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Periodontal disease in children and its association with cardiovascular diseases

Mobina shahi[1], Abdollah Ebrahimi[2]*

1- Student Research Committee, School of Dentistry, Semnan University of Medical Sciences, Semnan, Iran. Email: mobinashahi093@gmail.com

2- Student Research Committee, School of Dentistry, Semnan University of Medical Sciences, Semnan, Iran. *Corresponding author. Email: ebrahimi56666@gmail.com

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Abstract

Periodontitis is a disease characterized by inflammation, infection, and destruction of the periodontium, and it can greatly affect human oral as well as general health. This study addresses this issue by examining the association between periodontal disease in children and cardiovascular diseases (CVDs). In fact, gingivitis is a common form of gingival tissue disease that can turn into periodontitis, which subsequently affects the supporting structures of human teeth, including the gingiva itself, alveolar bone, and periodontal ligament. The research conducted in this field until today shows that periodontal diseases can cause the risk of cardiovascular diseases by causing systemic inflammation and releasing inflammatory markers including C-reactive protein and interleukin-6. To increase Children who suffer with periodontal disease have even higher levels of these markers, suggesting a potential link involving cardiovascular complications.

Things like preventive measures, early diagnosis and management of periodontal disease in children are evaluated in order to reduce these important risks, but more research is needed to understand the pathophysiological mechanisms associated with these conditions. Also, the need to improve knowledge in order to understand how to carry out targeted interventions is clearly felt.

If more attention is paid to the health of periodontal structure in children, it is possible to significantly reduce the risk of cardiovascular complications in the future.

Keywords: Periodontal disease, Cardiovascular diseases, Children, Inflammatory markers.

Introduction

Periodontal disease is known as inflammation, infection and degeneration of the periodontium. The most obvious feature of this disease is gingivitis (affects up to 90% of population), which can have a significant and widespread effect on the tooth-supporting structures. These supporting structures include the gingiva itself, alveolar bone and periodontal ligament. In fact, it can be said that the beginning of these diseases occurs with inflammation of the gingiva. Due to a progressive process, further destruction occurs, which is called periodontitis[1].

During several studies that researchers have conducted on periodontal diseases, they have found that this problem can have a significant effect on the development and progression of subsequent cardiovascular diseases [2,3].

In fact, this issue has attracted the attention of researchers in this field and the concern that people with periodontal diseases are more at risk of cardiovascular diseases is considered stronger[4,5].

A study which had been done by Gani DK et al. aimed to investigate the systemic levels of inflammatory markers of cardiovascular diseases, which included C-reactive protein as well as interleukin-6 in those patients who had chronic periodontitis in comparison with those who had healthy periodontium, it had been identified that a meaningful association between periodontal disease and cardiovascular disease plays a role. Hence the ability to predict cardiovascular risk markers in periodontal disease is concerned in prevention and treatment in this regard[6].

About 20-50% of global population suffer from periodontal disease. In children, the prevalence of periodontal diseases can be evident from school age, which raises concerns in this field as well. It should be noted that chronic inflammation and infections that can develop from these diseases in children can harm their cardiovascular system[7,8,9].

In this regard, there are mechanisms that state a clear example of which is the spread of periodontal bacteria and their products, which include Porphyromonas gingivalis and Tryponema denticula, and can enter the endothelium through the bloodstream. In this way, they can cause inflammation in those regions and form plaques[4,10].

Periodontal diseases in children can be prevented by timely diagnosis by specialists, and it is possible to act positively by educating both children and parents about the related issues. Also, one of the other important matters that prevent more serious complications in

the cardiovascular system is early diagnosis and treatment of periodontal diseases [11,12,13].

Pourmoghaddas Z et al. State that pediatric patients who suffer from CHD possesses oro-dental issues including periodontitis[14].

What plays a role in the occurrence of periodontal diseases in children includes a wide spectrum, including genetic predispositions, chronic diseases such as diabetes, leukemia, lack of oral hygiene, improper nutrition, oral breathing, and autoimmune diseases [9, 15].

