RESEARCH PAPER

Orthodontics and Cardiovascular Diseases: Exploring Inflammatory and Microbiological Considerations

Dr. Hemanth M[1], Dr. Anadha N Gujar[2*], Dr. K. Gnana Shanmugham[3], Dr. Adarsh S Naik[4]

[1]BDS, MDS, PhD, Principal and Head, Dayananda Sagar College of Dental Sciences and Hospital, Bangalore

[2*]BDS, MDS, PhD, Professor, Dept of Orthodontics, Dayananda Sagar College of Dental Sciences and Hospital, Bangalore

[3]BDS, MDS, Professor, Department of Orthodontics, Sree Balaji Dental College, Bharat Institute of Higher Education and Research, Chennai

[4]MBBS, MS, F.V.R.S, Associate professor, Dept of Ophthalmology, BGS Medical College and Hospital, Nagarur, Bangalore

Corresponding Author: Dr. Anadha N Gujar, BDS, MDS, PhD, Professor, Dept of Orthodontics, Dayananda Sagar College of Dental Sciences and Hospital, Bangalore

ABSTRACT

The significance of oral health in systemic disease is receiving more attention since cardiovascular disease continues to be a major source of morbidity and mortality worldwide. Although there has been much research on the connection between periodontal disease and cardiovascular disorders, less is known about how orthodontic therapy may affect cardiovascular health. By means of inflammatory, microbiological, and biomaterial-related pathways, such as cytokine release, procedure-associated bacteremia, oral microbiome dysbiosis, and possible systemic exposure to micro- and nanoplastics from orthodontic materials, orthodontic therapy may cause brief systemic biological reactions. Although there is currently little and mostly indirect evidence supporting a direct link between the mouth and the heart, these pathways offer a tenable biological foundation for a possible oral-cardiovascular connection. In a multidisciplinary context, this review summarizes the body of research on orthodontics and cardiovascular health, identifies important molecular pathways, and addresses clinical implications and potential future research avenues.

Keywords: Cardiovascular diseases; Cytokines; Inflammation; Orthodontics; Microbial pathogens.

How to cite this article: Hemanth M, Gujar AN, Shanmugham KG, Naik AS. Orthodontics and Cardiovascular Diseases: Exploring Inflammatory and Microbiological Considerations. Int J Drug Deliv Technol. 2026;16(15s): 905-912. DOI: 10.25258/ijddt.16.15s.101

Introduction

In a healthy mouth, the different oral microorganisms are known to exist in a symbiotic, balanced state. As long as the members of the healthy microbiota remain contained within the oral cavity, they are known to be non-pathogenic.[1] Oral cavity manipulation techniques have the potential to induce this bacteria into the bloodstream and result in local harm. The various groups of bacteria control the mouth cavity's normal and pathological states. The typical microbial flora's balanced state is disrupted during oral pathogenesis, which can also make oral disorders more severe.[1,2]

Bacterial pathogens can enter the bloodstream from the oral cavity through traumatic injuries to the mucosa or gingiva sustained during activities like chewing food or practicing oral hygiene, as well as diseases like periodontitis or dental caries and the complications they cause, and therapeutic interventions for their prevention and treatment.[3] This highlights the possibility of oral bacteremia, which might lead to infective endocarditis. Certain virulence factors and surface elements in different microbial species promote bacterial adherence to damaged endothelium walls and the thrombotic forms that follow. Infective endocarditis can be caused by several streptococcal, staphylococcal, and enterococcal species colonizing the endocardium.[4]

The placement of orthodontic appliances, such as brackets, tubes, band material, ligating materials, and arch-wires, inhibits proper oral hygiene, facilitates microbial adhesion, and creates new retentive areas for plaque and debris. This puts patients at risk for increased microbial burden and potential side effects, including gingival inflammation and white spot lesions.[5] More people are seeking orthodontic treatment these days to improve their quality of life and achieve a beautiful and

healthy smile. Numerous microorganisms naturally inhabit the mouth cavity; this ecological niche may serve as a reservoir for pathogenic and opportunistic microorganisms that could potentially induce systemic infections as well as cross-contamination.[6]

Orthodontic therapy may act as a transient systemic inflammatory stimulus with potential cardiovascular implications, although there is currently insufficient data to form clear conclusions about this association. Therefore, the goal of this review is to critically assess the information that is currently available about the connection between orthodontic treatment and cardiovascular health.

