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Tannerella forsythia, an orthodontic point of view

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Abstract
Introduction: *Tannerella forsythia*, is an anaerobic, Gram-negative microorganism closely related to periodontal disease. Factors such as poor dental hygiene, fixed orthodontic appliances, etc. can cause dysbiosis in the bacterial community.
Objective: To analyze the literature about the epidemiology, diagnostic methods, oral manifestations, relationship with systemic diseases and treatment of *Tannerella forsythia* in orthodontic patients.
Methodology: Using the keywords "*T. forsythia*", "orthodontics", "oral manifestations", "diagnostics", "treatment" and "epidemiology", the main public databases were searched, with emphasis on the last 5 years. It was evaluated with the PRISMA and AMSTAR-2 guidelines.
Results: At the national level, in 2019, cases of gingivitis and periodontal disease ranked fifth among the twenty main causes of diseases. As a diagnostic method, most of the studies used molecular biology (PCR) for the identification of bacterial DNA. Very few studies performed cultures for identification. *T. forsythia* is capable of inducing characteristic signs of gingivitis and periodontal disease. Non-surgical mechanical therapy remains the gold standard in its treatment. There are multiple diseases that can be related to the presence of *T. forsythia*, so its medical importance becomes more relevant and its control, essential.
Conclusion: *T. forsythia* is closely related to periodontal disease. Its presence is mainly found in the easily accumulated plaque in patients with fixed appliances. It is essential to diagnose it for a treatment that can avoid harm to the patient.

Keywords: *Tannerella forsythia*, orthodontics, diagnosis, treatment, epidemiology

1. Introduction
Tannerella forsythia is a microorganism that is closely related to periodontal disease. Periodontal disease is an infectious disease of periodontal tissues that can lead to tooth loss if it is not intervened in time [1]. In order to proliferate and persist, bacteria tend to live in biofilms. In the oral cavity, biofilms constitute what is known as "dentobacterial plaque" which can cause damage when accumulating for a long time. It is said that more than 300 bacterial species live inside a periodontal pocket [2]. According to Socransky and Haffajee, periodontal bacterial complexes can be grouped by color; *Tannerella forsythia*, is part of a group of bacteria called the "red bacterial complex", which includes *Porphyromonas gingivalis* and *Treponema denticola* [1, 3, 4]. In a healthy individual, without periodontal disease, bacteria exist in a natural balance with the host. However, different factors such as diabetes, smoking, genetic predisposition, poor dental hygiene, fixed orthodontic appliances, etc. can cause a dysbiosis in the bacterial community [5]. In the literature, it is mentioned that red and orange bacterial complexes are frequently associated with tissue inflammation during orthodontic treatments, so the appliances placed in the mouth have a close correlation with periodontal disease. However, correct alignment of the dental organs can provide long-term periodontal health benefits [6, 7]. There are not many studies about the impact of *T. forsythia* on patients treated with orthodontics, so the aim of this study is to analyze the literature about the epidemiology, diagnostic methods, oral manifestations, relationship with systemic diseases and treatment of *Tannerella forsythia* in orthodontic patients. Such research can help prevent any subsequent periodontal damage that may have a permanent impact on the patient.

2. Materials and Methods

Articles on the subject published through the PubMed, SCOPUS and Google Scholar databases were analyzed, with emphasis on the last 5 years. The quality of the articles was evaluated using PRISMA guidelines, i.e., identification, review, choice and inclusion. The quality of the reviews was assessed using the measurement tool for evaluating systematic reviews (AMSTAR-2). The search was performed using Boolean logical operators AND, OR and NOT. It was realized with the words "*Tannerella forsythia*", together with "orthodontics", "oral manifestations", "treatment" and "epidemiology. The keywords were used individually, as well as each of them related to each other.

3. Results & Discussion

3.1 Epidemiology

Periodontitis is a very common condition affecting approximately 15%-20% of the population worldwide at an age between 35-44 years [8]. *T. forsythia, T. denticola, C. rectus* and *P. nigrescens* are significantly more common in the samples obtained from the orthodontic patients [9-11].