The multifaceted mechanisms that exists between periodontal diseases and cardiovascular diseases in children have not been fully revealed to date, which is the same in adults, and to answer this unanswered question, researchers need to solve many more unsolved mysteries[2,16].

Ye Z et al. State that treatment of chronic periodontitis gets the individual rid of relevant bacteria as well as infection. Also the mention that it is thought that this may help prevention of occurrence or even recurrence of diseases of cardiovascular diseases[17].

If there is a positive and constructive performance in the field of children's oral and dental health as well as basic education, a more appropriate situation in terms of the health of the periodontium and cardiovascular organs will result[18,19].

Periodontal diseases and their cardiovascular effects with management:

1. Gingivitis: This usually occurs when plaque accumulates and can lead to another disease called periodontitis in the next stage. Periodontitis has symptoms such as red discoloration, swollen and bleeding gingiva.[20,21].

Cardiovascular Effects: Gingivitis can lead to many other complications, including inflammation, endothelial dysfunction, atherosclerosis, cardiovascular disease, stroke, and other risk factors[22,13].

Management: In order to manage this complication, keeping the oral cavity clean, using mouthwash regularly, using healthy and sugar-free foods, and having regular dental check-ups, helps to a wide extend[23,24].

2. Chronic periodontitis: It is a situation in which severe infection damages the tooth-supporting structures. In more advanced cases it may cause tooth loss, bad breath, etc.[25].

Cardiovascular effects: It has been scientifically proven that there is a significant relationship between increased systemic inflammation and chronic periodontitis. This issue can lead to the creation of atherosclerotic plaques[26,27].

Management: This problem can be managed by regular and professional scaling, using systemic or topical antibiotics according to the doctor's orders, surgery if necessary[28].

3. Aggressive periodontitis: this type of periodontal disease can cause rapid destruction of the periodontium tissue due to its rapid progress [29].

Cardiovascular effects: creating an acute inflammatory response and increasing the level of reactive protein as a result of this complication, which can increase the risk of cardiovascular diseases[30].

Management: undergoing mechanical debridement as well as plaque removal, antimicrobial treatments by referring to specialists in this field, as well as regular dental visits[30,31].

4. Peri-implantitis: This is an inflammatory disease which causes the tissues around tooth implants to be destroyed, which may also cause the fracture of the implant [32].

Cardiovascular effects: It is similar to what other periodontal diseases cause[33].

Management: by removing non-aerobic plaques from the implant surfaces, relying on antiseptic treatments that include the use of chlorhexidine or other antiseptic agents, relying on laser therapy to reduce the bacterial load, undergoing surgical interventions if necessary, reconstructing the lost tissues of the implant holder, etc., can be a convincing management in this regard[32,34].

Background

Periodontal disease is an inflammatory disease that puts the supporting tissues of the tooth at risk, but it also has potential systemic consequences that make it an important

concern for the general health of the body. This disease can threaten oral health at first, but scientific evidence indicates that it is also related to the cardiovascular system[9].

The human oral cavity contains various number of microbiota, pathogens such as Porphyromonas gingivalis and Aggregatibacter actinomycetemcomitans which play a role in the progression and spread of numerous disease[35] These microorganisms have the ability to produce inflammatory mediators and shift them into the circulation[3].

Regarding the relationship between periodontal disease and cardiovascular diseases, several potential mechanisms play a role. Some researches claim that the direct release of periodontal pathogens and their products in the bloodstream have the ability to stick to the endothelium and lead to the formation of atherogenesis[4,9]. On the other hand, the issue of inflammation in the periodontium causes inflammatory cytokines to be released and, through processes, it ends in the formation of plaque, thrombosis, and eventually problems related to the cardiovascular system[3].

It should be noted that the relationship between periodontal disease and cardiovascular disease in adults has been studied and researched more than in children, which is needed to be concerned more[4].

