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THE PATHOGENIC POTENTIAL OF PERIODONTAL BACTERIA

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Abstract: *In the present study we aimed to bring to the fore the most common bacteria with a role in the production of periodontal disease. We have also highlighted the way in which they act in the oral cavity, the way in which they are grafted onto the structures and tissues in the oral cavity and the concrete way in which they play their devastating role. Knowledge of the types of microbes involved in this disease can lead to the development of methods to eradicate them, so that this pathology, increasingly common especially in middle-aged and elderly people, can be stopped or even treated.*

INTRODUCTION

At birth, the oral cavity is free of microorganisms. After contact with the environment, colonization of the oral cavity begins, so at the age of one year the main microorganisms that make up normal microbiocenosis are present. Colonization of the oral cavity ends at about the age of 13 years. The continued appearance of some microorganisms depends on the secondary changes of the ecosystem environment of the oral cavity. In order for a bacterium to populate the oral cavity, it must be retained, but there is a possibility that it can be washed with saliva and removed by swallowing. It is known that the average rate of division of oral microorganisms is between 6 and 24 hours, and the average rate of saliva leakage is 500 + 600 ml / day. The fixation of microorganisms is done on a film that covers the membranes and teeth, and contains complex macromolecules. Thus, in the oral cavity, in adulthood, there are complex microorganisms in the category of gram-positive cocci (streptococcus, micrococcus, etc.), gram-positive bacteria (actinomzces, arachnia etc.), gram-negative bacilli (actinobacillus, prevotella etc.), other microorganisms. (treponema, candida etc). In the elderly, normal microbiocenosis of the oral cavity changes. It has been observed that S. mutans and S. sanguis disappear in total loss of teeth or periodontal disease, but these bacterial species reappear with the application of dentures.

The periodontal disease represents a chronic inflammatory condition of the gums. Periodontitis is manifested in the supporting tissues of the tooth on the arch: gum, periodontal ligament, alveolar bone. Periodontitis can lead to tooth loss by destroying the soft tissue and bone that supports the teeth. In the first phase there is inflammation of the gums - gingivitis. Normally, healthy gums are firm and pale pink. Gingivitis is manifested by changing the consistency of the gum - it becomes soft, and the colour - to purplish red. Also, the interdental papillae become inflamed and come off the teeth, there is pain, gingival itching, the gums bleed very easily, even when brushing with a soft hair.

Etiology and Pathogenesis

It is accepted that the microorganisms in the bacterial plaque that exist in the form of biofilms represent the primary etiological agents of periodontal disease. Biofilms are bacterial communities included in the matrix that adhere to each other, as well as on surfaces or interfaces. Enormous advances in biology and technology have provided even more sophisticated means of researching dental biofilms.(1)

It is considered that all the factors that influence the etiopathogenesis and the evolution of periodontopathy are favorable or predisposing, but they are not the cause of periodontopathy.

The causal factor is considered the microbial factor. It can be said that the determining factor is the body's immune response.(1) Periodontopathy is the result of the interaction between the bacterial complex in the bacterial plaque and the host's immune response, the ground. Some authors believe that occlusal trauma should be included as a causal factor.

The introduction of the GasPak (1) system and the anaerobic box allowed the discovery of many annoying planktonic anaerobic species in the oral cavity. Due to this progress in anaerobiosis, associated with epidemiological data, it has been possible to associate population changes to certain Gram-negative species in bacterial plaque biofilms with the onset and evolution of periodontal disease.(1) However, the application of DNA tests, PCR and confocal microscopy have deepened the understanding of the formation, maturation and ecology of bacterial plaque biofilms. Mature dental biofilms can include an increased variety of bacterial species.

