



REVIEW ARTICLE

RISK FACTORS FOR PERIODONTAL DISEASES

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ARTICLE INFO

Article history:

Received 3rd June 2015

Received in revised form 3rd June 2015

Accepted 6th June 2015

Keywords:

Risk Factor,Periodontal

Disease,Treatment Planning

ABSTRACT

Periodontal Diseases are infections, which are associated with specific pathogenic bacteria that colonize the subgingival area. Initiation & progression of periodontal infections are clearly modified by local & systemic conditions called risk factors. The local factors include pre-existing disease as evidenced by deep probing depths and plaque retention areas associated with defective restorations. Systemic risk factors recently have been identified by large epidemiologic studies using multifactorial statistical analyses to correct for confounding or associated co-risk factors. Recent Studies also point to several potentially important periodontal risk indicators. These include stress & coping behaviours, & osteopenia associated with periodontal disease including gender, age & hereditary factors. The study of risk in periodontal disease is a rapidly emerging field and much is yet to be learned.

INTRODUCTION:

It is of utmost importance to provide a clear analysis of the evidence supporting the important role of risk factors in determining the differences between individuals in susceptibility to periodontal disease and gain a deeper understanding of the role of risk factors in order to incorporate risk-factor modification in the management of periodontal disease. Focus will be specifically on systemic risk factors which are susceptible for periodontal disease that are relatively common in the population and are likely to have a substantial population-attributable risk.

Periodontal disease as an infection, and the overall role and definition of periodontal risk factors.

Risk is defined as the probability that an individual will get a specific disease in a given period. However, the

risk of developing the disease will vary from individual to individual.

Risk factors may be environmental, behavioural, or biologic factors that, when present, increase the likelihood that an individual will get the disease. For a risk factor to be identified, the exposure must occur prior to disease onset.

Risk indicators are probable or putative risk factors that have been identified in cross-sectional studies but not confirmed through longitudinal studies.

Risk predictors/markers, although associated with increased risk for disease, do not cause the disease.

The concept that rate of progression, age at onset, and severity of periodontal disease in an individual are often determined by systemic risk factors in the host is a recent concept,

made by understanding of the epidemiology of periodontal disease and the role of risk factors.

The mechanisms involved in the initiation and progression of periodontitis has developed from a

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simplicistic view of microbes directly causing clinical signs and symptoms of periodontitis, through understanding the importance of the immune system and the inflammatory response of the host which further describes periodontal disease, as a multifactorial disease that also is influenced by genetic and environmental risk factors.

Strength of evidence for risk factors

The strength of the contribution from each scientific report to the body of epidemiologic evidence is determined not only by the quality of the conduct of the study, but is limited by its design and methods that determine which conclusions about causality can be inferred from the results. Causality factors relevant in human health issues can be defined as: "a factor is a cause of a disease or health-related condition if its operation increases the frequency of the disease or condition."¹ The results of epidemiologic studies, potential risk factors can be identified which subsequently yield evidence that elucidates etiology and mechanisms by which risk factors operate at the basic molecular, cellular, and genetic levels. If a condition does not fulfill the causality criteria, but is frequently observed to be associated with studied outcome, it can still be considered as a risk factor which increases susceptibility to the infection. An important concept is the extent to which any risk factor contributes to periodontitis, is called the attributable risk.

INDIVIDUAL RISK FACTORS

- Gender, smoking, and alcohol (lifestyle)
- Diabetes
- Obesity and metabolic syndrome
- Osteoporosis, dietary calcium, and vitamin D
- Stress
- Genetic factors

GENDER, SMOKING AND ALCOHOL(LIFESTYLE)

Gender as a risk factor for periodontal disease

The most prevalent risk factor for periodontal disease is being of male sex. It has been recognized that men of all ages, race/ethnic groups, and geographic locations^{2,3,4} have significantly more periodontal disease than women, assessed by prevalence, extent, and severity, as well as by any parameter and case definition of periodontitis.⁵

Smoking as a risk factor for periodontal disease.

Cigarette smoking has long been associated with periodontal disease and tooth loss⁶. Smoking cigarettes, the source of more than 4,000 toxins, is a major risk factor for all cause mortality, cardiovascular disease, various cancers, and several chronic diseases⁷. An association between acute necrotizing ulcerative gingivitis and tobacco smoking was reported in 1947.⁸

The importance of cigarette smoking as a risk factor for periodontal disease is supported by: (i) consistency of results across many studies; (ii) strength of the association; (iii) dose-response of the association; (iv) temporal sequence of smoking and periodontal disease;

and (v) biologic plausibility⁹. Grossi and colleagues¹⁰ showed that as the number of pack years increased, the amount of attachment loss was greater. They also found that the amount of alveolar crest height loss was positively correlated with the number of pack years of smoking, showing a clear dose response. Following non-surgical periodontal therapy and smoking cessation, the subgingival microbiome is recolonized by a greater number of health-associated species along with a significantly lower prevalence and abundance of putative periodontal pathogens.¹¹

Longitudinal evidence for the benefits of smoking cessation on periodontal disease:

A study, by Bolin et al.¹², reported the results of a 10-year radiographic follow-up, showing that progression of alveolar bone loss was significantly reduced in those who had quit smoking during the study compared with continual smokers.

