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Inflammatory Markers in the Blood and Chronic Periodontitis

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***Abstract*—**Background: Plasma levels of inflammatory markers are the expression of the infectious wastes of existing periodontitis, as well as of existing inflammation everywhere in the body. Materials and Methods: The study consists of the clinical part of the measurement of inflammatory markers of 23 patients diagnosed with chronic periodontitis and the recording of parental periodontal parameters of patient periodontal status: hemorrhage index and probe values, before and 7-10 days after non-surgical periodontal treatment. Results: The level of fibrinogen drops according to the categorization of disease progression, active and passive, with the biggest % (18%-30%) at the fluctuation 10-20 mg/d. Fluctuations in fibrinogen level according to the age of patients in the range 0-10 mg/dL under 40 years and over 40 years was 13%-26%, in the range 10-20 mg/dL was 26%-22%, in the 20-40 mg/dL was 9%-4%. Conclusions: Non-surgical periodontal treatment significantly reduces the level of non-inflammatory markers in the blood. Oral health significantly reduces the potential source for periodontal bacteria, with the potential of promoting thromboembolism, through interaction between thrombocytes.

***Keywords*—**Chronic periodontitis, atherosclerosis, risk factor, inflammatory markers.

I. Background

IN more than two decades, data on the link between the presence of specific dental plaque bacteria and the existence and gravity of coronary arteries arising from atherosclerosis have increased. These results have led to a new outlook on atherosclerotic aetiology. Some mechanisms may start or exacerbate the atherosclerotic process, such as: activation of innate immunity, bacteremia due to dental treatment (iatrogene), and involvement of mediators activated by dental plaque and inclusion of cytokines from bacteria dental plaque [1].

Both periodontal disease and artherosclerosis may start in early childhood, but this does not mean anything about the appearance of the first symptoms of the disease, since the latter may not appear until adulthood. Lipid formation has been reported in 10-year-olds and the increased prevalence of obesity in children and adolescents is a risk factor that initially contributes to the development of lipid plaques in specific arteries [2]. Endothelial injury, caused by the formation of lipidic plaque in childhood, can lead to bacterial penetration as consequence of temporary bacteremia in the bloodstream after oral procedures for children as well as for patients with chronic periodontitis. Epidemiological studies have already shown that periodontitis is one of the risk factors for cardiovascular, pulmonary, renal, and infantile births in babies [3]. It can be assumed that dental plaque bacteria do not only affect local oral cavity but can also contribute to the development of some serious systemic illnesses.

Prevalence of cardiovascular disease in patients with periodontitis is 25-50% higher than in healthy individuals. Oral health (potential risk factor for periodontitis) and tooth loss (a possible consequence of periodontitis) are positively associated with coronary atherosclerotic loads [4]. A link between oral health and cardiovascular disease has been proposed for more than a century. Recently, potential links between periodontitis and atherosclerosis have been intensified and are continuing to be investigated for a possible escort and causality [1]-[11]. These data were the first attempts to collect information already published, and further on the collection of clinical data on cases presented at the University Dental Clinic "Çerçiz Mingomataj" at Albanian University and other Private Clinics, which were ready to join this initiative. Based on the fact that cardiovascular diseases are one of the primary cause factors of mortality in Albanian pollutants, but also in world medicine, [6] with the prevention of periodontal diseases, if it is possible, the periodontal treatment also counteracts the prevention of atherosclerosis as one of the causes of the further progression of existing cardiac diseases. This study aims at evaluating the effect of non-surgical periodontal treatment, expressed in the levels of periodontal indexes, in correlation with the quantitative and qualitative level, of the plasma inflammatory markers.