The literature describes that 60% of all orthodontic patients experience a variation in biofilm accumulation after the necessary appliance bonding. [12, 5]. Some studies; have analyzed the periodontal and microorganism change after orthodontic treatment. Three months after removal, a significant reduction of periodontopathogens such as *Tannerella forsythia* found during treatment was observed [13]. A study by Paolantonio and Cols., found that the frequency of subgingival pathogenic microbiota, significantly increased 1 month after application and was maintained up to three months after removal, which could mean an increased risk of periodontal disease [14]. It is important to highlight the degree of incidence in periodontal disease where periodontal pathogens such as *T. forsythia* play an important role. Therefore, orthodontists should take into account the priority in plaque control to avoid irreversible damage.

3.2 Diagnostic Methods

In most of the studies, molecular biology techniques were used for the extraction of bacterial DNA to identify *T. forsythia*. Samples were obtained by different methods. One fossil-based study used 344 microbiomes from human teeth that were 1000 to 2000 years old [8]. Another study used, in addition to DNA, plaque level, gingival bleeding level, probing depth and biofilm samples for PCR testing [15]. Association studies of *T. forsythia* with some other disease were also evaluated by molecular biology, where they identified the presence of the microorganism in a saliva sample [16]. In a study in which three types of orthodontic appliances were compared with the aim of evaluating the microbiota in each of them; they also isolated DNA by means of salivary samples to subsequently perform PCR and identify the microorganisms present, among which *T. forsythia* was mainly found [12]. Similar molecular biology methods (DNA hybridization) were performed for the identification of microorganisms isolated from the plaque found in the sulcus of a molar on which a metallic band was placed [17]. Another study reported the use of culture media in which an attempt was made to reproduce a bacterial environment for the growth of *T. forsythia*, subsequently with the help of an electron microscope a quantitative analysis of the bacteria was performed [18]. It is important to mention that, for a more accurate identification, most studies opted to perform molecular biology methods such as PCR for the identification of bacterial DNA. Very few studies were found that performed cultures for identification. Each study used a different sampling method according to their convenience.

3.3 Oral manifestations

T. forsythia is a microorganism that has been frequently associated with periodontal disease. Multiple studies have shown that there is a significantly higher frequency of *T. forsythia* in subgingival plaque in subjects with periodontal disease than in healthy subjects [19, 2]. Thus, its oral manifestations are directly related to the signs and symptoms of periodontitis [20]. High levels of *T. forsythia* have also been found in patients with gingival bleeding compared to those without gingival bleeding. Therefore, it can be attributed as one of the main clinical signs associated with its presence [21]. Importantly, *T. forsythia* causes a polymicrobial challenge to the immune system, which triggers a response that, under certain circumstances and in a subset of the population, leads to the progressive destruction of soft and hard tissues that characterizes periodontitis [22]. In a study correlating different periodontal pathogens with gingival enlargement during orthodontics, *T. forsythia* was found to be present [23]. Therefore, although *T. forsythia* is capable of inducing signs of periodontal disease such as the onset of connective tissue destruction and alveolar bone resorption [24]; a synergistic relationship between *T. forsythia* and other periodontal pathogens may be necessary to produce major gingival pathology, but it is demonstrable that its presence causes damage that may become irreversible in the patient's periodontium if not addressed in time. From a simple gingival inflammation and bleeding to the destruction of the gingiva.

3.4 Treatment

Scaling and root planing (SRP) are major components of any successful periodontal treatment. However, it is only effective in reducing bacterial load and does not completely eradicate all pathogens from deep pockets, either because of their presence in locations within periodontal tissues or in areas inaccessible to instrumentation [25, 26]. In such cases, adjunctive antibiotic therapy has been used. However, in any of these scenarios, the possibility of reinoculation and reinfection can cause recurrence of periodontal disease [27]. The protocol used considers the administration of amoxicillin and metronidazole alone in conjunction with non-surgical periodontal therapy. This combination has been repeatedly shown to be beneficial in the treatment of periodontitis [29]. Other studies show the efficacy of treatment combining mechanical scaling and root planning therapy with chlorhexidine gluconate for subgingival application. Where the data suggest that, combined with mechanical therapy, has a significantly greater and prolonged effect in the elimination of periodontal pathogens [25]. There are cases where a laser has been used that locally targets pathogens. In periodontal disease, the use of this laser is suggested as an adjunct in conjunction with scaling and root planing therapy [29, 30, 31]. Non-surgical mechanical therapy remains the gold standard in the treatment of periodontitis, as it removes or destroys subgingival biofilm. However, it is important to consider that there are adjuvants that can enhance efficacy in pathogen control.

