

CONNECTIONS BETWEEN PERIODONTAL DISEASE AND CARDIOVASCULAR DISEASE

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ABSTRACT

Cardiovascular disease and periodontal disease are two distinct conditions that have been found to be linked through various research studies. Periodontal disease is a chronic inflammatory condition that affects the supporting structures of the teeth, including the gums, periodontal ligament, and jawbone. It is primarily caused by the accumulation of dental plaque, a sticky film of bacteria that forms on the teeth. If left untreated, periodontal disease can lead to gum inflammation, gum recession, tooth loss, and even systemic health problems. Several mechanisms have been proposed to explain the potential link between periodontal disease and cardiovascular disease. Maintaining good oral hygiene and preventing or treating periodontal disease is important for overall health

Keyword: cardiovascular disease, periodontal disease, systemic health.

INTRODUCTION

Cardiovascular disease and periodontal disease are two distinct conditions that have been found to be linked through various research studies [1,2]. Although a causal relationship has not been definitively established, there is evidence to suggest that periodontal disease may contribute to an increased risk of cardiovascular disease [3].

Periodontal disease is a chronic inflammatory condition that affects the supporting structures of the teeth, including the gums, periodontal ligament, and jawbone [4]. It is primarily caused by the accumulation of dental plaque, a sticky film of bacteria that forms on the teeth. If left untreated, periodontal disease can lead to

gum inflammation, gum recession, tooth loss, and even systemic health problems [5,6].

Several mechanisms have been proposed to explain the potential link between periodontal disease and cardiovascular disease. One theory suggests that the oral bacteria and inflammatory mediators associated with periodontal disease can enter the bloodstream through inflamed gum tissues [7,8,9].

Once in the bloodstream, these bacteria and inflammatory molecules may contribute to the development and progression of cardiovascular disease by promoting inflammation in the arteries and contributing to the formation of arterial plaques [10].

In the last years, however, important advances have been made, not only in our understanding of the etiopathogenesis of periodontitis, or concerning the mounting evidence regarding the independent associations between periodontitis, diabetes, and cardiovascular disease, but also with many other systemic diseases including metabolic disease and obesity, rheumatoid arthritis, certain cancers, respiratory diseases, and cognitive disorders including Alzheimer's disease [11,12]. Research studies have shown associations between periodontal disease and several cardiovascular conditions, including coronary artery disease, stroke, and atherosclerosis. However, it's important to note that these associations do not necessarily imply causation. Other factors, such as smoking, poor diet, sedentary lifestyle, and genetic predisposition, also contribute to both periodontal disease and cardiovascular disease [13]. These shared risk factors could confound the relationship between the two conditions.

Nonetheless, maintaining good oral hygiene and preventing or treating periodontal disease is important for overall health. Regular brushing and flossing, routine dental check-ups, and professional cleanings can help reduce the risk of periodontal disease. If there is any cardiovascular disease or at risk for it, it's important to inform healthcare provider about oral health and work together to manage both conditions effectively.

HOW CAN CARDIOVASCULAR DISEASE CAN INFLUENCE ORAL HEALTH?

Cardiovascular diseases such as ischemic heart diseases or stroke are among the leading cause of deaths globally, and evidence

suggests that these diseases are modulated by a multifactorial and complex interplay of genetic, environmental, and lifestyle factors [14,15,16]. Cardiovascular disease (CVD) can have an impact on oral health through various mechanisms and interactions. Here are a few ways in which cardiovascular disease can influence oral health:

Medications: Many medications used to manage cardiovascular disease, such as anticoagulants (blood thinners) and antiplatelet agents, can increase the risk of bleeding during dental procedures or oral surgeries [17]. It is important for dental professionals to be aware of a patient's medication regimen to take appropriate precautions and minimize bleeding risks. The oral health is a major factor for a good quality of life for everyone. Bleeding disorders are inherited or acquired and can be a big challenge for dentists to provide the oral rehabilitation [18]. The management of oral rehabilitation depends on the severity of disease and the severity of oral procedures with a proper communication between the dentist and haematologist [19].

Oral Health Side Effects: Some medications used for managing cardiovascular conditions can have oral health side effects.

