevalence of medical conditions in each stage of periodontitis. 1.1% of hypertensive individuals had stage I periodontitis, 6.3% had stage II periodontitis, 21.1% had stage III periodontitis, and 71.5% had stage IV periodontitis. Patients with diabetes mellitus had 0% stage I periodontitis, 3.5% stage II periodontitis, 15.8% had stage III periodontitis, and 80.7% had stage IV periodontitis (Table 1).

### Prevalence of Periodontitis in CVD

The incidence and percentage of stages of periodontitis in CVD patients are shown in Figure 1. Stage IV was the most common stage of periodontitis with 69.3% (95) followed by stage III with 21.2% (29) then stage II with 5.1% (7) while the least common stage was stage I with 1.4% (2) as shown in Figure 1. The average tooth loss was 10.0± 8.1. Out of the 137 participants, 128 (93.4%) have missing teeth and 9 (6.6%) of them have all teeth present (Table 2).

### Correlation between Various Variables

Table 1 displays descriptive data from CVD patients with various stages of periodontitis. There was no significant association between gender and periodontitis stages (Table 1). There was a strong positive correlation between age and stage of periodontitis ( $r_s = 0.4$ ). The most advanced stage of periodontitis, which is stage IV, was more common in older patients and vice versa (Table 1).

### Discussion

Periodontal disease's significance in the etiology of cardiovascular disease has recently gained considerable attention. Previous research

has yielded conflicting results regarding whether periodontitis is associated with an increased risk of cardiovascular disease; however, numerous studies have shown that patients with chronic destructive periodontitis have evidence of systemic inflammation, which can link periodontitis and cardiovascular disease.<sup>18-21</sup> Furthermore, smoking, male gender, aging, and diabetes are all risk factors for periodontitis and cardiovascular disease.<sup>5</sup>

This study aimed to estimate the prevalence and severity of periodontitis in patients with CVD, as well as to develop an effective risk assessment criteria for CVD. A total of 137 participants were included. The mean age of the participants was (54.5 + 13.2) years and this was in agreement with previous studies that reported similar mean ages of participants.<sup>22,23</sup> In addition, gender distribution showed a higher prevalence of CVD in females (58.4%) than in males (41.6%) among the participants. This result contradicts other studies, which stated the number of males was significantly higher than female patients.<sup>3,24</sup> Although, there was a significant association between periodontal disease and CVD in men and women, no significant sex difference was found ( $P > 0.05$ ) and this result aligned with a study by Leng et al. who stated that the increased risk of CVD is associated with periodontal disease independent of sex.<sup>25</sup>

Periodontal clinical parameters such as plaque index (PI), bleeding on probing (BOP), and CAL were used to evaluate the condition of periodontal tissues. These are the most reliable parameters to assess periodontal health status and are commonly used in studies nowadays.<sup>22,23,26,27</sup> Considering plaque accumulation, the average score was notably high (82.5 ± 23.4) which has been testified by earlier studies.<sup>23,28</sup> suggested that high plaque scores in patients with CVD may be because of neglecting oral health care as a whole due to their systemic illness. Accordingly, it can be concluded that a high plaque score in the present study typically was the effect of poor oral hygiene. Additionally, inadequate oral hygiene in patients with CVD could be related to antidiuretic drugs, which could reduce salivary flow and decrease lubrication in the oral cavity, consequently, promoting dental biofilm accumulation.<sup>29</sup> In addition to the patients' substantial deposition of dental biofilm, the rate of gingival bleeding was (46.1%).

Regarding the frequency of periodontitis among CVD patients, there were 97% (133 out of 137 participants) have periodontitis which was in line with several studies that documented similar results.<sup>22,26,30</sup> Moreover, our results presented that 90.5% of the participants have severe forms of periodontitis (stage III & IV), but stage I periodontitis was the least prevalent stage of periodontitis (1.4%) followed by stage II (5.1%). These results agree with Schmalz et al. who concluded that the majority of the patients (88.7%) with severe heart failure had stage III or IV periodontitis.<sup>22</sup>

In addition, the average tooth loss was 10.0± 8.1. Out of the 137 participants, 128 (93.4%) have missing teeth and 9 (6.6%) of them have all teeth present.