3.5 Relationship of *T. forsythia* with other diseases

Esophageal cancer: It is the eighth most common cause of death in the world. Although much of the ethology of this type of cancer is attributed to lifestyle; an association of the

presence of *P. gingivalis* and *T. forsythia* has been attributed to an increased risk of this disease. According to the study developed by Malinowski and Cols. in 2019, it has been seen that *T. forsythia* could introduce pro-inflammatory cytokines such as IL-1β and IL-6 by CD4 cells [32].

Atherosclerosis: Lee and Cols. found that *T. fosythia* and BspA increased the progression of atherosclerotic lesions in mice. This process could be associated with down-regulation of lipid metabolism related to low gene expression. Mahalakshmi and Cols. conducted another study in which statistical significance was observed in the presence of *T. forsythia* and other periodontal pathogens with atherosclerosis [33, 34].

Rangé H and Cols. mention that there is a potential role of periodontal microorganisms, but that especially *T. forsythia*, is related to neutrophil activation within hemorrhagic atherosclerotic carotid plaques [35].

Rheumatoid arthritis: In addition, a statistically significant association of *T. forsythia* with high rheumatoid arthritis activity was presented [16].

Osteoporosis: In one study, periodontitis was detected in 77.1% of women with osteoporosis or osteopenia. In addition, a significant correlation was found between osteoporosis and missing teeth. Where *T. forsythia* and *C. rectus* were detected in 100% of the samples [36].

HIV: A study investigated the association between detectable human immunodeficiency virus (HIV) plasma viral load (HVL) and high levels of periodontal and non-periodontal microorganisms in the subgingival microbiota of people with HIV. Thus, detectable viral load in individuals with HIV was associated with elevated levels of known periodontal pathogens, such as *P. nigrescens*, *T. forsythia* and *E. corrodens*, etc [37].

Diabetes: Another disease that can be closely related to periodontal pathogens is diabetes. One study shows poor glycemic control; which is associated with increased levels and frequencies of periodontal pathogens in the subgingival biofilm of subjects with type 2 DM and periodontitis [38, 39].

There are multiple diseases that can be related to the presence of *T. forsythia* so its medical importance becomes more relevant and its control is essential.

4. Conclusions

The high incidence and prevalence of periodontal disease where *T. forsythia* plays an important role, increases the attention that orthodontists must have to avoid irreversible damage in patients. For diagnosis, most studies have opted for molecular biology methods such as PCR to identify bacterial DNA. The presence of *T. forsythia* can cause anything from simple inflammation and gingival bleeding to destruction of the patient's periodontium if not treated in time. There are multiple diseases that can be related to the presence of *T. forsythia* so the medical importance and control through oral hygiene in orthodontic patients is essential.

