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Impede Model of Periodontal Pathogenesis

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Abstract

Periodontal disease encloses the conditions and diseases associated with the periodontal tissue. The formation of dental plaque bio film along with microorganisms inhabiting within is the initial cause of its progression and advancement [(1)]. Many models have been involved to study the pathogenesis of periodontal disease and one among them is the Inflammation-Mediated Polymicrobial-Emergence and Dysbiotic-Exacerbation Model introduced by Van Dyke Et al. in 2020. This model revies how the inflammation mediates plaque-induced periodontitis. This explains the current concept of polymicrobial enzyme and dysbiotic exacerbation causing periodontitis [(2)].

Keywords: Dysbiotic, Polymicrobial, Periodontitis

Introduction

Periodontal disease mainly comprises gingivitis and periodontitis [(1)]. These inflammatory lesions are commenced by the presence of bacteria [(2)]. Gingivitis is mainly seen around the teeth, and as it progresses it advances into a dire form called periodontitis [(3)]. Periodontitis is commonly commenced by microbial

plaque, but it is also aggravated by factors like immune response and inflammatory response of individuals[4]. Studies have shown that periodontitis can be developed from systemic diseases such as kidney diseases, CVS, diabetic mellites, Alzheimer's, COPD, and even rheumatoid arthritis [3,5,6]. Medications such as anticholinergic, and antihistaminic drugs that decrease salivary flow can also cause overall inflammation over the mucosal surface[7]. Periodontitis can cause destruction of bone, periodontal ligament, soft tissue and can even lead to tooth loss[4]. Periodontopathogens not only affect the periodontium but can also bring out changes on the systemic health of individuals [8]. Bacterial accumulation is the chief causative reason for periodontitis[9], factors such as calculus, dental plaque, genetic and systemic factors, overhanging restorations, smoking, stress and developmental grooves also aggregates this disease[10].

Recent studies have shown that the microbial diversity of subgingival plaque increases as gingivitis/periodontitis develops. Unlike other infections, where diversity decreases due to specific pathogens and host defense mechanisms, periodontal disease actually shows an increase in diversity. However, it would be beneficial to have more studies that specifically differentiate between the early/moderate stages of the disease and the late-stage severe periodontitis associated with deep pockets. The periodontal pathogens like Porphyromon as gingival is and Treponema denticola are mostly found in deep periodontal pockets that are deeper than 4 mm. What's interesting is that they hang out together with other periodontal pathogens in little clusters on the surface layer of the biofilm near the lining of the pockets. This positioning allows them to release outer membrane vesicles filled with harmful stuff into the surrounding tissue and get access to the exudate from the inflamed tissue. It's also in line with how these species have a mutualistic relationship and cause disease[2].

In people who are more prone to it, the chronic inflammation and the anaerobic environment of the pocket can cause specific bacterial species to grow and spread. This, in turn, can worsen the inflammation and create a cycle where the inflammation feeds off itself, leading to uncontrolled inflammation and damage to the tissues. It's like a loop that keeps getting stronger and causing more harm.

The connection between the periodontal microbiome and the development of periodontitis is quite complex. It's been questioned whether specific pathogens are the main culprits in causing dysbiosis and disease, as there isn't a clear association between any particular pathogen and the initiation of disease in humans. Through analyzing plaque samples from healthy, gingivitis, and early periodontitis sites, we've learned that the bacteria responsible for starting the disease are mostly harmless "commensals," while the so-called "pathogens or pathobionts" associated with disease are only present in small amounts in the early stages. The shift to a dysbiotic microflora seems to be mainly driven by excessive and persistent inflammation, as well as the formation of pockets, which changes the environment for bacterial growth.