Molecular detection of microflora in the oral cavity has led to the identification of approximately 700 bacterial species or phylotypes.(1) In a standard bacterial plaque sample, approximately 50-60 species can be identified using 16S rRNA. 16S rRNA is an extremely conserved genetic sequence that allows estimating the distance of evolution and relevance to organisms.(1)

Definition of the disease

„The primary periodontal diseases are gingivitis and periodontitis. Gingivitis is characterized by reversible gingival inflammation without evidence of periodontal rupture".(5) Over time, untreated gingivitis can progress to destructive

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periodontitis.

Periodontitis, in contrast, is characterized by gingival inflammation that extends beyond the gingiva and causes irreversible breakdown of connective tissue attached to the root and resorption of alveolar bone. The progressive destruction of connective tissue and alveolar bone results in apical migration of the gingival epithelium and pocket formation. Ultimately, destruction of the periodontium leads to tooth mobility, reduced masticatory function, and eventual tooth loss.

Periodontal disease is caused by the accumulation of microorganisms around the tooth with the stimulation of the immune system; constitute a group of alterations of the periodontium, mostly of infectious origin.(6) It is classified as gingivitis, if it affects the protective tissue, or periodontitis, if the supporting tissues are involved. Periodontal disease is of inflammatory aetiology, of multifactorial origin, causes „progressive destruction of the dental support apparatus: loss of the periodontal ligament, bone destruction, formation of periodontal pockets, gingival recessions and tooth loss".(7) This host response to bacterial infection may be influenced by a number of risk factors that will affect susceptibility to disease development, rate of disease progression, and even response to treatment.

Periodontal diseases are the most common chronic inflammatory conditions worldwide, with a prevalence rate reaching up to 90%.(8) The global prevalence of periodontitis in the US is estimated at 47% in adults aged 30 years and older.(9)

In the etiopathogenesis of periodontal disease, the participation of microorganisms is essential, but they have been considered insufficient to explain periodontal destruction, so host factors, such as the immune response, environmental factors such as smoking, genetic factors, such as certain gene polymorphisms of cytokines, and systemic factors, such as diabetes, are determinants for the development of the disease.(10)

One of the main determinants of the development of periodontal disease is the increase in pathogenic bacteria within dental plaque, which activates a massive innate and adaptive immune response.(11) There are about 800 species of bacteria in the oral cavity and there is a complex interaction between the bacterial infection and the host response, „modified by behavioural factors, such as smoking, which result in periodontal disease".(12)

Periodontal disease is considered to be opportunistic polymicrobial infections. Putative bacterial pathogens associated with periodontal disease have been identified in subgingival biofilms. These include A. actinomycetemcomitans, P. gingivalis, Tannerella forsythia, Treponema denticola, Prevotella intermedia, Fusobacterium nucleatum, Eikenella corrodens, Campylobacter rectus, Parvimonas micra (formerly known as Peptostreptococcus micros) and Streptococcus intermedius.(1)

Three species - P. gingivalis, T. forsythia and T. denticola - have been designated as part of the "red complex, being involved in the progression of chronic periodontitis".(1) Aggregatibacter actinomycetemcomitans (formerly known as Actinobacillus actinomycetemcomitans) is a putative pathogen associated with aggressive forms of periodontitis. For the primary and secondary prevention of the disease, it is essential to identify the risk factors and associated factors for the application of effective interventions; In addition, periodontal disease must be diagnosed early in order to exercise adequate therapeutic actions that prevent the progression of the disease towards chronic and aggressive stages.(16)

Risk factors of periodontal diseases

The analysis of the effects of risk factors on periodontal diseases is complex, due to the incidence over a prolonged period of several factors, which may include confounding variables. On the other hand, the risk factor-disease association is not necessarily cause and effect; that is, casual and non-causal relationships may exist, which should be investigated in the future.