Epidemiological overview of non-communicable and cardiovascular diseases

Non-communicable diseases (NCDs) cause 41 million deaths annually, or 71% of all deaths worldwide, and are becoming more common due to an aging population, sophisticated diets, and sedentary lifestyles. In the United States, 80% of adults over 65 have one or more NCDs, and 77% have at least two. This results in a substantial burden of disease for both individuals and the healthcare system. Cardiovascular disease (CVD) is the leading cause of NCD burden worldwide, accounting for 17.9 million fatalities (a third of all deaths) and 45% of deaths caused by NCDs.[7]

Atherosclerotic disorders, primarily coronary heart disease, cerebrovascular disease, and peripheral vascular disease, are collectively referred to as CVD in this consensus report. Rheumatoid arthritis, psoriasis, systemic lupus erythematosus, and periodontitis are among the chronic infectious, inflammatory, and immune conditions that are linked to noticeably increased risks of adverse cardiovascular events. These findings are in line with the theory that long-term increases in the systemic inflammatory burden are causally linked to the onset of CVD and its aftereffects. Although there is evidence that more than 50 gene polymorphisms influence atherogenesis, effect sizes are small, and the main conventional risk factors for CVD continue to be lifestyle factors, primarily tobacco use, dyslipidemia, hypertension, and altered glucose metabolism.[8] The most severe type of periodontitis affects 11.2% of the world's population, making it the sixth most prevalent human disease. It is also an NCD with a high prevalence of 45% to 50% overall.[9]

Dysbiotic Oral Microbiota and the Development of Valvular Heart Disease

Unfortunately, over 50% of oral bacteria cannot be grown or identified, making oral dysbiosis a known risk factor for metabolic and cardiovascular diseases.[10] To better understand the interaction of synergistic and antagonistic interspecies as well as the imbalance of various bacteria that contribute to illness incidence, various culture-independent detection approaches have been developed in recent years. More than 300 of the 700 bacterial species found in the mouth cavity have been cultivated.[11,12]

The two most common microbially mediated oral diseases that affect people are periodontal disease and dental caries. As a colony of microbial cells embedded in an extracellular matrix, dental plaque is currently referred to as a polymicrobial biofilm. Dental plaque can be divided into two primary groups: subgingival, which occurs below the gingival margin, and supragingival, which occurs above the gingival margin. Numerous bacteria, including Firmicutes and Actinobacteria, are present in the former.[13] The majority of bacteria found in dental plaque are still members of the Streptococcus genus, which includes S. gordonii, S. mitis, S. mutans, and S. sanguis.[14] Actinomyces, Campylobacter, Capnocytophaga, Fusobacterium, Neisseria, and Veillonella are other bacteria that are frequently identified from dental plaque.[15,16]

Researchers have been concerned with the connection between heart disease and dental disease for decades. It is currently unknown if there is a direct correlation between these two conditions based on pathophysiological mechanisms that make periodontal disease an independent predictor of CVD or if there is a direct correlation because these two conditions frequently share several risk factors, such as smoking and an unhealthy diet.[17,18] Heart attacks, strokes, and other major cardiovascular events are more likely to occur in those with dental illness.[19,20]

Dental diseases with a potential to entrap a link with CVD included periodontal disease, vertical bone lesions, endodontic disease, dental caries, and dental infection.[21-23] The results of the study showed a positive correlation between the number of teeth lost, cardiovascular mortality, ischemic events, and abdominal aortic calcification.[19,20] Furthermore, a systemic sickness may be triggered by a lesion resulting from endodontic disease. Patients with CVD also exhibit poor oral hygiene and a dramatically reduced tooth count.[24-26]

Cytokine-mediated associations between Orthodontics and Cardiovascular disorders

Application of ideal force on the tooth induces the release of specific cytokines, producing alveolar bone remodeling. One type of environmental factor linked to the emergence of periodontal disease is orthodontic appliances.[27] Depending on the amount of cytokines released by the orthodontic force, the outcome may be either controlled tooth movement or gross resorption that compromises the periodontium.