Concerning the medical status of patients, our results demonstrated that hypertension and diabetes mellitus were the most prevalent medical conditions (69.3% and 41.6% respectively) and this was in accordance with previous studies, which confirmed that the most common medical problems in their studies were hypertension and diabetes mellitus.<sup>30</sup> Furthermore, our study also revealed the frequency of periodontitis with different stages among hypertensive and diabetic patients with CVD. Considering hypertension, the present study detected a high prevalence of severe periodontitis (Stage IV, 71.5%) in CVD patients. Similarly, Tadjoeeddin et al.<sup>30</sup> reported a high incidence of severe periodontitis (Stage III, 71.4%) in hypertensive patients. The association between periodontitis and hypertension could be attributed to many factors including stress, tobacco smoking, aging, socioeconomic factors and the amount of pathogenic periodontal bacteria.<sup>31-33</sup>

Regarding diabetes, our study documented a high frequency of severe periodontitis (Stage IV, 80.7%) in diabetic patients with CVD. This fact agrees with Schmalz et al.<sup>34</sup> who expressed a high frequency of severe periodontitis (70.9%) in diabetic patients with CVD, depending on the definition of the American Academy of Periodontology/Centers for Disease Control and Prevention (AAP/CDC) case definitions of 2007.<sup>35</sup> Moreover, Tadjoeeddin et al.<sup>30</sup> established a high frequency of severe periodontitis (Stage III, 83.1%) in diabetic patients. In addition, many patients with CVD have been receiving diabetes therapy for several years. Therefore, there is a general assumption that diabetes mellitus is the main cause of CVD. Furthermore, diabetes is considered a significant risk factor for severe periodontitis<sup>36</sup> and this could explain the link between CVD and periodontitis.

In our research, we also found a significant association between age and periodontitis stage ( $rs = 0.4$ ). Moreover, severe periodontitis (stage IV) was more prevalent among patients of older age and this fact was in agreement with other studies.<sup>37,38</sup> The alteration in the periodontium associated with the age of the patient supports the idea that age could be a risk indicator for periodontal disease progression.<sup>39</sup> The current study found a substantial link between periodontal disease and CVD, as well as a near-100% incidence of periodontal disease in CVD patients, and almost all CVD patients had a severe form of the disease with 90.5% having stage III and IV periodontitis. Although there was a positive correlation between periodontal disease and an increased risk of CVD, we cannot rule out the possibility that general risk factors such as tobacco use, male gender, race/ethnicity, stress, aging, and, in particular, diabetes, have an effect on the severity of periodontal disease and are also considered CVD risk factors. Periodontal disease was substantially associated with CVD; thus, periodontal parameters such as bleeding on probing (BOP), probing depth (PD), and clinical attachment level (CAL) may be effective risk assessment criteria for CVD. A high serum level of high-sensitivity CRP (HsCRP) is a biomarker of systemic inflammation that greatly increases the risk of CVD<sup>20,40</sup> and could be used to assess CVD risk. However, because HsCRP cannot be used to diagnose CVD with certainty, periodontal parameters and HsCRP could be utilized in conjunction with other risk factors. Therefore, our approach has been to evaluate the situation in which the dentist discovers severe periodontitis ( $PD \geq 6$  mm) and must determine whether to refer the patient for specialist evaluation. According to the literature, severe periodontitis is strongly associated with CVD. As a result, they could be used in conjunction with other risk factors such as obesity, tobacco smoking, race/ethnicity, stress, advancing age, hypertension, and, in particular, diabetes, and the patient should be referred for consultation if there is one positive dental risk factor and one positive general risk factor.

## Conclusion

To the best of our knowledge, this is the first study to estimate the prevalence and severity of periodontitis in Libyan population with CVD. Periodontitis is relatively common in patients with CVD. Therefore, more research is needed to determine the strength of the link between CVD and periodontal disease and if the management of periodontal disease could be beneficial for the CVD patient. We believe the optimal strategy for assessing the relationship between CVD and periodontal disease would be a longitudinal examination of systemic inflammatory markers and changes in periodontal parameters. Although, the current study does not prove causation, nonetheless, the results fit well with the existing literature's conclusions.

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## Competing Interests

The authors declare no conflict of interest.

