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Review Article

Genetic, environmental and microbiological causes of periodontal diseases

Yazeed Abdullah Alhabdan[1]*, Abdulhameed G. Albeshr[1], Shoroq Mansour Alqahtani[2], Rudaina Saud Khallaf[3], Khadijah Mustafa Saidi[4], Khalid Aymen Alqiraiqri[3], Bader Atallah Aljuaid[5], Alaa Abdulkalq Albasher[6], Naif Mayouf Alrasheedi[7], Dalal Mohammad Altheiaib[8], Ahmed Nayef Alsharif[9], Mohammed Abdulrahman Alnefaie[8]

[1]King Abdullah Medical City for National Guard, Riyadh, Saudi Arabia
[2]College of Dentistry, King Khalid University, Abha, Saudi Arabia
[3]College of Dentistry, King Abdulaziz University, Jeddah, Saudi Arabia
[4]General Dentist, Ministry of Health, Taif, Saudi Arabia
[5]Dental Department, Ad Dawadmi General Hospital, Ad Dawadmi, Saudi Arabia
[6]College of Dentistry, King Faisal Hospital, Al Ahsa, Saudi Arabia
[7]General Dentist, Ministry of Health, Uyun Aljaw, Saudi Arabia
[8]College of Dentistry, Majmaah University, Majmaah, Saudi Arabia
[9]College of Dentistry, Qassim University, Qassim, Saudi Arabia

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***Correspondence:**
Dr. Yazeed Abdullah Alhabdan,
E-mail: yah11@hotmail.com

ABSTRACT

Periodontal disease is a term that can be used to describe different oral conditions that occur to the gingiva, in addition to the bones and ligaments supporting the teeth. Periodontal diseases can develop secondary to inflammatory, developmental, genetic, traumatic, neoplastic, and metabolic disorders. In the present literature review, we aim to discuss the different genetic, environmental, and microbiological causes of periodontal diseases based on evidence from the current studies in the literature. Evidence regarding genetics is still not adequate, and further research is still needed to understand the main mechanism of this etiology furtherly. Different diseases and habitual factors can contribute periodontal diseases, mainly due to increased inflammation-induced pathological events. Further attention should be directed to preventing these events to intervene against the development of periodontal diseases adequately. Early interventions against these diseases can attribute to enhance the health and prognosis of the affected patients significantly. Microbiological causes are also important and usually develop mainly as a result of poor hygiene. Therefore, further interventional research should be directed towards raising awareness among individuals to reduce the incidence of the condition.

Keywords: Gingivitis, Periodontal diseases, Etiology, Genetics, Environmental, Pathophysiology, Microbiology

INTRODUCTION

Periodontal disease is a term that can be used to describe different oral conditions that occur to the gingiva, in addition to the bones and ligaments supporting the teeth.[1] Gingivitis is the initial process of the pathology of the condition, defined as inflammation of the gingiva, usually by a bacterial infection that has accumulated within the relevant teeth and dental plaque. Estimates show that the prevalence of gingivitis is 50-90% among the different settings, and the variability is mainly attributable to the different definitions of the condition.[2] When gingiva, ligament, and bone are lost, chronic periodontitis becomes the underlying pathology, usually associated

with a deep periodontal pocket that can eventually end up with teeth loss.

In addition to the significant impact on the oral health of the affected patients, evidence also shows that it can also contribute to the overall inflammation of the body and worsen the prognosis of other systemic conditions, including atherosclerosis and diabetes mellitus.[3-5] Periodontal diseases can develop secondary to different inflammatory, developmental, genetic, traumatic, neoplastic, and metabolic disorders. In the present literature review, we aim to discuss the different genetic, environmental, and microbiological causes of periodontal diseases based on evidence from the current studies in the literature.

LITERATURE SEARCH

To retrive relevant studies, we conducted an extensive literature search of the Medline, Cochrane, and EMBASE databases which was performed on 27th October 2021 using the medical subject headings (MeSH) or a combination of all possible related terms, accprding to the database. To avoid missing poetential studies, a further manual search for papers was done through Google Scholar, while the reference lists of the initially included papers. Studies discussing genetic, environmental and microbiological causes of periodontal diseases were screened for useful information, with no limitations posed on date, language, age of participants, or publication type.