The factors that have to power to „increase the risk of periodontal diseases can be classified into modifiable and non-modifiable".(17)

Modifiable risk factors

Smoking habit

It is the most important risk factor for periodontitis.(18) The negative effects on periodontal tissues of smoking cigarettes, tobacco, pipes or cannabis are similar. Smokers have a three times greater risk of presenting a severe form of periodontal disease than non-smokers.(17) Tobacco aggravates periodontal disease by promoting pathogenic bacterial invasion, suppressing immune defences, aggravating inflammation, and increasing alveolar bone loss.(19) Tobacco „affects the function and proliferation of periodontal cells, such as periodontal fibroblasts" and periodontal ligament cells, and induces apoptosis. A study showed that smoking interferes with redox homeostasis, alters antioxidant values and negatively influences periodontal disease.(20) Cementum is synthesized by cementoblasts during dental root formation and plays an essential role in anchoring the tooth to the alveolar bone.(21) Cementoblasts not only function as supporting cells of the periodontium, but also in the maintenance, development and regeneration of periodontal tissues. Nicotine causes destruction of periodontal tissue directly or through interaction with other factors. One study suggests that nicotine inhibits the migration and proliferation of cementoblasts and induces the synthesis of cytokines and reactive oxygen species by these cells.(21)

Poor oral hygiene

Poor oral hygiene is linked to periodontal disease, because it favours the deposition of bacteria and the formation of dental bacterial plaque on teeth and gums, with the consequent inflammatory change of the periodontal tissues. There is a strong association between poor oral hygiene and the high prevalence and severity of periodontal disease. In a 15-year prospective study, there was not found any deterioration of periodontal structures among people with adequate oral hygiene and professional dental care. Dietary sugars contribute to dental caries and periodontal disease because they are fermented by bacteria to acids that cause demineralization of tooth structure.(22) One study found poor oral hygiene and smoking as the main risk factors for chronic periodontitis in students.(16)

Hormonal changes in women

Hormonal changes in the female sex increase the probability of periodontal disease. „Women may experience gingival inflammation before menstruation and during ovulation", due to high levels of progesterone that block the repair of collagen fibers and cause vasodilation.(17) A study in China found a 73.9% prevalence of periodontal disease in women, mainly mild and moderate disease.(23) Similarly, „pregnant women frequently exhibit gingival changes, gingivitis, and sometimes localized growth of gingival tissues".(17) Fortunately, these inflammatory changes disappear within a few months of delivery, without causing persistent damage to the periodontal tissues. Estrogen deficiency after menopause can culminate in alveolar bone loss and eventually tooth loss. A longitudinal study in 42,171 postmenopausal women showed that treatment of osteoporosis with estrogen therapy reduced tooth loss.(17)

Diabetes mellitus

Type 2 diabetes mellitus „is preceded by systemic inflammation that causes decreased pancreatic beta cell

function, apoptosis, and insulin resistance".(16) High systemic inflammation causes the „entry of periodontal organisms and their virulence factors into the circulation, providing evidence for the effects of periodontitis on diabetes". The specific mechanism connecting diabetes to periodontal disease is not well understood.(14) It is suggested that diabetes participates in the alteration of the subgingival bacterial community that favors the growth of pathogens. Furthermore, the systemic levels of inflammatory mediators, such as C-reactive protein (CRP), TNF-α and IL-6, which are elevated in periodontal disease, could be a link between diabetes and periodontitis. Oxidative stress is likely to be an important link between the two diseases, due to the activation of common proinflammatory pathways.(14) Another mechanism could be the interactions between the products of advanced glycosylation and their receptors. Diabetes mellitus is associated with destruction of the periodontal ligament and loss of teeth. „Gingival fluids and saliva have higher concentrations of inflammatory mediators, such as cytokines, among diabetic patients with periodontitis compared with non-diabetics with periodontal disease".(17) A report provided by the „European Federation of Periodontology" and the „American Academy of Periodontology" identified a dose-response relationship between „the severity of periodontal disease and the adverse consequences of diabetes and that periodontal treatment was beneficial as antidiabetic medication".(16) One study in Sancti Spíritus, Cuba, found almost 80% of gingivitis and periodontitis in diabetic patients.(24)