## References

1. Katz, Joseph, Gavriel Chaushu, et al. On the association between hypercholesterolemia, cardiovascular disease and severe periodontal disease. *J Clin Periodontol.* 2001;28(9):865–868.
2. Beck James D, Paul Eke, Gerardo Heiss, et al. Periodontal Disease and Coronary Heart Disease: A Reappraisal of the Exposure. *Circulation.* 2005;112(1):19–24.
3. Howell T Howard, Paul M Ridker, Umed A Ajani, et al. Periodontal disease and risk of subsequent cardiovascular disease in U.S. male physicians. *J Am Coll Cardiol.* 2001;37(2):445–450.
4. Grau Armin J, Heiko Becher, Christoph M Ziegler, et al. Periodontal Disease as a Risk Factor for Ischemic Stroke. *Stroke.* 2004;35(2):496–501.
5. Demmer Ryan T, Moïse Desvarieux. Periodontal infections and cardiovascular disease. *J Am Dent Assoc.* 2006;137:S14–S20.
6. Gitlin JM, CD Loftin. Cyclooxygenase-2 inhibition increases lipopolysaccharide-induced atherosclerosis in mice. *Cardiovasc Res.* 2008;81:400–407.
7. Elburki, Muna S. The Etiology and Pathogenesis of Periodontal Disease 4, 2018.
8. Page Roy C. The pathobiology of periodontal diseases may affect systemic diseases: inversion of a paradigm. *Ann Periodontol.* 1998;3(1):108–120.
9. Elburki Muna S, Carlos Rossa, Morgana R Guimaraes, et al. A novel chemically modified curcumin reduces severity of experimental periodontal disease in rats: initial observations. *Mediators. Inflamm.* 2014;2014:1–10.
10. Elburki MS, DD Moore, NG Terezakis, et al. A novel chemically modified curcumin reduces inflammation-mediated connective tissue breakdown in a rat model of diabetes: periodontal and systemic effects. *J Periodontal Res.* 2017;52:186–200.
11. Slade Gary D, Elisa M Ghezzi, Gerardo Heiss, et al. Relationship between periodontal disease and c-reactive protein among adults in the atherosclerosis risk in communities study. *Arch Intern Med.* 2003;163.