5. References

1. Friedrich V, Janesch B, Windwarder M, Maresch D, Braun ML, Megson ZA, *et al*. *Tannerella forsythia* strains display different cell-surface nonulosonic acids: biosynthetic pathway characterization and first insight into biological implications. Glycobiology 2017;27(4):342-357.
2. Naginyte M, Do T, Meade J, Devine DA, Marsh PD. Enrichment of periodontal pathogens from the biofilms of healthy adults. Sci Rep 2019;9(1):5491.
3. Sekot G, Posch G, Messner P, Matejka M, Rausch-Fan X, Andrukhov O *et al*. Potential of the *Tannerella forsythia* S-layer to delay the immune response. J Dent Res 2011;90(1):109-14.
4. Singhrao SK, Harding A, Poole S, Kesavalu L, Crean S. *Porphyromonas gingivalis* Periodontal Infection and Its Putative Links with Alzheimer's Disease. Mediators Inflamm 2015;2015:137357.
5. Mombelli A, Almaghlouth A, Cionca N, Cancela J, Courvoisier DS, Giannopoulou C. Microbiologic Response to Periodontal Therapy and Multivariable Prediction of Clinical Outcome. J Periodontol 2017;88(12):1253-1262.
6. Bloch S, Thurnheer T, Murakami Y, Belibasakis GN, Schäffer C. Behavior of two *Tannerella forsythia* strains and their cell surface mutants in multispecies oral biofilms. Mol Oral Microbiol 2017;32(5):404-418.
7. Bergamo AZN, de Oliveira KMH, Matsumoto MAN, Nascimento CD, Romano FL, da Silva RAB, *et al*. Orthodontic appliances did not increase risk of dental caries and periodontal disease under preventive protocol. Angle Orthod 2019;89(1):25-32.
8. Philips A, Stolarek I, Handschuh L, Nowis K, Juras A, Trzciński D *et al*. Analysis of oral microbiome from fossil human remains revealed the significant differences in virulence factors of modern and ancient *Tannerella forsythia*. BMC Genomics 2020;21(1):402.
9. 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(3):260-5.
10. Kim SH, Choi DS, Jang I, Cha BK, Jost-Brinkmann PG, Song JS. Microbiologic changes in subgingival plaque before and during the early period of orthodontic treatment. Angle Orthod. 2012;82(2):254-60.
11. Choi DS, Cha BK, Jost-Brinkmann PG, Lee SY, Chang BS, Jang I *et al*. Microbiologic changes in subgingival plaque after removal of fixed orthodontic appliances. Angle Orthod 2009;79(6):1149-55.
12. 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;157(1):49-58.
13. Yáñez-Vico RM, Iglesias-Linares A, Ballesta-Mudarra S, Ortiz-Ariza E, Solano-Reina E, Perea EJ. Short-term effect of removal of fixed orthodontic appliances on gingival health and subgingival microbiota: a prospective cohort study. Acta Odontol Scand 2015;73(7):496-502.
14. 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(1):90.
15. Alves de Souza R, Borges de Araújo Magnani MB, Nouer DF, Oliveira da Silva C, Klein MI, Sallum EA, *et al*. Periodontal and microbiologic evaluation of 2 methods of archwire ligation: ligature wires and elastomeric rings. Am J Orthod Dentofacial Orthop. 2008;134(4):506-12.
16. Martínez-Rivera JI, Xibillé-Friedmann DX, González-Christen J, de la Garza-Ramos MA, Carrillo-Vázquez SM *et al*. Salivary ammonia levels and *Tannerella forsythia* are associated with rheumatoid arthritis: A cross sectional study. Clin Exp Dent Res 2017;3(3):107-114.