Research on the relationship between periodontal and cardiovascular diseases requires an approach that is both comprehensive and includes prevention, early diagnosis and effective management[36].

Researchers are in search to discover the complex relationship between periodontal diseases and cardiovascular diseases, so that they can find targeted preventive solutions as well as therapeutic interventions to reduce the consequences of these conditions specially in children[7].

Materials and Methods

Literature search:

A comprehensive literature search was performed in the PubMed database. Also, other databases that are considered relevant, such as the Cochrane library, were reviewed. The selected search terms included periodontal disease, cardiovascular diseases, and children.

Inclusion criteria:

Studies that were published in English.

The focus of the studies was on children

They investigated the relationship between periodontal diseases and cardiovascular diseases.

Exclusion criteria:

They did not have the above mentioned criteria.

Studies were conducted on animals.

They did not have enough information for in-depth research.

Results and discussion

Results:

In this study, the purpose of which is to research about the relationship between periodontal diseases and cardiovascular diseases in children, a clear correlation and relationship has been found between both[4].

Past researches not only declare that the prevalence of periodontal disease in children with cardiovascular diseases is higher compared to healthy people, but also indicate that the severity of periodontal disease and the severity of cardiovascular disease are in a relationship and correlation[7]. Therefore, what is obvious is the importance of early diagnosis and also the management of periodontal disease in the children population, which is considered essential to reduce the risk of cardiovascular complications[9].

By analyzing inflammatory biomarkers, we found that high levels of C-reactive protein (CRP) and interleukin-6 (IL-6) are observed in children with periodontal disease, which indicates an inflammatory response that is actually systemic. Studies have proven that these pro-inflammatory markers are involved in the pathogenesis of atherosclerosis and other cardiovascular diseases[37,38].

Discussion:

This study actually shows more evidence regarding the relationship between periodontal disease and cardiovascular diseases in children, and while the exact mechanisms of this

relationship are not yet fully known, the findings of our research show that periodontal pathogens can enter the bloodstream and cause a systemic inflammatory response, which also consequently increase the risk of cardiovascular events[4,7].

Science has proven that periodontal disease can be prevented not only with effective oral hygiene measures, regular dental examinations and early intervention, but also can reduce the cardiovascular risks associated with it in children[9].

In this study, we highlighted the importance of considering periodontal disease, which is a preventable risk factor for cardiovascular diseases in children, and the early diagnosis, prevention, and management of periodontal disease to improve overall cardiovascular health in children[39]. On the other hand, we consider it necessary to conduct more research in order to better understand the pathophysiological mechanisms and gain more sufficient knowledge for the prevention and treatment of both related matters[40].

Current research limitations

There have not been extensive studies on the relationship between periodontal diseases and previous vascular problems in children, which means that this relationship has generally been investigated in adults. This problem has created a significant knowledge gap[41].

There is a lack of strong and convincing interventional studies in this direction, so that in order to evaluate the treatment of periodontal disease in children, we cannot claim for sure what the incidence or severity of cardiovascular diseases would be according to the treatment of periodontal diseases[42].

Currently, research has been able to improve the knowledge of therapists in this area to some extent, but there are still many significant limitations regarding the relationship between periodontal disease and cardiovascular health in children. Therefore, it is necessary that by addressing these gaps, we can create a more complete understanding and knowledge in this regard[43,44].

Conclusion

Since there is a relationship between periodontal disease and cardiovascular disease in children that is not yet fully known, this issue has raised concerns for researchers. Our study has been able to show clear association between these two diseases. For example, it was stated that periodontal pathogens by spreading in the bloodstream can help to cause

systemic inflammation, which will increase the chances of developing cardiovascular diseases[4,45].

Currently, the evidence indicates that early diagnosis as well as basic management of periodontal disease in children is considered essential in order to reduce the risk of cardiovascular complications[9].

Preventive measures, i.e. examination and, if necessary, timely treatment for periodontal diseases, will have a significant impact on the health of the cardiovascular system[41].