According to the "Inflammation-Mediated Polymicrobial-Emergence and Dysbiotic-Exacerbation" (IMPEDE) Model introduced by Van Dyke et al. in 2020, inflammation plays a crucial role in the progression of periodontal disease. This model complements the current Classification of Periodontal Diseases, which views periodontitis as a continuum from health to disease with different stages of severity and complexity. In the IMPEDE model, inflammation is seen

as a principal driver of the clinical condition at each stage. The model recognizes five stages (0-4) representing the development, containment, or progression of health, gingivitis, and periodontitis. Through microbiome analyses and clinical studies, it has been observed that there are four distinct stages of bacterial transitions from health to late-stage periodontitis, driven by inflammation, pocket formation, and changes in bacterial composition. In the IMPEDE model, there are five stages in the development of periodontal disease. The first stage is Stage 0, which represents a healthy state. After that, we have four subsequent phases. The first phase is called gingivitis, where there's inflammation due to an overgrowth of plaque bacteria. The second phase is initiation/early periodontitis, where there's an increase in polymicrobial diversity and dysbiosis triggered by inflammation. And then there's the third phase is characterized by inflammation-mediated exacerbation of dysbiosis through a self-sustained feed forward loop. And finally, the fourth phase is late-stage periodontitis, where there's a decrease in polymicrobial diversity associated with the emergence of a polymicrobial infection. It's really interesting how these stages highlight the complex interactions between inflammation, dysbiosis, and the progression of periodontal disease[(2)].

Many models have been brought up to study the pathogenesis of periodontal disease for better diagnosis and treatment planning, and these include Linear Model (1960), Page and Schroeder Model (1979), Circa Model (1980), Critical Pathway Model (1996), Classical Model (1997), Multi-Level Hierarchical Model (2008), Biological Systems Model (2008), Generic Multicausality Model (2012), Keystone Pathogenesis Model (2012), Polymicrobial Synergy and Dysbiosis Model (2012), Revised Model (2013), Immunomicrobial Pathogenesis Model (2014), Polymicrobial Genetic Dysbiosis Model (2015), Contemporary Model (2015), Revised Page and Schroeder Model (2017), Inverted Model (2019) and IMPEDE Model (2020)[(11)].

Discussion

The IMPEDE model suggests that inflammation plays a significant role in each stage of periodontitis, acting as a principal driver of the clinical condition. The model identifies five stages (0-IV) which has been mentioned in figure 1 & 2 that encompass the transition from periodontal health to gingivitis and, if left untreated, to periodontitis. Stage I is gingivitis, where inflammation is initiated. Stage II is initiation/early periodontitis, characterized by the emergence of polymicrobial diversity. Stage III is advancing periodontitis, involving dysregulated inflammation and pocket formation. Finally, Stage IV is late-stage periodontitis, which involves inflammation-mediated dysbiosis, opportunistic infection, and advanced tissue destruction. It's interesting to see how inflammation can either worsen or be resolved with appropriate treatment, impacting the progression and outcome of periodontal disease[(2)].