Smoking as a risk factor for periodontal disease: pathogenic mechanisms:

These adverse effects fall into several categories regarding the effect of cigarette smoking on: microbiology (microbiota/periodontal pathogens) gingival blood flow polymorphonuclear neutrophil phagocytosis cytokine production (e.g., interleukin-1) CD3, CD4 and CD8⁺ T-cell subsets periodontal healing.¹³

Smoking was found to select for specific periodontal pathogens, including *P. gingivalis*, *Treponema denticola* and *T. forsythia*, and this was proposed to increase the risk for development and progression of periodontal disease.¹⁴ This was confirmed by Kazor et al.¹⁵ and Haffajee & Socransky¹⁶.

Smoking leads to peripheral vasoconstriction, probably associated with low doses of nicotine.^{17,18,19} Vasoconstriction can lead to reduced gingival bleeding and hence can cause the observation of less gingivitis and reduced gingival bleeding in smokers compared with nonsmokers. The compromised microvascular response, which could lead to reduced oxygen tension in the periodontal pocket and thus favor the overgrowth of anaerobes, such as *P. gingivalis* and *T. denticola*.

Smoking alters neutrophil function, mainly through the effects of nicotine. Nicotine also enhances the degranulation of neutrophils, making the neutrophils more sensitive to bacterial challenge.²⁰ Macrophages have also been implicated in the increased levels of tumor necrosis factor- α found in the gingival crevicular fluid of smokers, probably in response to the presence of nicotine. Tumor necrosis factor- α may also be expressed by peripheral neutrophils found in the periodontium, and increased levels of tumor necrosis factor- α may contribute to connective tissue and periodontal bone destruction. Proliferation, chemotaxis, and attachment of fibroblasts from the periodontium are inhibited by nicotine.^{50,51} Levels of interleukin-1 β in gingival crevicular fluid are reduced in periodontally diseased sites in smokers, but are enhanced in smokers who are periodontally healthy. This raises the possibility of an

imbalance in cytokine production that may affect the pathogenesis of periodontal disease in smokers.²³

Alcohol consumption as a risk factor for periodontal disease

Alcohol consumption may be associated, in a dose-dependent manner, with increased severity of clinical attachment loss.²⁴ In a study of data from NHANES III from 13,198 employed adults 20 years and older, there was a significant, linear relationship between number of alcoholic drinks per week and log clinical attachment loss ($P = 0.0001$).

DIABETES

Diabetes mellitus as a risk factor for periodontal disease

Diabetes mellitus is a metabolic disorder that occurs in several forms; however, all forms of diabetes mellitus are characterized by hyperglycemia. The abnormal glucose metabolism results from defects in insulin action or in insulin production (or in both in severe cases). Diabetes mellitus and periodontal disease are both chronic, common diseases in the population, especially in those over 65 years of age, and are related.

Two-way relationship between diabetes and periodontal disease

It has been suspected that diabetes contributes to poorer oral health because more people with diabetes have periodontal infections than do those without diabetes. The inter-relationship between diabetes and periodontal disease applies in both directions it is called a bidirectional (two-way) relationship^{25,26}.

The studies show, that the severity of periodontal disease is higher in individuals with mostly uncontrolled diabetes than in those with no diabetes from the same population^{27,28,29}. Also, the severity of periodontitis is greater in all age groups among those with diabetes and increases with age.

Prediabetes (impaired fasting glucose or glucose intolerance) as a risk factor for periodontal disease

'Prediabetes' or alternatively termed, are at high risk for diabetes, as measured by elevated glycated hemoglobin, impaired fasting glucose or impaired glucose tolerance. Prediabetes often leads to diabetes and is associated with major risk factors for cardiovascular disease and other diabetic complications³⁰. In an age- and sex-matched case-control study, subjects with prediabetes had moderate periodontal disease.

Those with abnormally high blood-glucose levels were significantly more likely to have severe periodontal conditions³¹. There was a significant association between elevated blood-glucose levels (≥ 120 mg/dl) and severe periodontal conditions. Compared with those with normal glucose levels, participants with hyperglycemia had more than double the risk (odds ratio = 2.46) for having severe periodontal conditions³². Thus, Katz concludes: 'The present study supports the existence of a two-way relationship between periodontal disease and

elevated glucose level in a large population³². The difference was seen after controlling for confounders, including age, gender, smoking, and body mass index.