II. Materials and Methods

The study involves the reprocessing of data collected in patients submitted to the University of Dentistry "Albanian University" and at private clinics in a period of 2 years, who willingly filled out the stages of the study protocol. After the study's involvement in the study was reached, patients underwent data recording procedures related to chronic periodontal disease. Examination of soft oral mucosal tissues of oral gingiva was done respecting the air-drying procedure and checking the mucosal relief. The signing of the consent by the patient was done after the patient was explained, in detail, the goals and studies, the stages of the protocol of involvement in the study [7].

With the aim of evaluating the level of fibrinogen and blood cells, patients underwent blood tests before and after periodontal treatment (predetermined time interval). Only patients who were diagnosed with chronic periodontitis were included in the study, based on the diagnostic criteria of this disease.

The purpose of the study involves the application of non-

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surgical periodontal surgery for the treatment of chronic peridodontitis. This type of disease with its characteristics responds well to non-surgical treatment with a treatment protocol of 2 or more stages of treatment, with a time interval of 1 week to 10 days. The treatment protocol was not included in the prescription of systemic antibiotics. This element was applied to evaluate the healing process under conditions of systemic disease deficiency [6]-[12].

Good information and consensus agreement are the stages before the application of the protocol of registration of values according to the patient evaluation indices from the periodontal point of view [7]. The need to re-elaborate the data of Heta et al. [13] is presented in the appendix to this study. Experiences in this field is a push for a return to this topic so important for the possible correlation between periodontitis and atherosclerosis, only the data on chronic periodontitis and only the clinical cases of patients with chronic periodontitis came to a halt. Out of the total of 54 patients, 23 of them were suffering from chronic periodontitis; the other group of patients was with refractory periodontitis and aggressive periodontitis. We point out that the three periodontal diseases (chronic periodontitis, aggressive periodontitis and refractory periodontitis) are diseases that have distinct clinical features that do not cover each other [14]. This fact is also mentioned in the selection criteria of patients for chronic periodontitis, the disease we are interested in in this study topic.

The criteria for selecting patients for chronic periodontitis are as follows: [15], [16]

- Swelling gingiva, colored gingiva, gingival bleeding
- Bone loss: vertical, horizontal
- Presence of the calculus in the dento-gingival connection.
- Presence of the red complex: *Bakteroides Gingivalis, Bacteroides Forsythus, Treponema Denticol*
- Systemic factors: diabetes
- Smoking
- Differential diagnosis is based on the patient's age, progression of the disease, lack of local factors that stimulate the plaque.
- Lack of pain.
- Chronic periodontitis does not advance at equal speeds in all areas.
- Chronic periodontitis accompanies the age, not a disease related to the age.

III. Results

The results obtained from the study are distributed according to the specifications in the Tables I-VI. Of the total of 54 patients diagnosed with one of three periodontal diseases included in the baseline study: refractory periodontal, aggressive periodontitis and chronic periodontitis, 23 patients met the predetermined criteria for chronic periodontitis. Table I and Fig. 1 show these data showing the percentage of chronic periodontitis, such as periodontal disease in relation to 2 other diseases.

The average age of patients is 42 years, regardless of the type of periodontitis (refractory, aggressive, or chronic periodontitis). For patients with chronic periodontitis, the average age of patients was 54 years for men and 45 for women. The average age, regardless the gender, is 50 years old. Table II and Fig. 2 summarize patients with chronic periodontitis, classified by the Mühleman index, as healthy and diseased, based on the values recorded. At health values according to the same index selected, we can rank 0-1 of index. These are the values that emphasize the immune system still at a high level to defeat the attack that originates from the onset of existing bacterial plaque that is acting in time.