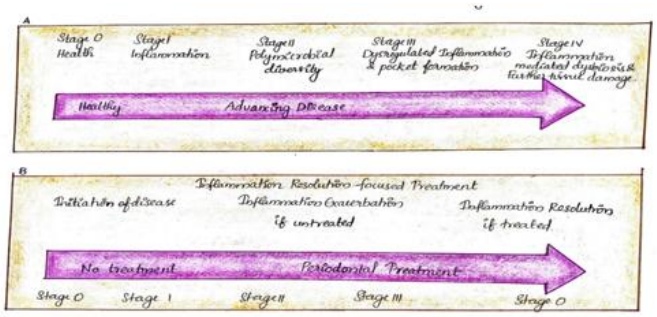

Figure 1: Impede and Periodontal Disease Stages

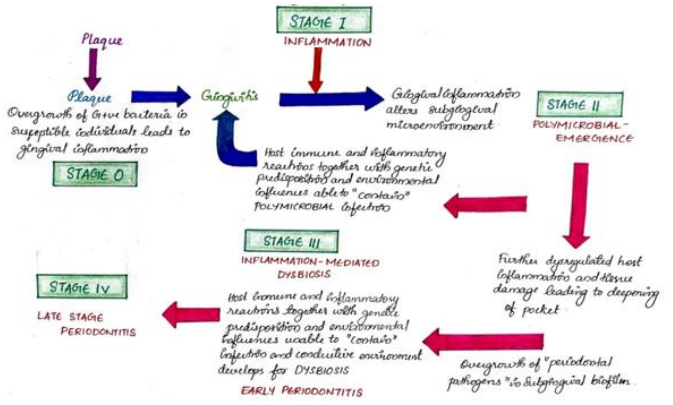

Figure 1: Inflammation-Mediated Polymicrobial-Emergence and Dysbiotic-Exacerbation

Stage 0: Periodontal Health

- Clinical inflammation is absent in this stage. Dominant gram - positive bacteria like streptococcus, coryne bacteria are seen.
- Chronic inflammation leads to the development of periodontal pocket.
- After completion of periodontitis treatment specific definitions were agreed to with regard to cases of gingival health or inflammation based on bleeding on probing and depth of the residual sulcus /pocket.
- It was accepted that, even following a successful therapy a patient with gingivitis can revert to a state of health, but a periodontitis patient remains a periodontitis patient for life.
- Periodontitis patients requires life-long supportive care to prevent recurrence of disease.
- Peri-implant health is defined both clinically and histologically. Clinically, it is characterized by an absence of visual signs of inflammation and bleeding on probing.
- Peri implant health can exist around implants with normal and reduced bone support. Probing depths compatible with peri-implant health is not possible to define.
- Lang and Bar told 2018 classification of periodontal health and gingival health:

1) Clinical gingival health on intact periodontium

2) Clinical gingival health on reduced periodontium

-Stable periodontitis patient

- Non periodontitis patient

Stage 1: Gingivitis (Inflammation)

Gingival inflammation is caused by overgrowth of gram-positive bacteria-in susceptible individuals.

Subgingival microenvironment is altered by gingival inflammation. Polymicrobial infection contains host immune and inflammatory reactions together with genetic predisposition and environmental influences.

Stage 2: Early Periodontitis (Polymicrobial Emergence)

Deepening of pocket is caused by further dysregulated host inflammation and tissue damage. Overgrowth of periodontal pathogens (pathobionts and symbionts) in the subgingival biofilm [2].

At oral and other epithelial sites, it is well established that a buildup of a commensal microbial biomass can trigger a switch from homeostasis (tolerance) to inflammation. An increase in diversity of the biofilm is caused by inflammation, which can still be associated with health at an epithelial site.To change the composition of the plaque with emergence of gram-negative species chronic inflammation is initiated .Disease causing species (pathobionts) and commensal (beneficial) species (symbionts),are the composition of diverse polymicrobial biofilm, which can be antagonistic to the pathogens. Unresolved chronic inflammation guides those subgingival ecological and environmental changes which in turn are intricately related to the host susceptibility (genes and environment) and disease (tissue damage and attachment loss). As discussed above, driving resolution of inflammation allowing the

commensal biofilm to return as the predominant microbiota helps this process to control at this stage [4].

Stage 3: Inflammation Mediated Dysbiosis:

Dysbiosis develops when the host inflammatory response, environmental stress and genetic predisposition unable to encounter inflammation [2].

Specific microbiological measure of dysbiosis helps in future diagnosis of periodontitis. Dysbiosis ratios, is defined as the percentage of genera associated with disease relative to the percentage of genera associated with the health, were calculated to distinguish disease from health[13].In susceptible people, emergence and proliferation of certain bacterial species is caused by chronic inflammation and anaerobic nature of pocket which may be may be present and an exacerbation of inflammation by the generation of a self-sustained feed forward loop to result in an uncontrolled inflammation and tissue destruction[2].

Stage 4: Late periodontitis

More gram-negative anaerobic species present in relation with the emergence of polymicrobial infection, there is a decrease in polymicrobial diversity. The emergence of disease associated pathogen will result in a dysbiotic state for the initiation of periodontitis. It is caused by inflammation mediated microbes [11].