According to a study, after three weeks of therapy with both aligners and the traditional labial fixed appliance, the levels of the six cytokines under investigation in GCF (IL-1α, IL-1ß, IL-2, IL-6, IL-8, and TNF-α) rose. While some cytokines rose more than others, others did not. The two groups' changes in cytokine levels from baseline to three weeks, however, differed only a little.[28] Determining the amounts of different cytokines during orthodontic treatment unquestionably aids in our comprehension of the fundamental process of bone metabolism.[29,30]

Fixed orthodontic treatment causes some changes in the mouth environment. A higher risk of caries and periodontal disorders results from increased plaque accumulation, a rise in the number of bacteria, and a reduction in pH. The decalcification of enamel might have detrimental consequences on the periodontium in addition to white spot lesions and caries.[28,31] Several factors, including surface features, influence microbial adhesion and plaque deposition, but bracket design is the most significant factor.8. Complex bracket designs lead to decreased self-cleaning efficiency, which leads to the accumulation of supragingival plaque. The positioning of the orthodontic brackets may have an impact on the biofilm's development.[32-33]

The mechanotransduction that takes place during the orthodontic tooth movement is what causes the cytokines to be released.[34,35] Even though cytokine generation during orthodontic treatment has been extensively studied, there have been variations in device design and applied forces. Through the release of certain cytokines, the tension exerted by the device during orthodontic therapy causes the periodontium to remodel, enabling regulated tooth movement.[36,37]

The use of lingual fixed appliances has increased due to the new need for aesthetics in orthodontic treatment; nevertheless, compared to labial fixed appliances, lingual fixed appliances have a higher risk of plaque formation because of where they are placed.[38] It has been demonstrated that TNF-α and IL-1 play a significant role in the development of periodontitis. Apart from being well-known inflammatory mediators, TNF-α and IL-1 have also been demonstrated to trigger additional inflammatory mediators, such as prostaglandin E2, matrix metalloproteinases, IL-8, IL-6, and others.[38,39]

According to another study, after three weeks of treatment, all of the cytokines (IL-1α, IL-1β, IL-2, IL-6, IL-8, and TNF-α) examined in the study showed a rise in their GCF levels in patients treated with both lingual and labial fixed appliances.[40] Additionally, lingual had greater cytokine levels. The lingual appliance may be putting more mechanical stress on the periodontium than the labial fixed appliance, as compared to the labial appliance. The way that plaque builds up in clear aligners and fixed lingual appliances differs.[40]

The gingival margins have long been thought to be the primary cause of periodontal disorders.[41] Since plaque adherence is caused by a variety of factors other than the bracket material, the orthodontic treatment revealed a change in the microbial population. The patient's age, salivary variables, kind of appliance, misaligned teeth, oral hygiene, and plaque accumulation may be impacted by systemic factors.[42]

Retention spaces are established for the buildup of plaque by fixed orthodontic appliances, impacting dental hygiene, raising the possibility of demineralization of enamel, caries, inflammation of the gingiva, and reduced periodontal health.[43] The periodontal status of adult patients using fixed buccal appliances and removable aligners was examined during a year of continuous orthodontic treatment, and found that the use of fixed buccal orthodontic appliances was linked to a reduction in periodontal health and elevated amounts of periodontopathic bacteria, in contrast to therapy with removable aligners for the course of the 12-month research.[43] The meta-analysis and systematic review conducted by Guo et al. revealed that the level of subgingival bacteria following orthodontic appliance implantation.[44,45]

Inflammation and Atherosclerosis: The oral-systemic link

An immune/inflammatory condition called atherosclerosis manifests as localized intimal thickening. Endothelial dysfunction is the trigger for atherogenesis. Although endothelial dysfunction first appears at the locations of arterial bifurcations, risk factors like

hypertension and hypercholesterolemia can also cause patches of endothelial dysfunction. Smooth muscle cell (SMC) migration and proliferation are stimulated by pro-inflammatory cytokines generated by activated macrophages or T-cells, which also contribute to the local inflammation of the lesion. As a result, inflammation is seen at every stage of lesion formation and contributes to both lesion instability and rupture.[46]

The oral biofilm's physical proximity to the periodontal vasculature makes it easier for oral bacteria to migrate systemically to distant locations from the oral cavity, like the heart. According to a review by Parahitiyawa et al., the sulcular epithelium is very thin and easily disrupted.[47] The sulcular epithelium can be disturbed by mastication, oral hygiene practices (tooth brushing and flossing), and periodontal operations (periodontal probing, tooth extractions, removal of subgingival plaque and calculus, as well as surgery), which can result in a bacteremic state.[48,49] The periodontal vasculature expands in both gingivitis and periodontitis, increasing its surface area and promoting bacteremia (reviewed in Parahitiyawa et al.[47] Due to a larger bacterial burden, people who practice poor oral hygiene are more likely to acquire bacteremia during periodontal procedures.[47-49]