Medicines

The vulnerability to infections and periodontal diseases is intensified when saliva flow is decreased with some medications. Hyposalivation has also been implicated in the risk of root caries, dental erosion, dental hypersensitivity, chronic mucositis, and oral candidiasis.(18) The most common medications that reduce the amount of saliva and lead to dry mouth are tricyclic antidepressants, atropine, antihistamines, and beta blockers.(17) Some drugs such as „phenytoin, cyclosporine and nifedipine induce abnormal growth of gingival tissues", which makes it difficult to remove dental plaque and aggravates periodontal disease.(17)

Stress

Stress reduces salivary secretions and favours the formation of dental plaque. A positive association has been observed between stress scores and salivary stress markers (cortisol, beta endorphin and alpha amylase), tooth loss, and probing depth of 5-8 mm.(17) A meta-analysis indicated that „stress is related to the immune system and different immunological changes occur in response to different stressful events". Chronic stress causes destruction of the periodontium in susceptible individuals.(18) However, the complex biological nature of stress limits the understanding of how it modulates periodontal health, which is made even more difficult by other acting environmental factors. Depressed people have a higher concentration of cortisol in the gingival crevicular fluid and respond less well to periodontal treatment.(17) Academic stress also causes poor oral hygiene and gingival inflammation, with an increase in the concentration of IL-1β.

Other factors

Other diseases associated with periodontal disease are cardiovascular and cerebrovascular diseases, metabolic diseases (obesity, metabolic syndrome), cancers, rheumatoid arthritis, and chronic obstructive pulmonary disease.(25) The main link between periodontal disease and systemic diseases could be the chronic inflammatory process that accompanies these disorders. This association is bidirectional, since these conditions influence each other.(26) In addition to endocrinopathies, such as diabetes, other diseases are linked to the destruction of the periodontium, such as immunosuppression (AIDS) and hematological disorders (neutropenia).(18) An inverse relationship has been found between dietary fiber intake and periodontal disease in US adults.(27) Other factors that increase the risk of periodontitis, such as low educational level and having non-private medical insurance, could be related more to the capacity for specialized dental care and the availability of financial resources.(28) In a study, patients with periodontitis more frequently reported a lower educational level, cigarette and alcohol consumption.(29) Systemic diseases such as diabetes, respiratory, blood, arthritis and drug treatment were more frequent in patients with periodontitis.

Non-modifiable risk factors

Non-modifiable risk factors include age, ethnicity, and genetic factors.(16)

Age

The risk of periodontal disease increases with aging, which explains the high prevalence of this disease in the elderly population.(23) It is suggested that age is a risk factor for alveolar bone and ligament loss, in addition to increased exposure time to local and general risk factors involved in tissue destruction.

Inheritance

Heredity is one of the factors associated with periodontal disease that makes some people more susceptible to the disease than others. It is argued that there is a complex interrelationship between genetic factors with environmental and demographic factors that demonstrate the wide variations between different ethnic and racial populations.(17) Within the genetic factors, polygenic inheritance seems to predominate in periodontal disease, rather than monogenic Mendelian inheritance.(18) An association of rs1537415, located in the glycosyltransferase gene (GLT6D1), with aggressive periodontitis and rs149133391 with chronic periodontitis was found among Latinos, Hispanics, and African-Americans.(30) In a small Italian population, associations were found between polymorphisms of EFCAB4B (rs242016) and localized periodontitis. Other associations between polymorphisms and periodontal disease have been reported. Aggressive periodontitis can also be influenced by genetic variations.(31)

Bacteria in the production of periodontal disease

Porpyromonas gingivalis is a gram-negative bacillus, naerobic, immobile. P. gingivalis has been isolated from periodontal lesions in subjects from several geographical areas, and the importance of this bacterium in the pathogenesis of periodontal disease is well documented. The role of this species is related to destructive periodontal lesions in humans as a primary pathogen in the etiology and pathogenesis of periodontal disease.(32) The pathogenicity of these microorganisms is multiple: first, several studies cite the role of proteolytic enzymes detected in the large amount of P. gingivalis, highlighting enzymes such as hyaloronidase, heparinase. Another pathogenetic mechanism in P. gingivalis involved in the progression of periodontal disease would be its invasive potential, being detected along with other bacterial species in gingival tissue in advanced periodontitis.