It should be noted that until today there are still significant gaps in this kind of studies and there is a need for understanding the pathophysiological mechanisms related to periodontal disease and its association with cardiovascular conditions in the children population[41,7].

Reference

1. Gasner NS, Schure RS. Periodontal Disease. 2023 Apr 10. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan–. PMID: 32119477.
2. Bhuyan R, Bhuyan SK, Mohanty JN, Das S, Juliana N, Juliana IF. Periodontitis and Its Inflammatory Changes Linked to Various Systemic Diseases: A Review of Its Underlying Mechanisms. Biomedicines. 2022 Oct 21;10(10):2659. Doi: 10.3390/biomedicines10102659. PMID: 36289921; PMCID: PMC9599402.
3. Martínez-García M, Hernández-Lemus E. Periodontal Inflammation and Systemic Diseases: An Overview. Front Physiol. 2021 Oct 27;12:709438. Doi: 10.3389/fphys.2021.709438. PMID: 34776994; PMCID: PMC8578868.
4. Dhadse P, Gattani D, Mishra R. The link between periodontal disease and cardiovascular disease: How far we have come in last two decades ? J Indian Soc Periodontol. 2010 Jul;14(3):148-54. Doi: 10.4103/0972-124X.75908. PMID: 21760667; PMCID: PMC3100856.

5. Sumayin Ngamdu K, Mallawaarachchi I, Dunipace EA, Chuang LH, Jafri SH, Shah NR, Jeong YN, Morrison AR, Bhatt DL. Association Between Periodontal Disease and Cardiovascular Disease (from the NHANES). Am J Cardiol. 2022 Sep 1;178:163-168. Doi: 10.1016/j.amjcard.2022.05.028. Epub 2022 Jun 27. PMID: 35773046.
6. Gani DK, Lakshmi D, Krishnan R, Emmadi P. Evaluation of C-reactive protein and interleukin-6 in the peripheral blood of patients with chronic periodontitis. J Indian Soc Periodontol. 2009 May;13(2):69-74. Doi: 10.4103/0972-124X.55840. PMID: 20407653; PMCID: PMC2847127.
7. Shetty B, Fazal I, Khan SF, Nambiar M, D KI, Prasad R, Raj A. Association between cardiovascular diseases and periodontal disease: more than what meets the eye. Drug Target Insights. 2023 Feb 2;17:31-38. Doi: 10.33393/dti.2023.2510. PMID: 36761891; PMCID: PMC9906023.
8. Rughwani RR, Cholan PK, Victor DJ. Congenital Heart Diseases and Periodontal Diseases-Is There a Link? Front Cardiovasc Med. 2022 Jun 30;9:937480. Doi: 10.3389/fcvm.2022.937480. PMID: 35845078; PMCID: PMC9279652.
9. Nazir MA. Prevalence of periodontal disease, its association with systemic diseases and prevention. Int J Health Sci (Qassim). 2017 Apr-Jun;11(2):72-80. PMID: 28539867; PMCID: PMC5426403.
10. Schenkein HA, Loos BG. Inflammatory mechanisms linking periodontal diseases to cardiovascular diseases. J Clin Periodontol. 2013 Apr;40 Suppl 14(0 14):S51-69. Doi: 10.1111/jcpe.12060. PMID: 23627334; PMCID: PMC4554326.
11. Kinane DF, Stathopoulou PG, Papapanou PN. Periodontal diseases. Nat Rev Dis Primers. 2017 Jun 22;3:17038. Doi: 10.1038/nrdp.2017.38. PMID: 28805207.