Orthodontic treatments and infectious endocarditis risk

After orthodontic appliances are placed, dental plaque and the germs that make it up have been shown to increase because these appliances create retentive areas that are difficult to effectively clean by brushing your teeth. After orthodontic bands were applied to the teeth, Bloom and Brown1 demonstrated that the oral microbiota was higher than it was before band placement. They suggested that the increased number of organisms was directly related to the number of bands placed in the mouth.[50]

Teeth cleaning and polishing have been linked to infectious endocarditis and bacteremia. As a result, this operation may put the patient at risk for infective endocarditis. Antibiotic prophylaxis is therefore necessary in susceptible patients for band implantation and removal, as well as any tooth polishing, according to the literature. Neither a confirmed case of infective endocarditis nor a substantial risk of bacteremia has ever been linked to the adjustment of permanent or removable orthodontic appliances. This is the reason the American Heart Association did not advocate prophylactic orthodontic appliance adjustment in their most current guidelines.[51]

Likewise, obtaining impressions for research models does not need prophylactic antibiotics and is not linked to a serious bacteremia that could result in infective endocarditis. In patients who are sensitive to infective endocarditis, exposing teeth, especially palatal canines, is a surgical procedure that could result in bacteremia and necessitates prophylactic antibiotics. The surgical site does not need additional antibiotics after the tooth is revealed and can be regarded similarly to an extraction site or erupting tooth.[52]

Compared to traction after replaced flap procedures, it has been suggested that traction after excisional exposure may lower the incidence of bacteraemia. The possibility of bacteremia during the traction phase may be the basis for this advice. Any tooth movement through a replacement flap, in our opinion, is comparable to hastened tooth eruption and shouldn't necessitate the use of preventative antibiotics.[53]

Before beginning any treatment, the cardiologist should fully understand the patient's condition. This may need additional confirmatory testing. When the orthodontist has all of this information, the patient and/or guardian should be asked for their informed permission. The authors believe that a treatment plan for patients at high risk of endocarditis should be realistic, doable, and not overly aggressive. Before beginning any orthodontic treatment, like with all patients, dental hygiene must be perfect.[52]

Patients at risk for infective endocarditis should maintain excellent oral hygiene because plaque buildup raises the possibility of serious bacteremia during treatment. Consideration must be given to stopping the appliance treatment if the patient's oral hygiene deteriorates during treatment and does not improve quickly. Prophylactic antibiotics should be administered to patients at "high" or "moderate" risk for operations known to be linked to bacteraemia.[52]

Possible cardiovascular implications of microplastic release from clear aligners

Microplastics and nanoplastics (MNPs) have been found to exist in both our bodies and our surroundings.[4] This raises questions about the potential for long-term wear of aligners and retainers to leach thermoplastic polymers, particularly MNPs. Wearing these devices for two years or more, in the case of retainers, is a common part of orthodontic therapy.[54]

These particles have been found in artery wall atheromas, which may be harmful to cardiovascular health, according to studies. Heart rate irregularities,

pericardial edema, myocardial fibrosis, and vascular effects such as hemolysis, thrombosis, and blood coagulation are among the cardiovascular consequences of MNPs. Furthermore, it has been discovered that MNPs worsen the cardiovascular toxicity of other environmental pollutants, which has an additional impact on the heart and blood vessels.[55]

Orthodontic treatment is still mainly underrepresented in oral-systemic research, despite a wealth of literature examining the link between periodontal disease and cardiovascular disorders. The effect of particular orthodontic materials or appliances on cardiovascular outcomes has not yet been directly assessed by any long-term clinical research. This demonstrates the need for further multidisciplinary research and reflects a large knowledge gap.