TABLE I
Patients Divided by Sex and Age, for the 3 Types of Periodontitis Included in the Baseline Study

Patients	Refractory periodontitis	%	Aggressive periodontitis	%	Chronic periodontitis	%	Value p
Female	8	15%	6	11%	5	9%	
Male	13	24%	4	7%	18	33%	0.0912
Total	21	39%	10	18%	23	42%	

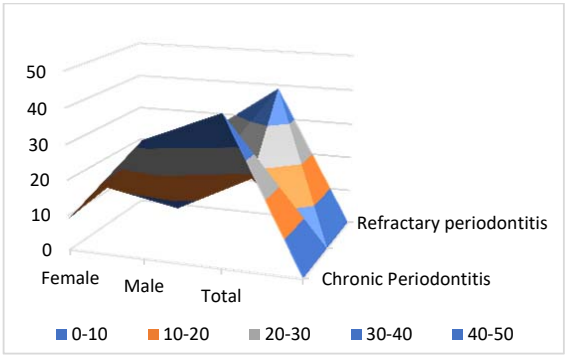

Fig. 1 Patients divided by sex and age, for the 3 types of periodontitis included in the baseline study

TABLE II
Value Fluctuations According to the Mühleman Index (IM), in Patients Divided before and after Periodontal Treatment

Patients	IM value 0-1	%	IM value 2-3	%	IM value 4-5	%	Value p
Before treatment	2	9%	13	57%	8	35%	0.0001
After treatment	17	74%	4	17%	2	9%	

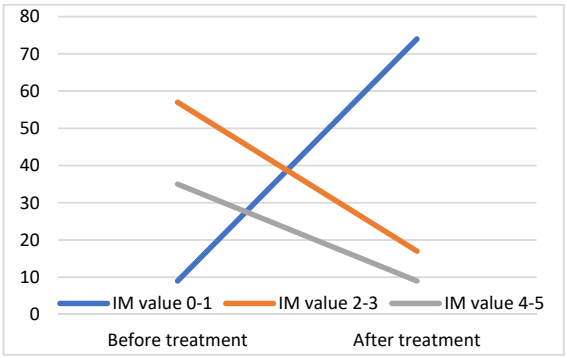

Fig. 2 Value fluctuations according to the Mühleman index, in patients divided before and after periodontal treatment

The p value indicates a very important statistical

correlation.

Table III and Fig. 3 show data on the fluctuation of probing values before and after treatment. The probes were divided into 3 categories: group 1: 0-2 mm, group: 2 3-4 mm and group 3: 5-6 mm.

TABLE III
VALUE FLUCTUATIONS ACCORDING TO PERIODONTAL PROBE VALUES, IN PATIENTS DIVIDED BEFORE AND AFTER PERIODONTAL TREATMENT

Patients	0-2 mm	%	3-4 mm	%	5-6 mm	%	Value p
Before treatment	0	0%	12	52%	11	48%	0.0001
After treatment	8	35%	10	43%	5	22%	

The p value indicates a very important statistical correlation.

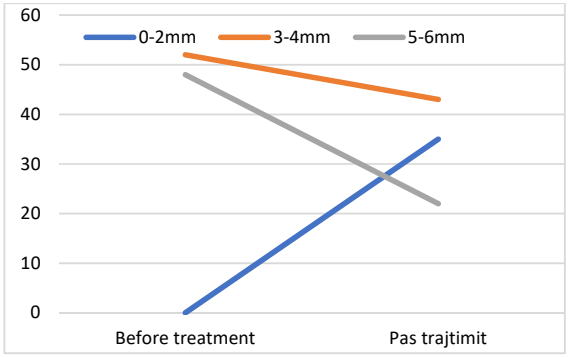

Fig. 3 Value fluctuations according to periodontal probe values, in patients divided before and after periodontal treatment.

Table IV and Fig. 4 reflect the group of patients based on the fibrinogen recorded plasma fluctuation level, 10 days post treatment.