For example, certain antihypertensive medications may cause dry mouth (xerostomia), which can increase the risk of tooth decay, gum disease, and oral infections. Additionally, medications like calcium channel blockers or angiotensin-converting enzyme (ACE) inhibitors may cause gum overgrowth (gingival hyperplasia) [20,21].

Inflammation and Periodontal Disease: There is evidence suggesting a bidirectional relationship between periodontal disease and cardiovascular disease.

Chronic inflammation, which is common in both conditions, may contribute to their association. Periodontal disease can

release bacteria and inflammatory mediators into the bloodstream, potentially promoting inflammation in blood vessels and increasing the risk of cardiovascular complications. Even if the aggressive factors are missing oral cavity is a favorable environment for the development of microbial germs or candidiasis in people with low local or general resistance, poor hygiene of oral cavity, or those wearing incorrectly adapted prostheses (irritating mechanical factor) [22].

Shared Risk Factors: Cardiovascular disease and periodontal disease share common risk factors, such as smoking, poor diet, obesity, and diabetes. These risk factors can contribute to both conditions and have a negative impact on oral health.

Endocarditis: Infective endocarditis is a rare but serious condition where bacteria from an oral infection enter the bloodstream and attach to damaged heart valves or other cardiovascular structures [23]. This can lead to infection and inflammation of the heart valves. Maintaining good oral hygiene and managing oral infections promptly are crucial to prevent the risk of infective endocarditis, especially in individuals with pre-existing heart conditions.

Taking in consideration connections between cardiovascular disease and oral health, it is important for individuals with cardiovascular disease to maintain good oral hygiene practices, schedule regular dental check-ups, and communicate with both their cardiologist and dentist to ensure coordinated care. Additionally, addressing shared risk factors, such as smoking cessation and a healthy diet, can benefit both cardiovascular health and oral health [24].

PHYSIOPATHOLOGY OF PERIODONTAL DISEASE

At present, periodontal disease is the main cause of tooth loss, dethroning dental

lesions of carious origin. The most important part of managing the patient with dental-periodontal injuries is to offer them the opportunity to regain functions (eg.masticatory, physiognomy, speech) [25].

Treatment is always tailored to the case and clinical situation and can range from simple to complex depending on the degree of periodontal damage. The aetiology of periodontitis is multifactorial. Subgingival dental biofilm elicits a host inflammatory and immune response, ultimately leading to irreversible destruction of the periodontium (alveolar bone and periodontal ligament) in a susceptible host. In order to successfully manage periodontitis, dental professionals must understand the pathogenesis, elimination of the causes and reduction of modifiable risk factors and treatment protocols. [26].

The physiopathology of periodontal disease involves a complex interplay between bacterial infection, host immune response, and other contributing factors. Here's an overview of the key factors involved:

Dental Plaque: Periodontal disease begins with the accumulation of dental plaque, a sticky biofilm that forms on the teeth. Plaque is primarily composed of bacteria, their byproducts, and food particles. When plaque is not adequately removed through oral hygiene practices, it can harden into tartar (calculus), providing a rough surface for further plaque accumulation [27].

Bacterial Infection: The bacteria present in dental plaque are predominantly gram-negative anaerobes, such as *Porphyromonas gingivalis*, *Treponema denticola*, and *Tannerella forsythia*. These bacteria have the ability to invade the gum tissues and initiate an immune response [28].

Inflammatory Response: The immune system recognizes the presence of bacteria and releases inflammatory mediators, such as

cytokines and chemokines, to combat the infection. These inflammatory molecules attract immune cells to the affected area, leading to the characteristic signs of inflammation—redness, swelling, and bleeding of the gums [29].

Destruction of Supporting Structures: Chronic inflammation and the ongoing immune response can result in the destruction of the supporting structures of the teeth [30].

This includes the gum tissues (gingiva), periodontal ligament, and alveolar bone. As the disease progresses, the gums may recede, forming periodontal pockets between the teeth and gums. Over time, the loss of bone support can lead to tooth mobility and eventual tooth loss.

Host Factors: The severity and progression of periodontal disease can be influenced by individual host factors. These include genetic predisposition, systemic conditions (e.g., diabetes), smoking, hormonal changes (e.g., during pregnancy), and certain medications (e.g., immunosuppressants).