Conclusion

Although orthodontic therapy is typically thought of as a localized dental intervention, new research indicates that it may cause systemic biological reactions through pathways related to inflammation, microbiology, and biomaterials. Several indirect mechanisms, including transient bacteremia, cytokine-mediated systemic inflammation, oral microbiome dysbiosis, and possible release of micro- and nanoplastics from orthodontic materials, support a plausible biological link between orthodontic therapy and cardiovascular disease, even though the current literature does not establish a direct causal relationship between the two. In vulnerable people with underlying cardiovascular risk factors, these interactions might be especially important. Further longitudinal and interdisciplinary research is necessary to elucidate the clinical importance of these correlations and to direct evidence-based orthodontic practice in medically challenged individuals, given the scant and mostly indirect character of current data.

References

1. Dubey R, Jalili VP, Jain S, Dubey A. Transient bacteremia consequent to tooth brushing in orthodontic patients. Progress in Orthodontics 2012;13(3):237-245.
2. Dubey R, Jain S, Dubey A, Chaukse A, Suma S, Shrivastava T. Correlation of Transient Bacteremia with Duration of Orthodontic Treatment. J Ind Orthod Soc 2014;48(4):301-308.
3. Roberts GJ. Dentists are innocent! ―Everyday‖ bacteremia is the real culprit: a review and assessment of the evidence that dental surgical procedures are a principal cause of bacterial endocarditis in children. Pediatr Cardiol. 1999; 20:317-25.
4. Erverdi N, Acar A, Is¸guden B, Kadir T. Investigation of bacteremia € after orthodontic banding and debanding following chlorhexidine mouth wash application. Angle Orthod. 2001; 71:190 4.
5. Papaioannou, William, et al. “Adhesion of Streptococcus mutans to different types of brackets.” The Angle Orthodontist 2007;77(6):1090-95.
6. Schwiertz, Andreas. Microbiota of the human body: Implications in health and disease. Advances in Experimental Medicine and Biology. Springer, 2016;902.
7. Sanz M, Marco Del Castillo A, Jepsen S, Gonzalez-Juanatey JR, D'Aiuto F, Bouchard P, Chapple I, Dietrich T, Gotsman I, Graziani F, Herrera D, Loos B, Madianos P, Michel JB, Perel P, Pieske B, Shapira L, Shechter M, Tonetti M, Vlachopoulos C, Wimmer G. Periodontitis and cardiovascular diseases: Consensus report. J Clin Periodontol. 2020 Mar;47(3):268-288.
8. Holdt, M. H., & Teupser, D. Genetic background of atherosclerosis and its risk factors. In the ESC textbook of preventive cardiology. Oxford, UK: Oxford University Press 2015:21-25.
9. Kassebaum, N. J., Smith, A. G. C., Bernabé, E., Fleming, T. D., Reynolds, A. E., Vos, T., … Oral Health Collaborators. Global, regional, and national prevalence, incidence, and disability adjusted life years for oral conditions for 195 countries. A systematic analysis for the global burden of diseases, injuries, and risk factors. Journal of Dental Research 2009-2015; 96(4), 380–387.
10. He,J.; Li, Y.; Cao, Y.; Xue, J.; Zhou, X. The oral microbiome diversity and its relation to human diseases. Folia Microbiol. 2015, 60, 69–80.
11. Figuero, E.; Sánchez-Beltrán, M.; Cuesta-Frechoso, S.; Tejerina, J.M.; del Castro, J.A.; Gutiérrez, J.M.; Herrera, D.; Sanz, M. Detection of periodontal bacteria in atheromatous plaque by nested polymerase