TABLE IV
FLUCTUATIONS IN THE NUMBER OF PATIENTS ACCORDING TO THE DIFFERENCE IN FIBRINOGEN VALUE BEFORE AND AFTER TREATMENT

Patients	0-10Mg/dL	%	10-20Mg/dL	%	20-Mg/dL	%	Total
Female	0	0%	5	22%	0	0%	5
Male	9	39%	6	26%	3	13%	18
Total	9	39%	11	48%	3	13%	23

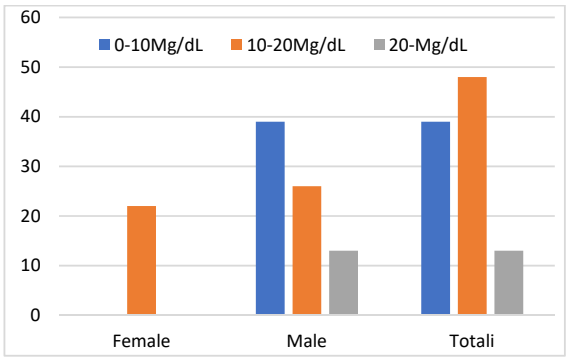

Fig. 4 The fluctuations of the number of patients according to the difference of fibrinogen value before and after treatment

Table V and Fig. 5 show the categories of patients divided according to fibrinogen fluctuations, up to the first phase of treatment of chronic periodontitis.

TABLE V
FIBRINOGEN FLUCTUATIONS AT MEASURABLE INTERVALS, ACCORDING TO THE DEGREE OF PROGRESSION OF PERIODONTAL DISEASE

Patients	0-10Mg/dL	%	10-20Mg/dL	%	20-Mg/dL	%
Active ill	2	9%	4	18%	0	0%
Passive healthy	7	30%	7	30%	3	13%
Total	9	39%	11	48%	3	13%

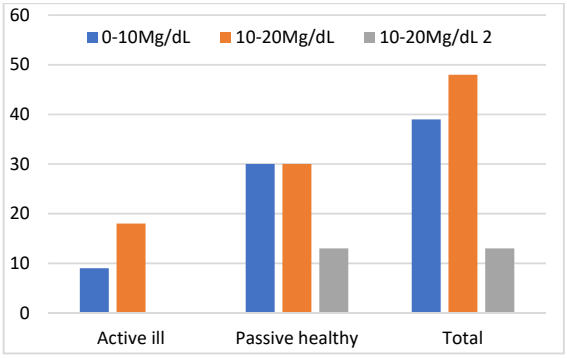

Fig. 5 Fibrinogen fluctuations at measurable intervals, according to the degree of progression of periodontal disease

The gingival index fluctuates in 1 evaluation value after non-surgical periodontal correct surgical treatment. Clinical data show that the average of bleeding areas and the depth of the probe are reduced by 60% and 2 mm.

In Table VI and Fig. 6 fluctuating values of fibrinogen are depicted depending on age. It is known that the risk of cardiac arrest is increasing from the age of 40 years. This is the age that increases the risk of periodontal problems and reduces the risk for oral cavity problems.

TABLE VI
FIBRINOGEN LEVEL FLUCTUATIONS IN THE DISTRIBUTION OF PATIENTS BY AGE LIMIT - 40 YEARS

Patients	0-10Mg/dL	%	10-20Mg/dL	%	20-Mg/dL	%
Age under 40 years	3	13%	6	26%	2	9%
Age 40 years over	6	26%	5	22%	1	4%
Total	9	39%	11	48%	3	13%

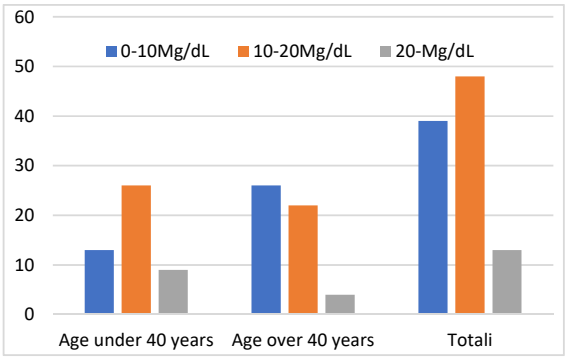

Fig. 6 Fibrinogen-level fluctuation dependence on patient division by age-limit - 40 years

IV. Discussions

The connection between periodontal disease and atherosclerosis is the subject matter of literature. Patients with periodontal disease share a large part of risk factors with patients suffering from cardiovascular disease, including age, gender (men more than females), lower socio-economic status, stress and smoking [17]. Moreover, a large portion of patients with periodontal disease also exhibit signs of cardiovascular disease [18]. These observations suggest that periodontal disease and atherosclerosis have almost the same etiology. Another study carried out a systematic review of data supporting or rejecting the link between the two diseases [19].