These factors can affect the immune response, making some individuals more susceptible to periodontal disease [31]. The bacterial infection and host immune response play central roles in the development of periodontal disease, but other factors, such as oral hygiene practices, nutrition, and systemic health, also contribute to its onset and progression. Effective management involves maintaining good oral hygiene, regular dental check-ups, and addressing any underlying risk factors or systemic conditions.

PHYSIOPATHOLOGY OF CARDIOVASCULAR DISEASE

The physiopathology of cardiovascular disease involves various processes that lead to the development and progression of conditions affecting the heart and blood vessels. Some of the factors involved are:

Atherosclerosis: Atherosclerosis is a major underlying process in many cardiovascular diseases. It starts with the accumulation of fatty deposits, primarily cholesterol and other lipids, within the inner lining (endothelium) of arteries. This build-up is known as plaque [32]. Over time, the plaque becomes hardened and can narrow the arterial walls, reducing blood flow and impeding the delivery of oxygen and nutrients to tissues.

Endothelial Dysfunction: Endothelial cells lining the arterial walls play a crucial role in maintaining vascular health. When exposed to risk factors like high blood pressure, smoking, high cholesterol levels, or inflammation, the endothelium can become damaged or dysfunctional [33, 34]. This leads to impaired regulation of blood flow, increased permeability, and the release of substances that promote inflammation and the formation of plaques.

Inflammation: Inflammatory processes play a significant role in cardiovascular disease. In response to endothelial dysfunction, immune cells (such as macrophages and T-lymphocytes) migrate into the arterial walls and accumulate in the plaques. Inflammatory mediators are released, triggering further damage to the arterial walls and promoting plaque progression [35].

Plaque Rupture and Thrombosis: Vulnerable plaques, which are characterized by a thin fibrous cap and a large lipid core, are prone to rupture. When a plaque ruptures, the contents, including lipid debris and pro-inflammatory substances, are exposed to the bloodstream. This triggers the formation of blood clots (thrombosis) at the site of rupture. If a blood clot completely blocks a coronary artery, it can lead to a heart attack. Similarly, if it occludes an artery in the brain, it can cause a stroke [36].

Hypertension: High blood pressure, or hypertension, is a significant risk factor for cardiovascular disease. It places

increased stress on the arterial walls, leading to endothelial dysfunction, inflammation, and accelerated atherosclerosis. Hypertension also contributes to the workload of the heart, potentially leading to heart failure or other cardiac complications [37].

Other Risk Factors: Several other factors contribute to the development of cardiovascular disease, including smoking, diabetes, obesity, sedentary lifestyle, unhealthy diet, genetic predisposition, and certain medical conditions (e.g., dyslipidemia). Major efforts should be directed towards the prevention of periodontal disease in patients at risk for osteoporosis. Patients with osteoporosis should benefit from frequent periodontal treatments, especially if periodontal disease is already present [38]. These factors can further promote inflammation, atherosclerosis, and other pathological processes.

It's important to note that cardiovascular disease encompasses a range of conditions, including coronary artery disease, heart failure, stroke, peripheral artery disease, and more. While the underlying mechanisms may vary slightly among these conditions, atherosclerosis and its associated processes form a common thread in the pathophysiology of cardiovascular disease. The prevention, diagnosis, and specific treatment of oral pathology in the context of cardiovascular disease and aplastic anemia improves the quality of life of these patients [39,40]. Managing cardiovascular disease involves lifestyle modifications, medications, and interventions to control risk factors, improve vascular health, and reduce the risk of complications.

HEART HEALTH AND PERIODONTAL DISEASE

Oral rehabilitation is a border specialty between dentistry and general medicine and aims to establish correct diagnoses that

ultimately lead to treatments capable of restoring mastication, phonation, dental and facial aesthetics, in the context in which the oral cavity is defined as a subset of the whole body that must function uniformly, without imbalances, which can have repercussions on the general state of health [41].

There is evidence to suggest that periodontal disease can affect heart health. While the exact nature of the relationship is still being studied, several mechanisms have been proposed to explain how periodontal disease may contribute to cardiovascular problems, such as:

Inflammation: Periodontal disease is characterized by chronic inflammation in the gums and supporting tissues of the teeth. This inflammation can lead to the release of inflammatory mediators into the bloodstream. These inflammatory molecules may contribute to the development and progression of cardiovascular disease by promoting inflammation in the blood vessels, leading to atherosclerosis (hardening and narrowing of the arteries) and increasing the risk of heart problems [42].