Indispensable part of periodontal disease pathogenesis is disease progression

Periodontal histopathogenesis

A series of stages are seen in development of periodontitis. Initial, early, established as well as advanced lesion. After the accumulation of bacterial plaque, initial lesion begins (after 2 to 4 days) [14]

An acute exudative vasculitis in the plexus of venules lateral to junctional epithelium, migration of polymorph nuclear cells (PMN)through the junctional epithelium in to gingival sulcus, co-exudation of fluid from sulcus and peri-vascular collagen are observed during the initial lesion. There is dense infiltrate of T lymphocytes and other mononuclear cells as well as by the pathological alteration of the fibroblast [14].

Moreover the established lesion develop after 2 to 3 weeks. There is increased number of activated B cell accompanied by loss of marginal gingival connective tissue matrix, but there is no bone loss In advanced lesion, plasma cells ate increase in number, gingival tissue is disturbed, there is destruction of alveolar bone and periodontal ligament. There is a conversion of junctional epithelium to pocket epithelium. formation of inflammatory infiltrate consisting of plasma cells and macrophages, loss of collagen attachment to root surface and there is resorption of alveolar bone[14].

Opportunistic polymicrobial infections

Microbial diversity of subgingival plaque increases from health to disease (gingivitis/periodontitis) shown by recent studies, which has been attributed to an increase in amount and range of nutrients provided by the exudates associated with chronic gingival inflammation. Increase in diversity is distinct from polymicrobial infections at other sites of the body where infection is characterized by a reduction in diversity due to increased specific pathogen abundance/competition as well as host defence mechanisms decreasing the viability/level of commensal species. Studies investigating the microbial diversity at periodontal sites have not differentiated between early/moderate disease and late-stage severe periodontitis associated with deep pockets. A study did differentiate between 6 mm pockets and those with depths >7–8 mm which showed that species richness as well as diversity were significantly higher in 6 mm pockets compared with that of the deeper pockets. Bacteroidetes and certain species were abundant in deep pocket. Majority (>50%) of species in the deeper

pockets is defined from families comprising known or suspected periodontal pathogens. More homogeneous were the subgingival microbial communities at diseased sites than those at healthy site suggesting a limited repertoire of species involved in disease progression. Results are consistent with a model of microbial succession in periodontitis in which disease-associated species initially invade/emerge in the healthy microbiota resulting in a diverse community comprising both health and disease-associated species. Transitional microbiota is temporally and spatially replaced by predominantly disease-associated species as disease (pocket depth and attachment loss) progress [2].

Conclusion

This model allows us to focus on the shift in microbial composition and restoration of microbiological balance or homeostasis due to inflammation [2].

Periodontitis can no longer be considered as a simple bacterial infection as well as a linear host response to microbial dysbiosis. Periodontitis is characterized by a self-perpetuating state of prolonged inflammation, which involves an interplay of a dysbiotic microbiome, a spectrum of host and environmental factors that subsequently leads to tissue destruction[11].Bacteria is the main etiological factor of periodontal disease, which are capable of activating the innate immune response of the host which induces an inflammatory response. Evolution of that inflammatory response culminates in the destruction of periodontal tissues [14]. There is an interaction of various susceptibility factors to influence the host response generally and the immune response specifically [4]