In response to questions such as "Does the periodontal disease affect the onset/progression of atherosclerosis and subsequent cardiovascular disease, stroke and peripheral vascular disease?", researchers identified 31 studies in humans. Although the authors did not perform meta-analysis due to differences in the reported results, the authors noted relative consistency (not absolute) and concluded, "Periodontal disease may be modestly associated with atherosclerosis, myocardial infarction, and other cardiovascular events". A consensus report approved by the American Academy of Periodontology recommends that "Patients and health workers should be informed that periodontal interventions can prevent the onset or progression of atherosclerotic-induced illnesses." That point of view and their consensus report, other meta-analyzes about the connection of cardiovascular disease and periodontitis have been reported and published [19]-[23].

Data in [24] reported a 20% risk increase for cardiovascular disease in patients with periodontal disease and an even greater risk of stroke ratio ranging from 2.85 to 1.74. In the same way, another study reported relative risk calculated 1.19 and 1.15 respectively. These meta-analyzes derived from human observational data suggest a modest but statistically significant increase in risk for cardiovascular disease with periodontal disease [24]-[27].

Recent findings from different studies in the worldwide population should also be considered. These studies include the Risk Study of Atherosclerosis in the Community (ARIC), the Health Professional Follow-up Study (HPFS). Periodontal data were collected from 6017 people, aged 52-75, who participated in the ARIC study [28]. The researchers evaluated the clinical presence of cardiovascular disease and subclinical atherosclerosis (BMI intima media thickness of the carotid artery (IMT) using B-mode ultrasound) as population-dependent variables. Individuals with large loss of attachment (≥ 10% of those with loss of applause > 3 mm) and large loss of teeth showed high chances of cardiovascular disease compared to individuals with low loss of attachment and tooth [28]-[32].

A second analysis showed a significant correlation between heavy periodontitis and carotid artery wall thickness after adaptation to co-variables such as age, sex, diabetes, lipid, hypertension and smoking [2]. Consequently, the ratio of chances of severe periodontitis (30% or more countries with ≥ 3 mm clinical loss of appetite) and carcinogenic subclinical atherosclerosis was 1.31.

In a third report, the researchers determined levels of IgG antibody (serum) specifically for 17 periodontal organisms using immunoblotting bacterial technique [2]. The researchers noted that the presence of *Campylobacter Rectus* antibody increased the risk of subclinical atherosclerosis twice. In particular, individuals with high levels of antibodies to *C. Rectus* and *Peptostreptococcus Micros* had almost twice the prevalence of carotid atherosclerosis compared to those individuals with only high *C. Titcus* antibodies (8.3% with 16.3%). Smoothing stratification indicated that all the significant microbial patterns for smokers were also significant for non-smokers except those with *Porphyromonas Gingivalis*. Thus, clinical signs of periodontitis are associated with cardiovascular disease and subclinical atherosclerosis in the ARIC population, and exposure to specific periodontal pathogens significantly increases the risk of atherosclerosis in smokers and non-smokers [32]-[35].

Results reported for periodontal disease and cardiovascular incidence were estimated in 2 stored databases, HPFS (n = 41407 males followed for 12 years) and NHS (n = 58974 females followed for 6 years) [33]. After control of important cardiovascular risk factors, males with a low oral tooth ratio (≤ 10) had a significantly higher risk compared with males with a higher number of present teeth (25 or more). The same result was also observed in women.