chain reaction. J. Periodontol. 2011, 82, 1469–1477.
12. Paster, B.J.; Olsen, I.; Aas, J.A.; Dewhirst, F.E. The breadth of bacterial diversity in the human periodontal pocket and other oral sites. Periodontol. 2006, 42, 80–87.
13. Peterson, S.N.; Meissner, T.; Su, A.I.; Snesrud, E.; Ong, A.C.; Schork, N.J.; Bretz, W.A. Functional expression of dental plaque microbiota. Front. Cell. Infect. Microbiol. 2014, 4, 108.
14. Arweiler, N.B.; Netuschil, L. The Oral Microbiota. Adv. Exp. Med. Biol. 2016, 902, 45–60.
15. Sreenivasan, P.K.; Prasad, K.V.V. Distribution of dental plaque and gingivitis within the dental arches. J. Int. Med. Res. 2017, 45, 1585–1596.
16. Tanner, A.; Kressirer, C.; Rothmiller, S.; Johansson, I.; Chalmers, N. The Caries Microbiome: Implications for Reversing Dysbiosis. Adv. Dent. Res. 2018, 29, 78–85.
17. Hujoel PP, Drangsholt M, Spiekerman C, Derouen TA. Examining the link between coronary heart disease and the elimination of chronic dental infections. The Journal of the American Dental Association. 2001; 132: 883–889.
18. Dhadse P, Gattani D, Mishra R. The link between periodontal disease and cardiovascular disease: how far we have come in the last two decades? Journal of Indian Society of Periodontology. 2010; 14: 148–154.
19. Meurman JH, Qvarnström M, Janket S, Nuutinen P. Oral health and health behavior in patients referred for open-heart surgery. Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology. 2003; 95: 300–307.
20. Aoyama N, Suzuki JI, Kobayashi N, Hanatani T, Ashigaki N, Yoshida A, et al. Associations among tooth loss, systemic inflammation and antibody titers to periodontal pathogens in Japanese patients with cardiovascular disease. Journal of Peri odontal Research. 2018; 53: 117–122.
21. Frisk F, Hakeberg M, Ahlqwist M, Bengtsson C. Endodontic variables and coronary heart disease. Acta Odontologica Scan dinavica. 2003; 61: 257–262.
22. Caplan DJ, Chasen JB, Krall EA, Cai J, Kang S, Garcia RI, et al. Lesions of Endodontic Origin and Risk of Coronary Heart Disease. Journal of Dental Research. 2006; 85: 996–1000.
23. Aldossri M, Farmer J, Saarela O, Rosella L, Quiñonez C. Oral Health and Cardiovascular Disease: Mapping Clinical Hetero geneity and Methodological Gaps. JDR Clinical & Translational Research. 2021; 6: 390–401.
24. Berlin-Broner Y, Febbraio M, Levin L. Association between apical periodontitis and cardiovascular diseases: a systematic review of the literature. International Endodontic Journal. 2017; 50: 847–859.
25. An GK, Morse DE, Kunin M, Goldberger RS, Psoter WJ. Association of Radiographically Diagnosed Apical Periodontitis and Cardiovascular Disease: a Hospital Records–based Study. Journal of Endodontics. 2016; 42: 916–920.
26. González Navarro B, Pintó Sala X, Jané Salas E. Relationship between cardiovascular disease and dental pathology. Systematic review. Medicina ClíNica. 2017; 149: 211–216.
27. Gelgor IE, Karaman A, Ercan E. Prevalence of malocclusion among adolescents in central anatolia. Eur J Dent. 2007;1:125–131.
28. Gujar AN, Baeshen HA, Alhazmi A, Bhandi S, Raj AT, Patil S, Birkhed D. Cytokine levels in gingival crevicular fluid during orthodontic treatment with aligners compared to conventional labial fixed appliances: a 3-week clinical study. Acta Odontol Scand. 2019 Aug;77(6):474-481.
29. Reynolds JJ, Meikle MC. Mechanisms of connective tissue matrix destruction in periodontitis. Periodontol 2000. 1997;14:144–157.
30. Båge T, Lindberg J, Lundeberg J, et al. Signal pathways JNK and NF kappa B, identified by global gene expression profiling, are involved in regulation of TNFalpha-induced mPGES-1 and COX-2 expression in gingival fibroblasts. BMC Genomics. 2010;11:241–250.
31. Gelgor IE, Karaman AI, Ercan E. Prevalence of malocclusion among adolescents in central anatolia. Eur J Dent 2007;1:125-31.