Bacterial Spread: The bacteria associated with periodontal disease can enter the bloodstream through the inflamed gum tissues. Once in the bloodstream, these bacteria can travel to other parts of the body, including the heart and its surrounding tissues. Bacterial colonization in the heart can cause infections, such as endocarditis (infection of the inner lining of the heart) or infective pericarditis (infection of the outer lining of the heart) [43].

Immune Response: The immune system plays a role in both periodontal disease and cardiovascular disease. In periodontal disease, the immune response to the bacteria and their byproducts can contribute to tissue destruction and inflammation. This immune response can also affect the cardiovascular

system by promoting inflammation and contributing to the development of atherosclerosis [44].

Shared Risk Factors: Periodontal disease shares common risk factors with cardiovascular disease, such as smoking, poor diet, obesity, and diabetes. These risk factors can increase the likelihood of both conditions and have negative effects on heart health [45]. While the evidence suggests a link between periodontal disease and heart health, it's important to note that having periodontal disease does not necessarily mean a person will develop cardiovascular disease.

Many other factors, such as genetics, lifestyle choices, contribute to the development of cardiovascular problems. However, maintaining good oral hygiene and managing periodontal disease is still important for overall health and may help reduce the risk of cardiovascular complications.

It is advisable to consult with both a dentist and a healthcare provider to ensure coordinated care and management of oral and cardiovascular health.

Prevention/education activities will play a key role in ensuring proper oral health of the population and will have to address issues such as oral hygiene, access to services and the effects of adopting undesirable behaviors (smoking, poor nutrition, alcohol consumption, etc.) on the oral cavity [46].

Use of the internet for obtaining relevant information regarding health is a very common practice nowadays [47]. Dental anxiety represents a major obstacle when it comes to seeking early consultation on oral and dental-periodontal problems. Anxious patients often postpone visits to

dental offices until the time when dental-periodontal treatment is absolutely necessary. Anxious patients suffer from poor oral health, compared to non-anxious patients [48].

CONCLUSIONS

It's important to note that periodontal disease is a multifactorial condition, and the exact mechanisms underlying its progression are still being investigated. Moderate and severe forms of periodontal disease increase the systemic inflammatory level, a characteristic common to all chronic inflammatory diseases.

Only starting a treatment to reduce the effects of periodontal disease with minimal reduction of clinical signs leads to a significant decrease in the systemic level of inflammation. In untreated periodontal diseases, the same bacterial strains that we usually find in periodontal pockets have been found in atheromatous plaques in the blood vessels of those suffering from cardiovascular disease.

Treating periodontal disease in the dental office, dentists also directly address to cardiovascular disease, minimizing the risks of myocardial infarction and stroke.