In a second report, researchers assessed the relationship between periodontal disease and increases in biomarkers for cardiovascular disease (serum) in a cross-sectional study in a part of HPFS patients (n = 468 males),fibrinogen, factor VII, indigenous plasmid activator (t-PA), LDL cholesterol, Von Willenbrand factor and TNF 1 and 2 receptor (tumor necrosis factor) [29].

In a multi-variable study, controlling age, smoking, alcohol consumption, physical activity and aspiration, periodontal disease was associated with higher levels of CRP (30% higher), t-PA (11% higher) and LDL cholesterol (11% higher). These analyzes show a significant association between the number of teeth and the risk of cardiovascular disease, as well as between periodontal disease and serum endothelial dysfunction and dyslipidemia [32]-[35].

The appearance of periodontal disease affecting the appearance of arteriosclerosis was as follows: 39% refractory periodontal 39%, aggressive periodontist 185 and chronic periodontitis 42%. The gingival bleeding index before and after non-surgical periodontal treatment ranged from 9% to 17% in the interval 0-1, ranging from 2-3 to 57% to 17%, in the 4-5 interval of 35% to 9%. The pre-and post-treatment probe fluctuations in the 0-2 mm range ranged from 0% to 35%, in the 3-4 mm range was 52% to 43%, in the 5-6 mm range was 45% to 22%.

The number of patients divided by gender in the fluctuation range of fibrinogen values before and after treatment ranged from 0 to 10 mg/dL female: male 0%-39%, in the range 10-20 mg/dL was 22%-26%, in the range of 20-40 Mg/dL was 0%-13%.

Fibrinogen fluctuations according to the categorization of

disease progression rate in active and passive healthy ratio in the 0-10 mg/dL range was 9%-30%, in the range of 10-20 mg/d, was 18%-30% in the interval 20-40 Mg/dL was 0%-13%.

Fluctuations in the level of fibrinogen according to the age of patients in the range 0-10 mg/dL under 40 years and over 40 years, was 13%-26%, in the range of 10-20 mg/dL was 26%-22%, at interval 20-40 Mg/dL was 9% -4%.

The bulk of the published articles aimed at analyzing the relationship between atherosclerosis and chronic periodontitis at the level of group control studies. This relationship between these two inflammatory-based diseases has increased the attention, which is reflected in the addition of periodical publications 2012-2019.

V. Conclusions

The reduction in fibrinogen levels after non-surgical periodontal treatment, indicates a significant association between the presence of active chronic periodontitis and the possibility of arteriosclerosis. In cases of periodontal evaluation of the oral condition before and after periodontal treatment, it is advisable to select two indices that correlate well with each-other, for the most efficient evaluation of the patient's periodontal status.

Supplementary Materials:

Author Contributions: Literature research was conducted by Dr. Saimir Heta. It was his insistent work that made it possible to reach the conclusions in this article.

Conflicts of Interest: We declare that there is no conflict of interest between the authors and the material presented in this article.

References

[1] Jirina Bartova, Pavla Sommerova, Yelena Lyuya-Mi, et al., "Periodontitis as a Risk Factor of Atherosclerosis," Journal of Immunology Research, vol. 2014, Article ID 636893, 9 pages, 2014.

[2] J. D. Beck and S. Offenbacher, "The association between periodontal diseases and cardiovascular diseases: a state-of-the-science review," Annals of Periodontology, vol. 6, no. 1, pp. 9–15, 2001.

[3] A. P. Dasanayake, "Poor periodontal health of the pregnant woman as a risk factor for low birth weight," Annals of Periodontology, vol. 3, no. 1, pp. 206–212, 1998.

[4] M. S. Gomes, P. Chagas, D. M. Padilha et al., "Association between self-reported oral health, tooth loss and atherosclerotic burden," Brazilian Oral Research, vol. 26, no. 5, pp. 436–442, 2012.