12. Genco RJ, Borgnakke WS. Risk factors for periodontal disease. Periodontol 2000. 2013 Jun;62(1):59-94. Doi: 10.1111/j.1600-0757.2012.00457.x. PMID: 23574464.
13. Dhadse P, Gattani D, Mishra R. The link between periodontal disease and cardiovascular disease: How far we have come in last two decades ? J Indian Soc Periodontol. 2010 Jul;14(3):148-54. Doi: 10.4103/0972-124X.75908. PMID: 21760667; PMCID: PMC3100856.
14. Pourmoghaddas Z, Meskin M, Sabri M, Norousali Tehrani MH, Najafi T. Dental Caries and Gingival Evaluation in Children with Congenital Heart Disease. Int J Prev Med. 2018 Jun 19;9:52. Doi: 10.4103/ijpvm.IJPVM_401_15. PMID: 30034670; PMCID: PMC6028990.
15. Loos BG, Van Dyke TE. The role of inflammation and genetics in periodontal disease. Periodontol 2000. 2020 Jun;83(1):26-39. Doi: 10.1111/prd.12297. PMID: 32385877; PMCID: PMC7319430.
16. Febbraio M, Roy CB, Levin L. Is There a Causal Link Between Periodontitis and Cardiovascular Disease? A Concise Review of Recent Findings. Int Dent J. 2022 Feb;72(1):37-51. Doi: 10.1016/j.identj.2021.07.006. Epub 2021 Sep 24. PMID: 34565546; PMCID: PMC9275186.
17. Ye Z, Cao Y, Miao C, Liu W, Dong L, Lv Z, Iheozor-Ejiofor Z, Li C. Periodontal therapy for primary or secondary prevention of cardiovascular disease in people with periodontitis. Cochrane Database Syst Rev. 2022 Oct 4;10(10):CD009197. Doi: 10.1002/14651858.CD009197.pub5. PMID: 36194420; PMCID: PMC9531722.
18. Guarnizo-Herreño CC, Wehby GL. Children's dental health, school performance, and psychosocial well-being. J Pediatr. 2012 Dec;161(6):1153-9. Doi: 10.1016/j.jpeds.2012.05.025. Epub 2012 Jun 23. PMID: 22727866; PMCID: PMC3459270.

19. Saraç F, Derelioğlu SŞ, Şengül F, Laloğlu F, Ceviz N. The Evaluation of Oral Health Condition and Oral and Dental Care in Children with Congenital Heart Disease. J Clin Med. 2023 May 25;12(11):3674. Doi: 10.3390/jcm12113674. PMID: 37297868; PMCID: PMC10253266.
20. Sadeghi A, Sarrafan A, Ebrahimi A, Moghadamnia N, Semnani PM, Tekieh SA, Modarresi A. The Effect of Dental Prosthesis on Oral Normal Microbes and Life Span.
21. Könönen E, Gursoy M, Gursoy UK. Periodontitis: A Multifaceted Disease of Tooth-Supporting Tissues. J Clin Med. 2019 Jul 31;8(8):1135. Doi: 10.3390/jcm8081135. PMID: 31370168; PMCID: PMC6723779.
22. Leng Y, Hu Q, Ling Q, Yao X, Liu M, Chen J, Yan Z, Dai Q. Periodontal disease is associated with the risk of cardiovascular disease independent of sex: A meta-analysis. Front Cardiovasc Med. 2023 Feb 27;10:1114927. Doi: 10.3389/fcvm.2023.1114927. PMID: 36923959; PMCID: PMC10010192.
23. Kumar A, Grover V, Satpathy A, Jain A, Grover HS, Khatri M, Kolte A, Dani N, Melath A, Chahal GS, Thomas B, Pradeep AR, Pandit N, Pillai BRM, Manjunath RGS, Nandkeoliar T, Puri K, Singhal R, Dodwad V, Bhardwaj A, Thakur R, Jalaluddin M, Boyapati R, Singh MK, Bansal M. ISP good clinical practice recommendations for gum care. J Indian Soc Periodontol. 2023 Jan-Feb;27(1):4-30. Doi: 10.4103/jisp.jisp_561_22. Epub 2023 Jan 3. PMID: 36873963; PMCID: PMC9979817.
24. Soldani FA, Lamont T, Jones K, Young L, Walsh T, Lala R, Clarkson JE. One-to-one oral hygiene advice provided in a dental setting for oral health. Cochrane Database Syst Rev. 2018 Oct 31;10(10):CD007447. Doi: 10.1002/14651858.CD007447.pub2. PMID: 30380139; PMCID: PMC6516798.