Reference

1. Abdulkareem AA, Al-Taweel FB, Al-Sharqi AJB, Gul SS, Sha A, Chapple ILC. Current concepts in the pathogenesis of periodontitis: from symbiosis to dysbiosis. J Oral Microbiol. 2023 Apr 2;15(1):2197779. Doi: 10.1080/20002297.2023.2197779. PMID: 37025387; PMCID: PMC10071981.
2. Van Dyke TE, Bartold PM, Reynolds EC. The Nexus Between Periodontal Inflammation and Dysbiosis. Front Immunol. 2020 Mar 31;11:511. Doi: 10.3389/fimmu.2020.00511. PMID: 32296429; PMCID: PMC7136396.
3. Baeza M, Morales A, Cisterna C, Cavalla F, Jara G, Isamitt Y, Pino P, Gamonal J. Effect of periodontal treatment in patients with periodontitis and diabetes: systematic review and meta-analysis. J Appl Oral Sci. 2020 Jan 10;28:e20190248. Doi: 10.1590/1678-7757-2019-0248. PMID: 31939522; PMCID: PMC6919200.
4. Kinane DF. Causation and pathogenesis of periodontal disease. Periodontol 2000. 2001;25:8-20. Doi: 10.1034/j.1600-0757.2001.22250102.x. PMID: 11155179.
5. Chapple IL, Genco R; working group 2 of the joint EFP/AAP workshop. Diabetes and periodontal diseases: consensus report of the Joint EFP/AAP Workshop on Periodontitis and Systemic Diseases. J Periodontol. 2013 Apr;84(4 Suppl):S106-12. Doi: 10.1902/jop.2013.1340011. PMID: 23631572.
6. Bui FQ, Almeida-da-Silva CLC, Huynh B, Trinh A, Liu J, Woodward J, Asadi H, Ojcius DM. Association between periodontal pathogens and systemic disease. Biomed J. 2019 Feb;42(1):27-35. Doi: 10.1016/j.bj.2018.12.001. Epub 2019 Mar 2. PMID: 30987702; PMCID: PMC6468093.
7. Williams RC. Periodontal disease. N Engl J Med. 1990 Feb 8;322(6):373-82. Doi: 10.1056/NEJM199002083220606. PMID: 2405268.

8. 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
9. Lamont RJ, Hajishengallis G. Polymicrobial synergy and dysbiosis in inflammatory disease. Trends Mol Med. 2015 Mar;21(3):172-83. Doi: 10.1016/j.molmed.2014.11.004; PMID: 25498392
10. Shi B, Chang M, Martin J, Mitreva M, Lux R, Klokkevold P, Sodergren E, Weinstock GM, Haake SK, Li H. Dynamic changes in the subgingival microbiome and their potential for diagnosis and prognosis of periodontitis. mBio. 2015 Feb 17;6(1):e01926-14. Doi: 10.1128/mBio.01926-14; PMID: 25691586
11. Avula H, Chakravarthy Y. Models of periodontal disease pathogenesis: A journey through time. J Indian Soc Periodontol. 2022 May-Jun;26(3):204-212. Doi: 10.4103/jisp.jisp_294_21. Epub 2022 May 2. PMID: 35602539; PMCID: PMC9118949.
12. Caton JG, Armitage G, Berglundh T, Chapple ILC, Jepsen S, Kornman KS, Mealey BL, Papapanou PN, Sanz M, Tonetti MS. A new classification scheme for periodontal and peri-implant diseases and conditions – Introduction and key changes from the 1999 classification. J Periodontol. 2018 Jun;89 Suppl 1:S1-S8. Doi: 10.1002/JPER.18-0157. PMID: 29926946.
13. Meuric V, Le Gall-David S, Boyer E, Acuña-Amador L, Martin B, Fong SB, Barloy-Hubler F, Bonnaure-Mallet M. Signature of Microbial Dysbiosis in Periodontitis. Appl Environ Microbiol. 2017 Jun 30;83(14):e00462-17. doi: 10.1128/AEM.00462-17. PMID: 28476771; PMCID: PMC5494626.
14. Luis Muñoz-Carrillo J, Elizabeth Hernández-Reyes V, Eduardo García-Huerta O, Chávez-Ruvalcaba F, Isabel Chávez-Ruvalcaba M, Mariana Chávez-Ruvalcaba K, et al. Pathogenesis of Periodontal Disease [Internet]. Periodontal Disease - Diagnostic and Adjunctive Non-surgical Considerations. IntechOpen; 2020. Available from: http://dx.doi.org/10.5772/intechopen.86548