32. Socransky SS, Haffajee AD, Smith C, Dibart S. Relation of counts of microbial species to clinical status at the sampled site. J Clin Periodontol 1991;18:766-75.
33. Lee SM, Yoo SY, Kim HS, Kim KW, Yoon YJ, Lim SH, et al. Prevalence of putative periodontopathogens in subgingival dental plaques from gingivitis lesions in Korean orthodontic patients. J Microbiol 2005;43:260-5.
34. Andrade I, Silvana R, Taddei SR, et al. Inflammation and tooth movement: the role of cytokines, chemokines, and growth factors. Semin Orthod. 2012;18:257–269.
35. Ren Y, Vissink A. Cytokines in crevicular fluid and orthodontic tooth movement. Eur J Oral Sci. 2008;116:89–97.
36. Castroflorio T, Gamerro EF, Caviglia GP. Biochemical markers of bone metabolism during early orthodontic tooth movement with aligners. Angle Orthod. 2017;87:74–81.
37. Rody WJ, Wijegunasinghe M, Wiltshire WA, et al. Differences in the gingival crevicular fluid composition between adults and adolescents undergoing orthodontic treatment. Angle Orthod. 2014;84:120–126.
38. Serra E, Perinetti G, D'Attillo M, Cordella C, Poalantani M, Festa F, et al. Lactate dehydrogenase activity in gingival crevicular fluid during orthodontic treatment. Am J Orthod 2003;124:206-11.
39. Alfaqeeh SA, Anil S. Gingival crevicular fluid flow rate and alkaline phosphatase level as potential marker of active tooth movement. Oral Health Dent Manag 2015;13:458-63.
40. Gujar AN, Baeshen HA, Alhazmi A, Ghoussoub MS, Raj AT, Bhandi S, Sarode SC, Awan KH, Birkhed D, Patil S. Comparison of biochemical markers of bone metabolism between conventional labial and lingual fixed orthodontic appliances. Niger J Clin Pract. 2020 Apr;23(4):568-573.
41. 18. Hirsch DI,Kulbersh R, KaczynskiR. Assessmentof pretreatment or thodontic patients using the BANA test. N-benzoyl-DL-arginine naphthylamide. Am JOrthodDentofacial Orthop1997;112:154-8.
42. Forsberg CM, Brattstr€om V, Malmberg E, Nord CE. Ligature wires and elastomeric rings: two methods of ligation, and their associa tion with microbial colonization of Streptococcus mutans and lac tobacilli. Eur J Orthod 1991;13:416-20.
43. 34. Karkhanechi M, Chow D, Sipkin J, Sherman D, Boylan RJ, Norman RG, et al. Periodontal status of adult patients treated with fixed buccal appliances and removable aligners over one year of active orthodontic therapy. Angle Orthod 2013;83:146-51.
44. Guo R, Lin Y, Zheng Y, Li W. The microbial changes in subgingival plaques of orthodontic patients: a systematic review and meta analysis of clinical trials. BMC Oral Health 2017;17:90.
45. Gujar AN, Al-Hazmi A, Raj AT, Patil S. Microbial profile in different orthodontic appliances by checkerboard DNA-DNA hybridization: An in-vivo study. Am J Orthod Dentofacial Orthop. 2020 Jan;157(1):49-58
46. Valtonen VV. Role of infections in atherosclerosis. Am Heart J 1999; 138: 4313.
47. Parahitiyawa NB, Jin LJ, Leung WK, Yam WC, Samaranayake LP. Microbiology of odontogenic bacteremia: beyond endo carditis. Clin Microbiol Rev 2009; 22: 4664.
48. Heart, Stroke, and Vascular Diseases Australian Facts 2004. Canberra: Australian Institute of Health and Welfare, National Heart Foundation of Australia, National Stroke Foundation Australia; 2004.
49. Crouse JR. Progress in coronary artery disease risk factor research: what remains to be done? Clin Chem 1984; 30: 11257.
50. Hussein, Emad & Acar, Ahu & Aksoy, Alev & Kadir, Tanju & Caldemir, Seniz & Erverdi, Nejat. (2009). Investigation of bacteremia after toothbrushing in orthodontic patients.KOREAN J ORTHOD. 39. 10.4041/kjod.2009.39.3.177.
51. Dajani AS, Taubert KA, Wilson W, Bolger AF, Bayer A, Ferrieri P, et al. Prevention of bacterial endocarditis, recommendations by the of the American Medical Association. J Am Heart Assoc. 1997;277:1974–1801.
52. Yadav SK, Kedia NB, Kedia G, Kumar K. Infective endocarditis: An Orthodontist's perspective. IP Indian J Orthod Dentofacial Res 2020;6(2):39-43.

53. HobsonRS,Clark JD. Management of the orthodontic patient 'at risk' from infective endocarditis. Br Dent J. 1995;178:289–95.
54. Ali N, Katsouli J, Marczylo EL, Gant TW, Wright S, de la Serna JB. The potential impacts of micro-and-nano plastics on various organ systems in humans. EBioMedicine 2024;99:104901.
55. Marfella R, Prattichizzo F, Sardu C, Fulgenzi G, Graciotti L, Spadoni T, et al. Microplastics and nanoplastics in atheromas and cardiovascular events. N Engl J Med 2024;390:900-10.