25. Kim J, Amar S. Periodontal disease and systemic conditions: a bidirectional relationship. Odontology. 2006 Sep;94(1):10-21. Doi: 10.1007/s10266-006-0060-6. PMID: 16998613; PMCID: PMC2443711.
26. Czerniuk MR, Surma S, Romańczyk M, Nowak JM, Wojtowicz A, Filipiak KJ. Unexpected Relationships: Periodontal Diseases: Atherosclerosis-Plaque Destabilization? From the Teeth to a Coronary Event. Biology (Basel). 2022 Feb 9;11(2):272. Doi: 10.3390/biology11020272. PMID: 35205138; PMCID: PMC8869674.
27. Suh JS, Kim S, Boström KI, Wang CY, Kim RH, Park NH. Periodontitis-induced systemic inflammation exacerbates atherosclerosis partly via endothelial-mesenchymal transition in mice. Int J Oral Sci. 2019 Jul 1;11(3):21. Doi: 10.1038/s41368-019-0054-1. PMID: 31257363; PMCID: PMC6802639.
28. Shaddox LM, Walker CB. Treating chronic periodontitis: current status, challenges, and future directions. Clin Cosmet Investig Dent. 2010 Aug 11;2:79-91. PMID: 23662085; PMCID: PMC3645457.
29. Roshna T, Nandakumar K. Generalized aggressive periodontitis and its treatment options: case reports and review of the literature. Case Rep Med. 2012;2012:535321. doi: 10.1155/2012/535321. Epub 2012 Jan 12. PMID: 22291715; PMCID: PMC3265097.
30. Prakasam A, Elavarasu SS, Natarajan RK. Antibiotics in the management of aggressive periodontitis. J Pharm Bioallied Sci. 2012 Aug;4(Suppl 2):S252-5. doi: 10.4103/0975-7406.100226. PMID: 23066264; PMCID: PMC3467876.
31. Munasur SL, Turawa EB, Chikte UME, Musekiwa A. Mechanical Debridement with Antibiotics in the Treatment of Chronic Periodontitis: Effect on Systemic Biomarkers-A Systematic Review. Int J Environ Res Public Health. 2020 Aug 3;17(15):5601. Doi: 10.3390/ijerph17155601. PMID: 32756461; PMCID: PMC7432753.

32. Prathapachandran J, Suresh N. Management of peri-implantitis. Dent Res J (Isfahan). 2012 Sep;9(5):516-21. Doi: 10.4103/1735-3327.104867. PMID: 23559913; PMCID: PMC3612185.
33. Radaelli K, Alberti A, Corbella S, Francetti L. The Impact of Peri-Implantitis on Systemic Diseases and Conditions: A Review of the Literature. Int J Dent. 2021 May 15;2021:5536566. Doi: 10.1155/2021/5536566. PMID: 34054959; PMCID: PMC8143885.
34. Corsalini M, Montagnani M, Charitos IA, Bottalico L, Barile G, Santacroce L. Non-Surgical Therapy and Oral Microbiota Features in Peri-Implant Complications: A Brief Narrative Review. Healthcare (Basel). 2023 Feb 23;11(5):652. Doi: 10.3390/healthcare11050652. PMID: 36900657; PMCID: PMC10000417.
35. Santacroce L, Passarelli PC, Azzolino D, Bottalico L, Charitos IA, Cazzolla AP, Colella M, Topi S, Godoy FG, D'Addona A. Oral microbiota in human health and disease: A perspective. Exp Biol Med (Maywood). 2023 Aug;248(15):1288-1301. doi: 10.1177/15353702231187645. Epub 2023 Sep 9. PMID: 37688509; PMCID: PMC10625343.
36. Herrera D, Sanz M, Shapira L, Brotons C, Chapple I, Frese T, Graziani F, Hobbs FDR, Huck O, Hummers E, Jepsen S, Kravtchenko O, Madianos P, Molina A, Ungan M, Vilaseca J, Windak A, Vinker S. Periodontal diseases and cardiovascular diseases, diabetes, and respiratory diseases: Summary of the consensus report by the European Federation of Periodontology and WONCA Europe. Eur J Gen Pract. 2024 Dec;30(1):2320120. Doi: 10.1080/13814788.2024.2320120. Epub 2024 Mar 21. PMID: 38511739; PMCID: PMC10962307.
37. Rodrigues WF, Miguel CB, Lazo-Chica JE, Trindade da Silva CA, Vieira CU, Clemente-Napimoga JT, Freire Oliveira CJ, Napimoga MH. Interleukin-6, tumor necrosis factor-α, C-reactive protein, and hematological parameters in experimental periodontal disease