[5] P. P. Hujoel, M. Drangsholt, C. Spiekerman, and T. A. DeRouen, "Periodontal disease and coronary heart disease risk," The Journal of the American Medical Association, vol. 284, no. 11, pp. 1406–1410, 2000.

[6] World Health Organisation- Cardiovascuval Diseases (CDVs) https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds)

[7] Ilma Robo, Saimir Heta, Fjona Hamzai, Vera Ostreni. The Effect of Conservative Periodontal Therapy in Patients with Systemic Diseases. Archives of Internal Medicine Research 2 (2019): 040-049.

[8] Carranza – Clinical periodontology; Mosby 2009; Kapitulli Mjekësia Periodontale.

[9] D.E. Newby, N.R. Grubb, A. Bradbury; "Davidson's Principles & Practice of Medicine" 21st ed. 2010.

[10] Brian L. Mealey, Perry R. Klokkevold "Carranza's Clinic Periodontology 11th ed. 2012.

[11] D.E. Newby, N.R. Grubb, A. Bradbury "Davidson's Principles & Practice of Medicine" 21st ed. 2010.

[12] M. John Novak and Karen F. Novak "Carranza's Clinic Periodontology 11th ed. 2012

[13] S. Heta et al.; "Niveli plazmatik i markerave të inflmacionit, si shprehës i ndërlidhjes së periodontitit me arteriosklerozën"; Albanian Stomatological Journal; Vëll.15; Nr.1-2 (56, 57); Mars 2017. nëntor 2017.

[14] Walker CB; "Refractory periodontitis or recurrence of disease"; J ClinPeriodontol. 1996 Mar;23(3 Pt 2):289-92.

[15] Shaddox, Luciana M; Walker, Clay B (2010-08-11). "Treating chronic periodontitis: current status, challenges, and future directions". Clinical, Cosmetic and Investigational Dentistry. 2: 79–91. ISSN 1179-1357. PMC 3645457. PMID 23662085.

[16] Heitz-Mayfield LJ, Schätzle M, Löe H, et al. (October 2003). "Clinical course of chronic periodontitis. II. Incidence, characteristics and time of occurrence of the initial periodontal lesion". J. Clin. Periodontol. 30 (10): 902–8. doi:10.1034/j.1600-051X.2003.00399.x. PMID 14710770. Archived from the original on 2013-01-05.

[17] Beck JD, Offenbacher S, Williams R, Gibbs P, Garcia R.; "Periodontitis: a risk factor for coronary heart disease?"; Ann Periodontol. 1998 Jul;3(1):127-41. Review.

[18] Mattila KJ.; "Dental infections as a risk factor for acute myocardial infarction."; Eur Heart J. 1993 Dec;14 Suppl K:51-3. Review.

[19] Essentials of Clinical Periodontology and Periodontics 3rd Ed. (fq. 45-46)

[20] Newman Carranza's Clinical Periodontology 11th Ed. (fq. 349)

[21] Clinical Problem Solving in Periodontology &Implantology (Elsevier) (fq. 13)

[22] Carranza – Clinical periodontology; Mosby 2009; Kapitulli Epidemiologjia.

[23] Hani H. Mawardi,Lena S. Elbadawi,Stephen T. Sonis, "Current understanding of the relationship between periodontal and systemic diseases"; Saudi Med J. 2015; 36(2): 150–158.

[24] Bozoglan A, Ertugrul AS, Taspınar M, Yuzbasioglu B; "Determining the relationship between atherosclerosis and periodontopathogenic microorganisms in chronic periodontitis patients."; Acta Odontol Scand. 2017 May;75(4):233-242. doi: 10.1080/00016357.2017.1280739. Epub 2017 Jan 24.