DISCUSSION

Different etiologies have been proposed for developing periodontal diseases. In the present section, we will shed more light on the role of these etiologies in developing the condition. Among the different factors, studies have stratified the risk of developing periodontal diseases secondary to these etiologies based on the risk of these factors, which might be modifiable or not. Among the non-modifiable risk factors, genetics have been reported by various investigations that studied the impact of genetics on the development of periodontal diseases among twins and families. In Indonesia, a previous investigation suggested that genetics usually contribute to developing a less severe condition of chronic periodontal diseases.[6,7] The authors concluded this as they included young siblings that did not receive regular dental care and still did not suffer from a chronic severe condition of periodontitis. Accordingly, different research investigations and protocols have been declared to investigate the association between the different types of periodontal diseases and the associated polymorphism and genes, and whether they can significantly impact the course of the disease. In chronic periodontitis, it has been proposed that various types of genes are involved in developing the condition. Furthermore, it has been demonstrated that these genes also vary based on the different communities and ethnicities. Genetics and polymorphisms that are responsible for cytokine production have been a focus of research investigations.[8] On the other hand, it was also demonstrated that genes and polymorphisms that are single-nucleotide have no apparent role in the pathogenesis and development of periodontal diseases.[9,10] The role of familial aggregation has been proposed in the literature among the different family studies. However, it should be noted that most of these studies lack sufficient evidence regarding whether genetic or environmental factors are the main accusants in developing the condition. This has been proposed because it is well known that environmental factors usually have a significant role in the development of genetic modifications. Therefore, their might be indirectly responsible for genetic-induced periodontal diseases. Chromatin changes and acetylation or methylation of the DNA bases are the main mechanisms by which the patterns of gene expressions are usually altered by epigenetic changes. Accordingly, the reliability of genetic coding can also be significantly impacted secondary to these events.[11] On the other hand, evidence in the literature is also poor regarding the role of epigenetics in modulating genes that are responsible for the inflammatory and anti-inflammatory events in the pathology of periodontal diseases.[12] Researching the role and mechanisms of periodontal diseases is a new concept in recent decades, and it has been demonstrated to have a significant role in acquiring more knowledge about the pathogenesis and mechanisms of developing periodontal diseases. This can also provide a possible relation between the effect of genetics and the different phenotypes and forms of periodontal diseases, and provide more information about the potential risk factors and susceptibility of some individuals over others.

As we previously mentioned, environmental causes might attribute to a significant change in the genetics of individuals leading to the development of polymorphisms that can predispose to the development of periodontal diseases. There are many other modifiable and non-modifiable factors and disorders that can be linked to the pathogenesis of periodontal diseases. For instance, psychological and physical stress might be involved in the process of developing periodontal disease. However, the exact mechanism of the condition is still poorly understood, and further research is still needed.[13,14] In this context, previous investigations have demonstrated that being predisposed to significant risk factors and suffering from stressful conditions and psychological disorders might restrain the affected patient from dealing with these events, which can significantly expose him to these risk factors, contributing to the pathogenesis of the disease.[15,16] Impaired host response is also another important factor to consider when discussing the pathogenesis of the disease because the role of the immune response has been previously well discussed in interventing against the pathology of the different inflammatory diseases, like periodontitis (Figure 1). Accordingly, the presence of an underlying condition that can impair the immune host response can be a significant factor for developing periodontal diseases. Some of these

conditions might include thrombocytopenia, leukemia, cyclic neutropenia, agranulocytosis, and leukocyte adhesion deficiency. Being affected with HIV and AIDS can also impair the immune response and has been reported to be a significant factor for developing periodontal diseases among the different investigations in the literature. Although it has been demonstrated that being infected with HIV does not have a significant factor on the development and pathogenesis of periodontal diseases as significant as other risk factors,[17] it has been reported that the immunocompromised status that is associated with the disease is remarkably associated with distinctive types of periodontitis and necrotizing gingivitis.[18] During World War I, the prevalence of acute gingivitis was very high, and therefore, it was called trench mouth disease. Many risk factors attributed to the development of the condition, including fatigue, stress, poor hygiene, and malnutrition, and the disease was generally characterized by bleeding gums, pain, low-grade fever, halitosis, cervical lymphadenopathy, and malaise. Nevertheless, recent evidence indicates that the prevalence of the condition is not as high among HIV patients as in the previous decades, and some patients only suffer from necrotizing mucositis and necrotizing ulcerative periodontitis. Evidence indicates that the prevalence of periodontal problems is not a common condition among HIV-positive patients. On the other hand, a previous investigation also indicated that a CD4+ count <200 cells/µL strongly predicts the presence of necrotizing ulcerative periodontitis in these patients.[19] As a result of the increased efficacy and availability of highly active antiretroviral therapies, the incidence of oral disorders has significantly decreased since then among HIV-positive patients.[20,21] However, in countries where there is less availability of adequate management modalities, as in sub-Saharan Africa and other less-developed regions, the prevalence of oral symptoms among HIV-positive patients is still high.[22,23]

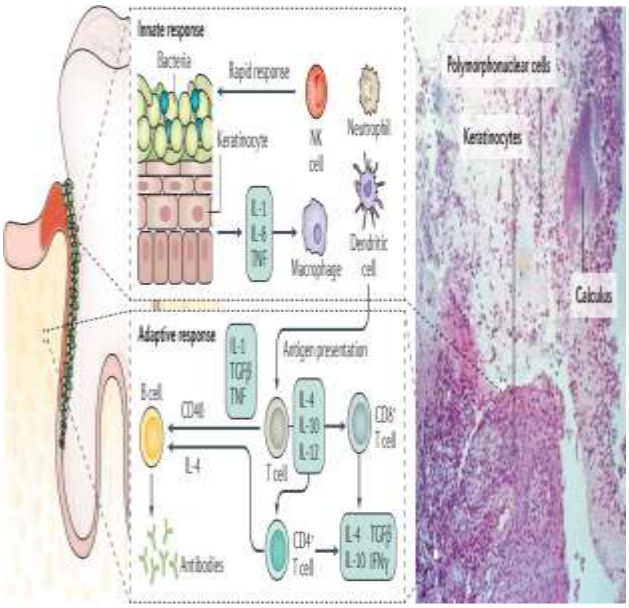

Figure 1: Immune response in periodontitis.[45]