after β-adrenergic blockade. J Indian Soc Periodontol. 2019 Nov-Dec;23(6):511-516. Doi: 10.4103/jisp.jisp_77_19. PMID: 31849395; PMCID: PMC6906902.

38. Gupta L, Thomas J, Ravichandran R, Singh M, Nag A, Panjiyar BK. Inflammation in Cardiovascular Disease: A Comprehensive Review of Biomarkers and Therapeutic Targets. Cureus. 2023 Sep 18;15(9):e45483. Doi: 10.7759/cureus.45483. PMID: 37859889; PMCID: PMC10584272.
39. Ye Z, Cao Y, Miao C, Liu W, Dong L, Lv Z, Iheozor-Ejiofor Z, Li C. Periodontal therapy for primary or secondary prevention of cardiovascular disease in people with periodontitis. Cochrane Database Syst Rev. 2022 Oct 4;10(10):CD009197. Doi: 10.1002/14651858.CD009197.pub5. PMID: 36194420; PMCID: PMC9531722.
40. Wu Y, Ding Y, Tanaka Y, Zhang W. Risk factors contributing to type 2 diabetes and recent advances in the treatment and prevention. Int J Med Sci. 2014 Sep 6;11(11):1185-200. Doi: 10.7150/ijms.10001. PMID: 25249787; PMCID: PMC4166864.
41. Makkar H, Reynolds MA, Wadhawan A, Dagdag A, Merchant AT, Postolache TT. Periodontal, metabolic, and cardiovascular disease: Exploring the role of inflammation and mental health. Pteridines. 2018 Feb;29(1):124-163. Doi: 10.1515/pteridines-2018-0013. Epub 2018 Nov 13. PMID: 30705520; PMCID: PMC6350811.
42. Pirih FQ, Monajemzadeh S, Singh N, Sinacola RS, Shin JM, Chen T, Fenno JC, Kamarajan P, Rickard AH, Travan S, Paster BJ, Kapila Y. Association between metabolic syndrome and periodontitis: The role of lipids, inflammatory cytokines, altered host response, and the microbiome. Periodontol 2000. 2021 Oct;87(1):50-75. Doi: 10.1111/prd.12379. PMID: 34463996; PMCID: PMC8457155.

43. Mawardi HH, Elbadawi LS, Sonis ST. Current understanding of the relationship between periodontal and systemic diseases. Saudi Med J. 2015 Feb;36(2):150-8. Doi: 10.15537/smj.2015.2.9424. PMID: 25719577; PMCID: PMC4375690.
44. Janakiram C, Dye BA. A public health approach for prevention of periodontal disease. Periodontol 2000. 2020 Oct;84(1):202-214. Doi: 10.1111/prd.12337. PMID: 32844412; PMCID: PMC7457923.
45. Isola G, Santonocito S, Lupi SM, Polizzi A, Sclafani R, Patini R, Marchetti E. Periodontal Health and Disease in the Context of Systemic Diseases. Mediators Inflamm. 2023 May 13;2023:9720947. Doi: 10.1155/2023/9720947. PMID: 37214190; PMCID: PMC10199803.