Actinobacillus actinomycetemcomitans is a species of Gram-negative microaerophilic bacilli, bacilli that colonize the oral cavity in very small amounts or not at all in healthy individuals, the presence of these bacteria is increased and closely related to the progression of periodontal disease in children, adolescents and adults. Actinobacillus actinomycetemcomitans produces biologically active

substances which, individually or collectively, may be involved in the production of periodontal disease. The pathogenic mechanism of A. actinomycetemcomitans can be considered the property of this species to inhibit the activity of fibroblasts, endothelial and epithelial cells without killing them. Lipopolysaccharides found in these bacteria, like all lipopolysaccharides in Gram-negative bacteria, are virulence factors in the production of periodontal disease. In addition, consistently endotoxin can stimulate bone resorption in vitro.(32)

Prevotella intermedia and Prevotella nigrescens, both previously referred to as P. intermedia, are Gram-negative, anaerobic bacilli that can be isolated from the subgingival sites of healthy patients and those suffering from various forms of periodontal disease. These species, which are frequently isolated from healthy and affected areas (in contrast to P. gingivalis), are considered to be commensal, being part of the human-resident flora.(31) There are therefore pathogenic-opportunistic bacteria that can be associated with ulcer-necrotic gingivitis, with gingivitis during pregnancy and puberty, but also with periodontal diseases that occur in people with diabetes. The virulence of these bacteria is primarily due to the ability to adhere to the host tissue, with the main colonization mechanism being collagen binding, which allows the bacterium to attach to the cell matrix.(33)

Bacteroides forsytus is a gram-negative, anaerobic bacillus, associated with advanced and destructive periodontitis and refractory periodontitis (RA), being one of the prevalent species of this form of periodontal disease. B. forsztus possesses an enzyme that is found on surfaces similar to that of trypsin, which allows the identification of this species by enzymatic tissue. Many researchers mention high levels and proportions of spirochete in some forms of periodontal disease. The association between spirochetes and periodontal disease results from the observation that they were found in large numbers in plaque, in the short story of diseased sites, being undetectable or present in small numbers in healthy periodontal tissue, which is why spirochetes are considered periodontopathogenic bacteria.(33)

The role of spirochetes in the etiology and pathogenesis of periodontal disease, whether or not they are causative agents, remains a controversial issue. What is unanimously admitted is that oral spirochetes are a valuable indicator for monitoring the status of the disease, their presence indicating an active disease.

CONCLUSIONS

Periodontal diseases are a multifactorial group of disorders of the protective tissues (gingivitis) or support tissues of the tooth (periodontitis), where infectious and inflammatory factors are involved. In these diseases, innate and acquired immunity plays an important role with a chronic inflammatory process that, from a reversible phase that includes gingivitis, can progress to irreversible damage to the supporting tissue of the tooth, known as periodontitis. Periodontal disease risk factors include modifiable and non-modifiable factors. Among the modifiable factors, there are: smoking, poor oral hygiene, hormonal changes in women, diabetes mellitus, medications and systemic diseases and among the non-modifiable factors, we can mention: age, ethnicity and genetic factors predominate. The identification of these risk factors allows the design and application of health promotion and prevention strategies to prevent the development and progression of periodontal diseases.

Although it is generally accepted that the microflora of advanced periodontitis is mostly anaerobic Gram-negative bacilli, there are authors who also mention the presence of Gram-positive aerobic bacilli. The literature of recent years clearly emphasizes that one cannot speak of a methodology of various forms of periodontal disease. It is obvious that destructive periodontal disease is the result of a complex correlation between members of the subgingival microflora and non-bacterial factors, especially host and environmental factors. Microorganisms are the predominant factors. Without them, there would be no infection, and therefore the disease would be triggered when the bacteria combined with either a compromised host or an environmental factor that knew the host's susceptibility to infectious agents. The nonspecific plaque hypothesis seems to be gaining ground over the specific one. Accordingly, periodontal disease results from the accumulation of dental plaque and bacteria in it, rather than a specific association between certain microorganisms and various forms of periodontal disease than the involvement of a specific periodontopathogen.