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REFERENCES

1. Aarabi G., Zeller T., Seedorf H., Reissmann D. R., Heydecke G., Schaefer A.S., & Seedorf U. Genetic susceptibility contributing to periodontal and cardiovascular disease. *Journal of Dental Research*, 2017;96, 610–617.
2. Ahn Y.B., Shin M.S., Han D.H., Sukhbaatar M., Kim M.S., Shin H.S., Kim H.D. Periodontitis is associated with the risk of subclinical atherosclerosis and peripheral arterial disease in Korean adults. *Atherosclerosis*, 2016:311.
3. Achterberg, T. (2022). Reviewing the Mechanisms and Causal Relationship Between Periodontitis and Cardiovascular Disease.
4. Dahiya P., Malhotra A., Pajnoo, A., Gupta R., & Kamal R. Comparative evaluation of efficacy of topical and intra-sulcular application of Co-enzyme Q10 in the non-surgical treatment of periodontal diseases. *Journal of Indian Society of Periodontology*, 2022: 26(6), 533-538.
5. Broomhead T., Gibson B., Parkinson C.R., Vettore M.V., Baker S.R. (2022). Gum health and quality of life—subjective experiences from across the gum health-disease continuum in adults. *BMC Oral Health*, 22(1), 512.
6. Butera, A., Gallo, S., Pascadopoli, M., Maiorani, C., Milone, A., Alovise, M., & Scribante, A. (2022). Paraprobiotics in non-surgical periodontal therapy: Clinical and microbiological aspects in a 6-month follow-up domiciliary protocol for oral hygiene. *Microorganisms*, 10(2), 337.
7. Xu, B., & Han, Y. W. (2022). Oral bacteria, oral health, and adverse pregnancy outcomes. *Periodontology 2000*, 89(1), 181-189.
8. Jiang, M., Li, Z., & Zhu, G. (2022). The role of endoplasmic reticulum stress in the pathophysiology of periodontal disease. *Journal of Periodontal Research*, 57(5), 915-932.
9. Loos, B. G., & Van Dyke, T. E. (2020). The role of inflammation and genetics in periodontal disease. *Periodontology 2000*, 83(1), 26-39.
10. Schenkein, H. A., Papapanou, P. N., Genco, R., & Sanz, M. (2020). Mechanisms underlying the association between periodontitis and atherosclerotic disease. *Periodontology 2000*, 83(1), 90-106.
11. Genco, R. J., & Sanz, M. (2020). Clinical and public health implications of periodontal and systemic diseases: An overview. *Periodontology 2000*, 83(1), 7-13.
12. Cojocaru, E., Cojocaru, C., Antoniu, S.A., Stafie, C.S., Rajnoveanu, A., Rajnoveanu, R.M. Inhaled interferons beta and SARS-COV2 infection: a preliminary therapeutic perspective. *Expert Rev Respir Med* 2021,16:1-5.
13. Orlandi, M., Graziani, F., & D'Aiuto, F. (2020). Periodontal therapy and cardiovascular risk. *Periodontology 2000*, 83(1), 107-124.
14. Hamza SA, Asif S, Khurshid Z, Zafar MS, Bokhari SAH. Emerging Role of Epigenetics in Explaining Relationship of Periodontitis and Cardiovascular Diseases. *Diseases*. 2021; 9(3):48.
15. Andreea Clim, Ana-Maria Pop, Mărănducă Minela Aida, Loredana Liliana Hurjui, Irina Grădinaru, Ionela Lăcrămioara Șerban. The multidisciplinary team approach to oral rehabilitation of patients with valvular heart disease. *Romanian Journal of Oral Rehabilitation* Vol. 11, No. 4, October - December 2019, p.113-119.
16. Cojocaru, C., Cojocaru, E., Turcanu, A.M., Zaharia, D.C. Clinical challenges of SARS-CoV-2 variants. *Experimental and Therapeutic Medicine* 2022; 23:416.
17. Lu, S. Y., Lin, L. H., & Hsue, S. S. (2018). Management of dental extractions in patients on warfarin and antiplatelet therapy. *Journal of the Formosan Medical Association*, 117(11), 979-986.
18. Cristina Claudia Tărniceriu, Delianu Carmen, Tănase Daniela Maria, Grădinaru Irina, Mitrea Mihaela, Hurjui Ion, Armencia Adina Oana, Jipu Raluca, Loredana Liliana Hurjui. The multidisciplinary team approach to oral rehabilitation of patients with inherited