17. Do Nascimento C, Pita MS, Pedrazzi V, de Albuquerque Junior RF, Ribeiro RF. *In vivo* evaluation of Candida spp. adhesion on titanium or zirconia abutment surfaces. Arch Oral Biol 2013;58:853-861.
18. Shimotahira N, Oogai Y, Kawada-Matsuo M, Yamada S, Fukutsuji K, Nagano K, *et al*. The surface layer of *Tannerella forsythia* contributes to serum resistance and oral bacterial coaggregation. Infect Immun. 2013;81(4):1198-206.
19. Haffajee AD, Cugini MA, Tanner A, Pollack RP, Smith C, Kent RL Jr, *et al*. Subgingival microbiota in healthy, well-maintained elder and periodontitis subjects. J Clin Periodontol 1998;25(5):346-53.
20. Socransky SS, Smith C, Haffajee AD. Subgingival microbial profiles in refractory periodontal disease. J Clin Periodontol 2002;29(3):260-8.
21. Persson GR, Hitti J, Paul K, Hirschi R, Weibel M, Rothen M *et al*. *Tannerella forsythia* and *Pseudomonas aeruginosa* in subgingival bacterial samples from parous women. J Periodontol 2008;79(3):508-16.
22. Holt SC, Ebersole JL. *Porphyromonas gingivalis*, *Treponema denticola*, and *Tannerella forsythia*: the "red complex", a prototype polybacterial pathogenic consortium in periodontitis. Periodontol 2000, 2005;38:72-122.
23. Gong Y, Lu J, Ding X. Clinical, microbiologic, and immunologic factors of orthodontic treatment-induced gingival enlargement. Am J Orthod Dentofacial Orthop. 2011;140(1):58-64.
24. Chukkapalli SS, Rivera-Kweh MF, Velsko IM, Chen H, Zheng D, Bhattacharyya I *et al*. Chronic oral infection with major periodontal bacteria *Tannerella forsythia* modulates systemic atherosclerosis risk factors and inflammatory markers. Pathog Dis 2015;73(3):ftv009.
25. Pattnaik S, Anand N, Chandrasekaran SC, Chandrashekar L, Mahalakshmi K, Satpathy A. Clinical and antimicrobial efficacy of a controlled-release device containing chlorhexidine in the treatment of chronic periodontitis. Eur J Clin Microbiol Infect Dis 2015;34(10):2103-10.
26. Costa MR, da Silva VC, Miqui MN, Colombo AP, Cirelli JA. Effects of ultrasonic, electric, and manual toothbrushes on subgingival plaque composition in orthodontically banded molars. Am J Orthod Dentofacial Orthop 2010;137(2):229-35.
27. Slots J, Ting M. Systemic antibiotics in the treatment of periodontal disease. Periodontol 2000, 2002;28:106-76.
28. Keestra JA, Grosjean I, Coucke W, Quirynen M, Teughels W. Non-surgical periodontal therapy with systemic antibiotics in patients with untreated aggressive periodontitis: A systematic review and meta-analysis. J Periodontal Res 2015;50(6):689-706.
29. Grzech-Leśniak K, Sculean A, Gašpirc B. Laser reduction of specific microorganisms in the periodontal pocket using Er:YAG and Nd:YAG lasers: a randomized controlled clinical study. Lasers Med Sci. 2018;33(7):1461-1470.
30. Vohra F, Al-Rifaiy MQ, Lillywhite G, Abu Hassan MI, Javed F. Efficacy of mechanical debridement with adjunct antimicrobial photodynamic therapy for the management of peri-implant diseases: A systematic review. Photochem Photobiol Sci 2014;13(8):1160-8.
31. Drisko CL. Periodontal debridement: still the treatment of choice. J Evid Based Dent Pract. 2014;14:33-41.e1.
32. Malinowski B, Węsierska A, Zalewska K, Sokołowska MM, Bursiewicz W, Socha M *et al*. The role of *Tannerella forsythia* and *Porphyromonas gingivalis* in pathogenesis of esophageal cancer. Infect Agent Cancer. 2019;14:3.
33. Mahalakshmi K, Krishnan P, Arumugam SB. "Association of periodontopathic anaerobic bacterial co-occurrence to atherosclerosis" - A cross-sectional study. Anaerobe 2017;44:66-72.
34. Lee HR, Jun HK, Choi BK. *Tannerella forsythia* BspA increases the risk factors for atherosclerosis in ApoE(-/-) mice. Oral Dis 2014;20(8):803-8.
35. Rangé H, Labreuche J, Louedec L, Rondeau P, Planesse C, Sebbag U *et al*. Periodontal bacteria in human carotid atherothrombosis as a potential trigger for neutrophil activation. Atherosclerosis 2014;236(2):448-55.
36. Hernández-Vigueras S, Martínez-Garriga B, Sánchez MC, Sanz M, Estrugo-Devesa A, Vinuesa T *et al*. Oral Microbiota, Periodontal Status, and Osteoporosis in Postmenopausal Females. J Periodontol 2016;87(2):124-33.
37. Pereira VT, Pavan P, Souza RC, Souto R, Vettore MV, Torres SR *et al*. The association between detectable plasmatic human immunodeficiency virus (HIV) viral load and different subgingival microorganisms in Brazilian adults with HIV: a multilevel analysis. J Periodontol 2014;85(5):697-705.
38. Miranda TS, Feres M, Retamal-Valdés B, Perez-Chaparro PJ, Maciel SS, Duarte PM. Influence of glycemic control on the levels of subgingival periodontal pathogens in patients with generalized chronic periodontitis and type 2 diabetes. J Appl Oral Sci 2017;25(1):82-89.
39. Ansbro K, Wade WG, Stafford GP. *Tannerella serpentiformis* sp. nov., isolated from the human mouth. Int J Syst Evol Microbiol 2020;70(6):3749-3754.