Future investigations into the properties of various microorganisms in the oral cavity, their interactions and especially the rapid development of modern methods of studying molecular ones in the first place, will lead to a better understanding of periodontal disease and the conversion of these notions into practical, useful applications, including enrichment of diagnosis and treatment.

REFERENCES

1. Mârțu, S. Retrospectiva istorică și conceptele actuale în etiopatogenia și clasificarea bolilor parodontale. Date din literatură. Romanian Journal of Medical and Dental Education, 2015, 4(2):27-40.
2. Lim G, Janu U, Chiou LL, Gandhi KK, Palomo L and John V. Periodontal Health and Systemic Conditions. Dent J. 2020;8:130:2-12.
3. Eke PI, Thornton-Evans GO, Wei L, Borgnakke WS, Dye BA and Genco RJ. Periodontitis in US Adults: National Health and Nutrition Examination Survey 2009-2014. J Am Dent. Assoc. 2018;149:576-588.e6.
4. 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;29(1):124-163.
5. Silva N, Abusleme L, Bravo D, Dutzan N, Garci -Sesnich J, Vernal R, et al. Host response mechanisms in periodontal diseases. J Appl Oral Sci. 2015;23(3):329-355.
6. Martínez Pérez ML, Camejo Roviralta L, Sánchez Sánchez RJ. Relación entre la enfermedad periodontal y la cardiopatía isquémica. CCM. 2019;23(4):1-20.
7. Sen S, Giamberardino LD, Moss K, Morelli T, Rosamond WD, Gottesman RF, et al. Periodontal Disease, Regular Dental Care Use, and Incident Ischemic Stroke Stroke. 2018;49(2):355-362.
8. Aguilar Soto FE, Sosa Morales FJ, Bojórquez Anaya Y, Fontes García Z. Periodontitis una enfermedad multifactorial: Diabetes Mellitus. RICS. 2017;6(11):61-86.
9. Orejuela Correa CT. Mechanism of inflammation in response to periodontal disease. Pathogenesis; therapy [Thesis]. Lima, Perú: Universidad Inca Garcilaso de La Vega; 2017.
10. Rafiei M, Kiani F, Sayehmiri K, Sayehmiri F, Tavirani M, Majid Dousti, Abdolkarim Sheikhi. Prevalence of Anaerobic Bacteria (*P. gingivalis*) as Major Microbial Agent in the Incidence Periodontal Diseases by Meta-analysis. J Dent Shiraz Univ Med Sci. 2018;19(3):232-242.