[25] Bokhari SA, Khan AA, Butt AK, Hanif M, Izhar M, Tatakis DN, Ashfaq M; "Periodontitis in coronary heart disease patients: strong association between bleeding on probing and systemic biomarkers."; J ClinPeriodontol. 2014 Nov;41(11):1048-54. doi: 10.1111/jcpe.12284. Epub 2014 Sep 11.

[26] Gocke C, Holtfreter B, Meisel P, Grotevendt A, Jablonowski L, Nauck M, Markus MR, Kocher T.; "Abdominal obesity modifies long-term associations between periodontitis and markers of systemic inflammation."; Atherosclerosis. 2014 Aug;235(2):351-7. doi: 10.1016/j.atherosclerosis.2014.05.926. Epub 2014 May 22.

[27] Saffi MA, Furtado MV, Montenegro MM, Ribeiro IW, Kampits C, Rabelo-Silva ER, Polanczyk CA, Rösing CK, Haas AN.; "The effect of periodontal therapy on C-reactive protein, endothelial function, lipids and proinflammatory biomarkers in patients with stable coronary artery disease: study protocol for a randomized controlled trial.";Trials. 2013 Sep 6;14:283. doi: 10.1186/1745-6215-14-283.

[28] Androsz-Kowalska O, Jankowski K, Rymarczyk Z, Kowalski J, Pruszczyk P, GórskaR.;"Correlation between clinical parameters of periodontal disease and mean platelet volume in patients with coronary artery disease: a pilot study."; Kardiol Pol. 2013;71(6):600-5. doi: 10.5603/KP.2013.0124.

[29] López NJ, Chamorro A, Llancaqueo M.; "Association between atherosclerosis and periodontitis.; Rev Med Chil. 2011 Jun;139(6):717-24. doi: /S0034-98872011000600004. Epub 2011 Sep 14. Spanish.

[30] López NJ, Quintero A, Casanova PA, Ibieta CI, Baelum V, López R.; "Effects of periodontal therapy on systemic markers of inflammation in patients with metabolic syndrome: a controlled clinical trial.'; J Periodontol. 2012 Mar;83(3):267-78. doi: 10.1902/jop.2011.110227. Epub 2011 Jul 12.

[31] Yu KM, Inoue Y, Umeda M, Terasaki H, Chen ZY, Iwai T.; "The periodontal anaerobe Porphyromonasgingivalis induced platelet activation and increased aggregation in whole blood by rat model."; Thromb Res. 2011 May;127(5):418-25. doi: 10.1016/j.thromres.2010.12.004. Epub 2011 Feb 18.

[32] Buhlin K, Hultin M, Norderyd O, Persson L, Pockley AG, Rabe P, Klinge B, Gustafsson A.; "Risk factors for atherosclerosis in cases with severe periodontitis."; J ClinPeriodontol. 2009 Jul;36(7):541-9. doi: 10.1111/j.1600-051X.2009.01430.x.

[33] Amabile N, Susini G, Pettenati-Soubayroux I, Bonello L, Gil JM, Arques S, Bonfil JJ, Paganelli F.; "Severity of periodontal disease correlates to inflammatory systemic status and independently predicts the presence and angiographic extent of stable coronary artery disease."; J Intern Med. 2008 Jun;263(6):644-52. doi: 10.1111/j.1365-2796.2007.01916.x. Epub 2008 Jan 16.
[34] Leivadaros E, van der Velden U, Bizzarro S, ten Heggeler JM, Gerdes VE, Hoek FJ, Nagy TO, Scholma J, Bakker SJ, Gans RO, ten Cate H, Loos BG.; "A pilot study into measurements of markers of atherosclerosis in periodontitis."; J Periodontol. 2005 Jan;76(1):121-8.
[35] Ebersole JL, Cappelli D, Mott G, Kesavalu L, Holt SC, Singer RE.; "Systemic manifestations of periodontitis in the non-human primate."; J Periodontal Res. 1999 Oct;34(7):358-62.