- coagulopathies. Romanian Journal of Oral Rehabilitation. Vol. 12, No. 2, April - June 2020, p.137-144.
19. Claudia Cristina Tarniceriu, Loredana Liliana Hurjui, Daniela Maria Tanase, Ion Hurjui, Mihaela Mitrea, Ludmila Lozneanu, Carina Balcos, Adina Armencia, Irina Gradinaru. The impact of the anemic syndromes on the anatomical structures of the oral cavity. Romanian Journal of Oral Rehabilitation Vol. 13, No.4 October-December 2021, p.54-59.
 20. Ustaoglu, G., Erdal, E., & Karaş, Z. (2021). Influence of different anti-hypertensive drugs on gingival overgrowth: A cross-sectional study in a Turkish population. *Oral Diseases*, 27(5), 1313-1319.
 21. Rajak, D., Sahu, D., Jain, A., Khan, R., Khare, B., Jain, P. K., & Thakur, B. S. (2022). Review on Toxicity of Antihypertensive Drugs. *Asian Journal of Dental and Health Sciences*, 2(4), 64-68.
 22. Loredana Liliana Hurjui, Irina Gradinaru, Claudia Dorus, Daniela Maria Tanase, Adina Armencia, Ion Hurjui, Claudia Cristina Tarniceriu, Mihaela Mitrea, Ludmila Lozneanu, Carina Balcos, Ionela Lăcrămioara Şerban. Oral mucosa - pathophysiological and pharmacotherapeutic aspects. Romanian Journal of Oral Rehabilitation. Vol. 13, No.4 October-December 2021, p.108-114.
 23. Coll, P. P., Lindsay, A., Meng, J., Gopalakrishna, A., Raghavendra, S., Bysani, P., & O'Brien, D. (2020). The prevention of infections in older adults: oral health. *Journal of the American Geriatrics Society*, 68(2), 411-416.
 24. Sharma, P. (2019). An Update on the Links Between Periodontal Health and General Health. *Primary Dental Journal*, 8(4), 22-27.
 25. Mihaela Mitrea, Claudia Rusu, Irina Grădinaru, Adina Oana Armencia, Simona Niculescu, Cristina Claudia Tărniceriu, Loredana Liliana Hurjui, Raluca Jipu, Edlibi Al Hage Walid, Hurjui Ion. Case report and literature review regarding reconstruction of fracture mandible with implants, Romanian Journal of Oral Rehabilitation. Vol. 12, No. 2, April - June 2020, p.220-228.
 26. Mihaela Mitrea, Edlibi Al Hage Walid, Radu Razvan Maxim, Simona Partene Vicoleanu, Gabriela Dumachita Sargu, Niculescu Simona, Liliana Loredana Hurjui, Irina Gradinaru, Cristina Claudia Tarniceriu, Claudia Florea, Norina Consuela Forna. Intervention for replacing missing teeth at patients with periodontitis Romanian Journal of Oral Rehabilitation. Vol. 13, No.4 October-December 2021, p.92-103.
 27. Abdulkareem, A. A., Al-Taweel, F. B., Al-Sharqi, A. J., Gul, S. S., Sha, A., & Chapple, I. L. (2023). Current concepts in the pathogenesis of periodontitis: from symbiosis to dysbiosis. *Journal of Oral Microbiology*, 15(1), 2197779.
 28. Mohanty, R., Asopa, S. J., Joseph, M. D., Singh, B., Rajguru, J. P., Saidath, K., & Sharma, U. (2019). Red complex: Polymicrobial conglomerate in oral flora: A review. *Journal of family medicine and primary care*, 8(11), 3480.
 29. Ramadan, D. E., Hariyani, N., Indrawati, R., Ridwan, R. D., & Diyatri, I. (2020). Cytokines and chemokines in periodontitis. *European journal of dentistry*, 14(03), 483-495.
 30. Könönen, E., Gursoy, M., & Gursoy, U. K. (2019). Periodontitis: a multifaceted disease of tooth-supporting tissues. *Journal of clinical medicine*, 8(8), 1135.
 31. Graves, D. T., Ding, Z., & Yang, Y. (2020). The impact of diabetes on periodontal diseases. *Periodontology 2000*, 82(1), 214-224.
 32. Ahmad, P., Alvi, S. S., Iqbal, D., & Khan, M. S. (2020). Insights into pharmacological mechanisms of polydatin in targeting risk factors-mediated atherosclerosis. *Life sciences*, 254, 117756.
 33. Xu, S., Ilyas, I., Little, P. J., Li, H., Kamato, D., Zheng, X., ... & Weng, J. (2021). Endothelial dysfunction in atherosclerotic cardiovascular diseases and beyond: from mechanism to pharmacotherapies. *Pharmacological Reviews*, 73(3), 924-967.
 34. Domokos-Hancu, B., Man, M.A., Trofor, A.C., Pop, C.M., Gavrilesu, C.M., Cojocaru, E.,