11. Corona Martínez JD, Pérez Soto E, Sánchez Monroy V. Identificación molecular de bacterias en salud y enfermedad periodontal. Rev Odont Mex. 2019;23(1):23-30.
12. Franco C, Hernández Ríos P, Sorsa T, Biguetti C, Hernández M. Matrix Metalloproteinases as Regulators of Periodontal Inflammation. Int J Mol Sci. 2017;18(2):440.
13. Nazir MA. Prevalence of periodontal disease, its association with systemic diseases and prevention. Int J Health Sci (Qassim). 2017;11(2):72-80.
14. Mariotti A and Hefti AF. Defining periodontal health. BMC Oral Health. 2015;15(Suppl 1):6.
15. Zhang Y, He J, He B, Huang R, Li M. Effect of tobacco on periodontal disease and oral cancer. Tob Induc Dis. 2019;17:40.
16. Chang CH, Han ML, Teng NC, Lee CY, Huang WT, Lin CT, et al. Cigarette Smoking Aggravates the Activity of Periodontal Disease by Disrupting Redox Homeostasis-An Observational Study. Sci Rep. 2018;8:11055.
17. Chen CS, Lee SS, Yu HC, Huang FM, Chang YC. Effects of nicotine on cell growth, migration, and production of inflammatory cytokines and reactive oxygen species by cementoblasts. J Oral Sci. 2015;10(2):154-160.
18. Najeeb S, Zafar MS, Khurshid Z, Zohaib S, Almas K. The Role of Nutrition in Periodontal Health: An Update. Nutrients. 2016;8(9):530.
19. Jiang H, Su Y, Xiong X, Harville E, Wu H, Jiang Z, et al. Prevalence and risk factors of periodontal disease among pre-conception Chinese women. Reprod Health. 2016;13(1):141.
20. Yanes Ruiz Y, Rubio Ríos G, Torres López MC, Cañizares Obregón Y. Factores de riesgo relacionados de la enfermedad periodontal. Pacientes diabéticos. Zaza del Medio. Taguasco. 2010. Gac Méd Espirit. 2016;18(1):14-21.
21. Roa Ignacio, del Sol Mariano. Obesidad, glándulas salivales y patología oral. Colomb Med. 2018;49(4):280-287.
22. Nagpal R, Yamashiro Y, Izumi Y. The Two-Way Association of Periodontal Infection with Systemic Disorders: An Overview. Mediators Inflamm. 2015;2015: 793898.
23. Nielsen SJ, Trak Fellermeier MA, Joshipura K, Dye BA. Dietary Fiber Intake Is Inversely Associated with Periodontal Disease among US Adults. J Nutr. 2016;146(12):2530-2536.
24. Pardo Romero Fredy F, Hernández Luis J. Enfermedad periodontal: enfoques epidemiológicos para su análisis como problema de salud pública. Rev Salud Púb. 2018;20(2):258-264.
25. Maya Ramírez JC, Sánchez Lopera N, Posada López A, Agudelo-Suárez AA, Botero Javier E. Condición periodontal y su relación con variables sociodemográficas y clínicas en pacientes adultos de una institución docencia-servicio. Rev Odont Mex. 2017;21(3):165-172.
26. Morelli T, Agler CS, Divaris K. Genomics of periodontal disease and tooth morbidity. Periodontol 2000. 2020;82(1):143-156.
27. Frías Muñoz M, Araujo Espino R, Martínez Aguilar VM, Correa Alcalde T, Aguilera Galaviz LA, Gaitán Fonseca C. Aggressive Periodontitis and its Multidisciplinary Focus: Review of the Literature. ODOVTOS-Int J Dent Sc. 2017;19(3):27-33.
28. Hurtado Camarena A, Bojoroquez Anaya Y, de Lourdes Montano Perez M and Lopez Mendosa JA. Bacterias asociadas a enfermedades periodontales. Oral. 2016;17(54):1374-1378.
29. Farias Rodriguez F. Enfermedad periodontal y microorganismos periodontopatogenos. Revista de la Faculdad de Odontologia. 2018;1-22.
30. Morelli T, Agler CS, Divaris K. Genomics of periodontal disease and tooth morbidity. Periodontol 2000. 2020;82(1):143-156.
31. Frías Muñoz M, Araujo Espino R, Martínez Aguilar VM, Correa Alcalde T, Aguilera Galaviz LA, Gaitán Fonseca C. Aggressive Periodontitis and its Multidisciplinary Focus: Review of the Literature. ODOVTOS-Int J Dent Sc. 2017;19(3):27-33.
32. Hurtado Camarena A, Bojoroquez Anaya Y, de Lourdes Montano Perez M and Lopez Mendosa JA. Bacterias asociadas a enfermedades periodontales. Oral. 2016;17(54):1374-1378.
33. Farias Rodriguez F. Enfermedad periodontal y microorganismos periodontopatogenos. Revista de la Faculdad de Odontologia. 2018;1-22.