12. Meurman Jukka H, Mariano Sanz, Sok-Ja Janket. Oral health, atherosclerosis, and cardiovascular disease. *Crit Rev Oral Biol Med*. 2004;15:403–413.
13. D’Aiuto F, M Parkar, G Andreou, et al. Periodontitis and systemic inflammation: control of the local infection is associated with a reduction in serum inflammatory markers. *J Dent Res*. 2004;83:156–160.
14. Ridker Paul M, Eleanor Danielson, Francisco A H Fonseca, et al. Rosuvastatin to prevent vascular events in men and women with elevated c-reactive protein. *N Engl J Med*. 2008;359:2195–2207.
15. Tonetti Maurizio S, Henry Greenwell, Kenneth S Kornman. Staging and grading of periodontitis: framework and proposal of a new classification and case definition. *J Periodontol*. 2018;45:S149–S161.
16. Lange DE, HC Plagmann, A Eenboom, et al. A. Clinical methods for the objective evaluation of oral hygiene. *Dtsch Zahnarzt Z*. 1977;32(1):44–47.
17. Ainamo J, I Bay. Problems and proposals for recording gingivitis and plaque. *Int Dent J*. 1975;25(4):229–235.
18. Desvarieux Moïse, Ryan T Demmer, Tatjana Rundek, et al. Relationship between periodontal disease, tooth loss, and carotid artery plaque: the oral infections and vascular disease epidemiology study (INVEST). *Stroke* 34(9):2120–2125.
19. Offenbacher Steven, James D Beck, Kevin Moss, et al. Results from the periodontitis and vascular events (pave) study: a pilot multicentered, randomized, controlled trial to study effects of periodontal therapy in a secondary prevention model of cardiovascular disease. *J Periodontol*. 2009;80(2):190–201.
20. Muhsin, Jasim M. The possible connection of periodontal diseases (pd) with cardiovascular disease (cvd) and prostatitis in sample of iraqi patients. *Muthanna Medical Journal*. 2019;6:1–12.
21. Trevisan, Maurizio, Joan Dorn. The Relationship Between Periodontal Disease (PD) And Cardiovascular Disease (CVD). *Mediterranean Journal of Hematology and Infectious Diseases*. 2010;2:e2010030.
22. Schmalz Gerhard, Alina Hennecke, Rainer Haak, et al. Secondary analysis of potential associations between oral health and infection-related parameters in patients with severe heart failure—results of a German cohort. *BMC Cardiovasc Disord*. 2023;23(1):573.
23. Wojtkowska Agnieszka, Tomasz Zapolski, Joanna Wysokińska-Miszczuk, et al. The inflammation link between periodontal disease and coronary atherosclerosis in patients with acute coronary syndromes: case-control study. *BMC Oral Health*. 2021;21(1):5.
24. Larvin Harriet, Jing Kang, Vishal R Aggarwal, et al. Risk of incident cardiovascular disease in people with periodontal disease: A systematic review and meta-analysis. *Clin Exp Dent Res* 2021;7(1):109-122.
25. Leng, Yurong. Periodontal disease is associated with the risk of cardiovascular disease independent of sex: A meta-analysis. *Front Cardiovasc Med*, 2023.
26. Schmalz Gerhard, Sven-Paul Zöbisch, Jens Garbade, et al. No Association between Clinical Periodontal Conditions and Microbiological Findings on Driveline of Patients with Left-Ventricular Assist Devices (LVAD). *Antibiotics (Basel)*. 2021;10(10):1219.
27. Nakayama Yohei, Shinichi Tabe, Arisa Yamaguchi, et al. Identification of Nutritional Factors to Evaluate Periodontal Clinical Parameters in Patients with Systemic Diseases. *Nutrients*. 2023;15(2):365.
28. Rodean Ioana-Patricia, Luminița Lazăr, Vasile-Bogdan Halațiu, et al. Periodontal Disease Is Associated with Increased Vulnerability of Coronary Atheromatous Plaques in Patients Undergoing Coronary Computed Tomography Angiography—Results from the Atherodent Study. *J Clin Med*. 2021;10(6):1290.
29. I Hanim Afzan, Nur Karyatee K, Fatimah Zahra, et al. Periodontal Health of Pre-Dialysis Chronic Kidney Disease Patients in a Northeast Peninsular Malaysia Tertiary Hospital. *Malays J Med Sci*. 2020;27(1):106–114.
30. Tadjoeidin Ete Ss, Nabila P Dewi, Yuniarti Soeroso, et al. Stage and grade determination of periodontitis accompanied by systemic conditions and diseases according to American Academy of Periodontology 2017 Classification: Study at Dental Hospital, Faculty of Dentistry, Universitas Indonesia. *Journal of Dentomaxillofacial Science*. 2021;6:88.
31. Engström Sevek, Lars Gahnberg, Hans Högberg, et al. Association between High Blood Pressure and Deep Periodontal Pockets. *Ups J Med Sci*. 2007;112(1):95–103.
32. Lockhart Peter B, Ann F Bolger, Panos N Papapanou, et al. Periodontal Disease and Atherosclerotic Vascular Disease: Does the Evidence Support an Independent Association?. *Circulation*. 2012;125(20):2520–2544.
33. Desvarieux Moïse, Ryan T Demmer, David R Jacobs, et al. Periodontal bacteria and hypertension : the oral infections and vascular disease epidemiology study ( INVEST ). *J Hypertens*. 2010;28(7):1413–1421.
34. Schmalz Gerhard, Nora Schiffers, Sandra Schwabe, et al. Dental and periodontal health , and microbiological and salivary conditions in patients with or without diabetes undergoing haemodialysis. *Int Dent J*. 2017;67(3):186–193.
35. Page Roy C, Paul I Eke. Case Definitions for Use in Population-Based Surveillance of Periodontitis. *J Periodontol*. 2007;78(7 Suppl):1387–1399.
36. Gayathri S, Koshi Elizabeth, Arun Sadasivan, et al. Effect of Initial Periodontal Therapy on Serum Nitric Oxide Levels in Chronic Periodontitis Patients with or without Type 2 Diabetes Mellitus. *J Contemp Dent Pract*. 2019;20(2):197–203.
37. Wulandari Pitu, Dody Widkaja, Aini Hariyani Nasution, et al. Association between age, gender and education level with the severity of periodontitis in pre-elderly and elderly patients. *Dental Journal*. 2022.
38. Södal Anne Thea Tveit, et al. Periodontitis in a 65-year-old population: risk indicators and impact on oral health-related quality of life. *BMC Oral Health*. 2022;22(2):640.
39. Huttner Eder Abreu, Denise Cantarelli Machado, Rogério Belle De Oliveira, et al. Effects of human aging on periodontal tissues. *Spec Care Dentist*. 2009;29(4):149–155.
40. Stankovic B, I Minic. The Role of Periodontal Disease in Etiology of Myocardial Infarction. *Archives of Medicine*. 2019;11.