Reports also indicate that diabetes mellitus might be a significant risk factor for developing periodontal diseases through different mechanisms and mainly through the development of an immunocompromised status. Among the different studies in the literature, evidence is almost consistent, indicating a significant association between diabetes and periodontal diseases. These investigations have demonstrated that the prevalence of periodontal diseases among patients with different types of diabetes is significantly higher among these patients as compared to the other population without diabetes.[24,25] It has been furtherly demonstrated that patients with controlled diabetes do not have a significantly higher risk than non-diabetic patients. On the other hand, it has been well established that uncontrolled diabetes is associated with various complications, including nephropathy, retinopathy, macrovascular diseases, and neuropathy, in addition to periodontal diseases.[24,26] The association between diabetes and the risk of developing periodontal diseases is logical due to the strong evidence that adequately elaborated the microscopic and macroscopic events of the disease. Reduced monocyte response to the antigens from dental plaques and impaired wound healing, and the reduced chemotactic response of the neutrophils to the local inflammatory events, which are common mechanisms in diabetes, are mainly responsible for developing periodontal diseases in these settings.[27,28] It has been furtherly demonstrated that the role of bacterial infections in the gingiva seems to be non-significantly different between the diabetic and nondiabetic populations.[29] Nutrition also plays an essentail factor as a major contributor the general health and gingival health, and impaired nutritional status can significantly be associated with an increased risk of developing periodontal diseases. For instance, scurvy has been associated with vitamin C deficiency as a result of increased periodontal inflammation, reduced collagen maintenance and formation, tooth loss, and hemorrhage. However, evidence from many large previous epidemiological investigations did not significantly associate the development of periodontal diseases and hypovitaminosis. In depleted or poor countries, the impact of trace elements, vitamins, and proteins deficiencies is important in the development of periodontal diseases. Nevertheless, evidence regarding these events is not clear, and the mechanisms are poorly underreported. For instance, cancrum oris has been estimated to be significantly prevalent in Sub-Saharan Africa. The clinical devastating oral manifestations of the condition are usually initially observed as acute necrotizing ulcerative gingivitis. Further evidence also indicates that populations with immunocompromised status following viral infection (particularly measles), have an unusual oral bacterial infection, or suffer from a significant malnutrition status (including Kwashiorkor) are the most susceptible for developing periodontal diseases in these communities.[30]

Osteoporosis has also been reported to contribute to the development of periodontal diseases.[31,32] Besides, tobacco

use and smoking habits were also reported to increase the risk of developing periodontitis and other oral-related conditions that might end up with teeth loss and edentulism.[33,34] Although alcohol consumption has been reported to attribute to the development of periodontal disease, evidence is still scarce, and further investigations are still needed.[35] The role of microbiological etiologies has also been extensively established by many investigations. Evidence shows that the frequencies of gram-negative organisms significantly increase as maturation of the dental plaque occurs and becomes significantly associated with the development of periodontal diseases.[36,37] Further evidence also showed that the supragingival growth of bacteria significantly exceeds the growth in other oral parts by more than 10 times.[38] Bacterial counts are also variously observed in the periodontal pocket and within a shallow healthy cervice. Investigations show that cleaning the mouth at least every 2 days can significantly keep oral health normally with the normal physiological bacterial counts.[39] However, it has been demonstrated that achieving this is difficult among the public, and the common approaches to increase awareness about these events seem to be non-significant.[40] Certain bacterial species have been reported to attribute to the development and pathology of periodontal diseases. Evidence shows that spirochaete *Treponema denticola*, *Tannerella forsythensis*, and *Porphyromonas gingivalis* are the main pathogens that can cause periodontal conditions.[41] Increased release of collagenases, leucotoxins, fibrinolysins, and other toxic substances from these bacterial species attributes to the main pathology of the condition. *Actinobacillus actinomycetemcomitans*, viral infections (especially by herpes), and fungal infections (especially by *Candida albicans*) can also be attributed to developing periodontal diseases. Therefore, certain concerns should be provided to these etiologies to adequately diagnose and manage the affected patients.[42-44]

CONCLUSION

Evidence regarding genetics is still not adequate, and further research is still needed to furtherly understand the main mechanism of this etiology. Different diseases and habitual factors can attribute to the development of periodontal diseases, mainly due to increased inflammation-induced pathological events. Further attention should be directed to preventing these events to adequately intervene against the development of periodontal diseases. Early interventions against these diseases can attribute to significantly enhance the health and prognosis of the affected patients. Microbiological causes are also important and usually develop mainly due to poor hygiene. Therefore, further interventional research should be directed towards raising awareness among individuals to reduce the incidence of the condition.

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