- Cernomaz, A., Lesan, A., Boerescu, C., Barbu, R.M., Popescu, F. Biochemistry in Assessing the Inflammatory Response of the Respiratory System Due to Experimental Exposure to Glass Fibres. *Materiale plastice*, 2019, 56(1): 285-290.
35. Tsoupras, A., Lordan, R., & Zabetakis, I. (2019). Inflammation and cardiovascular diseases. In *The impact of nutrition and statins on cardiovascular diseases* (pp. 53-117). Academic Press.
36. Campbell, B. C., De Silva, D. A., Macleod, M. R., Coutts, S. B., Schwamm, L. H., Davis, S. M., & Donnan, G. A. (2019). Ischaemic stroke. *Nature reviews Disease primers*, 5(1), 70.
37. Saheera, S., & Krishnamurthy, P. (2020). Cardiovascular changes associated with hypertensive heart disease and aging. *Cell transplantation*, 29.
38. Loredana Liliana Hurjui, Ion Hurjui, Carmen Delianu, Cristina Claudia Tărniceriu, Alexandra Maria Mârțu, Carina Balcoș, Raluca Jipu, Adina Oana Armencia, Ion Andrei Hurjui, Ruxandra Maria Hârțan, Irina Grădinaru. Biological markers importance in the diagnosis of osteoporosis. *Romanian Journal of Oral Rehabilitation* Vol. 12, No. 4, October - December 2020, p.181-189.
39. Cristina Claudia Tărniceriu, Anca Haisan, Ludmila Lozneanu, Daniela Maria Tănase, Irina Grădinaru, Mihaela Mitrea, Ion Hurjui, Loredana Liliana Hurjui. Aplastic anemia and health of the oral cavity-clinical considerations. *Romanian Journal of Oral Rehabilitation* Vol. 14, No. 1, January - March 2022, p.157-161.
40. Cojocaru, E., Cojocaru, C., Saramet, B.I., Diculencu, D. Identification Mycobacterium tuberculosis complex using an immunochromatographic test. *Romanian Biotechnological Letters* 2012, 17(4):7525-7528.
41. Irina Gradinaru, Raluca Jipu, Loredana Liliana Hurjui, Arina Alice Ciocan Pendefunda, Adina Oana Armencia, Mihaela Mitrea, Magda-Ecaterina Antohe. Current aspect of metal-ceramic-biomaterial restorations and technology. *Romanian Journal of Oral Rehabilitation* Vol. 12, No. 2, April - June 2020, p.116-127.
42. Larsson, L., Kavanagh, N. M., Nguyen, T. V., Castilho, R. M., Berglundh, T., & Giannobile, W. V. (2022). Influence of epigenetics on periodontitis and peri-implantitis pathogenesis. *Periodontology 2000*, 90(1), 125-137.
43. Nappi, F., Iervolino, A., & Singh, S. S. A. (2021). The new challenge for heart endocarditis: from conventional prosthesis to new devices and platforms for the treatment of structural heart disease. *BioMed Research International*, 2021.
44. Zhong, C., Yang, X., Feng, Y., & Yu, J. (2020). Trained immunity: an underlying driver of inflammatory atherosclerosis. *Frontiers in Immunology*, 11, 284.
45. Nibali, L., Gkraniias, N., Mainas, G., & Di Pino, A. (2022). Periodontitis and implant complications in diabetes. *Periodontology 2000*, 90(1), 88-105.
46. Adina Oana Armencia, Irina Bamboi, Loredana Hurjui, Irina Grădinaru, Irina Zetu, Irina Bamboi, Magda Ecaterina Antohe, Carina Balcos. Economic evaluation of dental care prevention programs: cost-efficiency analysis. *Romanian Journal of Oral Rehabilitation* Vol. 14, No. 2, April-June 2022, p.153-165.
47. Carina Balcos, Loredana Hurjui, Irina Gradinaru, Ion Hurjui, Livia Bobu, Irina Bamboi, Dana Budala, Dana Baci, Daniela Argatu, Magda Barlean, Adina Armencia, Ramona Feier. The role of the internet in promoting dental health and changing behavior among the adult population in Iasi. *Romanian Journal of Oral Rehabilitation*. Vol. 13, No. 2, April – June 2021, p.104-114.
48. Carina Balcos, Ramona Feier, Iulia Săveanu, Livia Bobu, Radu Sireteanu, Loredana Hurjui, Irina Grădinaru, Dana Budală, Raluca Jipu, Magda Bârlean, Adina Armencia. Dental anxiety and oral health among students in Iasi. *Romanian Journal of Oral Rehabilitation*. Vol. 13, No. 1, January-March 2021, p.328-340.