Gestational diabetes as a risk factor for periodontal disease

Women with a history of gestational diabetes vs. 4.8% for those without any history of any form of diabetes³³. The other study found that in pregnant women, the prevalence of periodontitis was 44.8% in those with gestational diabetes vs. 13.2% in those with no evidence of diabetes. In nonpregnant women, the prevalence of periodontitis was 40.3% in those with type 1 or type 2 diabetes, 25.0% in those with a history of gestational diabetes and 13.9% in those without diabetes, and the differences were statistically significant. It is important to note that nonsurgical periodontal treatment of pregnant women is probably safe for both the mother and the child^{34,35}, and hence management of periodontal disease during pregnancy may be an option to modify the increased risk of worsening periodontal disease in pregnant women.

Mechanisms to explain the role of diabetes mellitus in periodontitis.

Inflammation is a central feature of both diabetes and periodontal disease, and inflammatory processes are up-regulated in the periodontal tissues of patients with diabetes. The levels of interleukin-1 β and prostaglandin E₂ are higher in the gingival fluid of patients with type 1 diabetes than in the gingival fluid of diabetes free individuals with the same level of periodontal disease³⁶. Both type 1 and type 2 diabetes mellitus are also associated with elevated levels of systemic markers of inflammation³⁷. Many of the complications of diabetes may be associated with elevation of inflammatory pathways. Hyperglycemia can result in increased inflammation, oxidative stress, and apoptosis, and hence contribute to enhanced periodontal destruction³⁸.

Role of advanced glycation end-products and of receptors for advanced glycation end-products.

The receptors for advanced glycation end-products are elevated in patients with diabetes. This is important because the interaction of these receptors with advanced glycation end-products, which are elevated in patients with diabetes, plays a role in the development of diabetic complications such as cardiovascular disease and kidney disease³⁹. In humans, the levels of advanced glycation end-products in serum are also associated with the extent of periodontitis in adults with type 2 diabetes mellitus⁴⁰.

Alteration and capacity for repair in periodontitis associated with diabetes.

Patients with diabetes have increased apoptosis, which is associated with delayed wound healing⁴¹. It is likely that apoptosis plays a role in the increased severity of periodontitis in patients with diabetes. Periodontal organisms interfere with the capacity for repair in inflamed periodontal tissues in patients with diabetes by enhancing the death of matrix-producing cells.

Altered native immune responses in patients with diabetes.

Patients with diabetes have been shown to have impaired neutrophil chemotaxis^{42,43}.

Patients with type 2 diabetes have also been shown to have impaired neutrophil adherence and phagocytosis^{44,45}. In a study of patients with severe periodontitis it was found that patients with diabetes and severe periodontitis have depressed neutrophil chemotaxis compared with nondiabetic subjects with periodontitis or with diabetic subjects with mild periodontitis^{46,47}. Furthermore, diabetes may lead to increased severity of periodontal disease as a result of defective neutrophil apoptosis^{48,49}. This, in turn, could lead to increased retention of neutrophils in the periodontium, resulting in increased tissue destruction as a result of the release of reactive oxygen species and histolytic enzymes from neutrophils.

Effects of periodontitis on the levels of glycated hemoglobin and on diabetes complications: possible mechanisms.

Periodontitis increases the levels of proinflammatory and prothrombotic mediators in serum^{50,51}. Hence, it is possible that systemic inflammation associated with the local inflammatory response triggered by periodontal microflora leads to insulin resistance. For example, tumor necrosis factor- α , which is elevated in the plasma of patients with periodontitis⁵², is known to promote insulin resistance by interfering with insulin signaling^{53,54,55,56}. Periodontal therapy appears to be able to reduce systemic inflammatory mediators, such as C-reactive protein, tumor necrosis factor- α , interleukin-6, and others, as well as to increase adiponectins in individuals with diabetes^{57,58,59,60}. The reduction of these inflammatory mediators by periodontal treatment may result in increased insulin sensitivity with improved control of glycated hemoglobin. In turn, this improvement in glycated hemoglobin can lead to a reduction in the complications of diabetes mellitus that are associated with periodontitis, including cardiovascular and renal complications⁶¹.

OBESITY AND METABOLIC SYNDROME

Obesity as a risk factor for periodontal disease

Obesity is an emerging major public health problem, as the prevalence of obesity and overweight has trebled since the 1980s⁶². Overweight and obesity are defined by measures such as body mass index, waist : hip ratio, waist circumference, body weight, and body-weight changes.

Evidence for association of obesity with periodontal disease.

Suvan et al.⁶³ reviewed cross-sectional studies, most of which show greater severity and/or prevalence of periodontal disease in individuals who are either overweight or obese. The odds ratios were adjusted for age, gender, smoking, alcohol consumption, and frequency of tooth brushing. Hence, it appears from the

association studies that there is consistency in the association of obesity with periodontal disease. The strength of association is reasonable, with odds ratios ranging from 1.88 to 4.40, and the dose response is clear.

Mechanisms by which obesity may lead to increased periodontal disease

Haffajee & Socransky⁶⁴ compared periodontally healthy and gingivitis subjects with chronic periodontitis subjects. They found that the numbers of *T. forsythia* were significantly higher in obese individuals suffering from gingivitis, but who were otherwise periodontally healthy, compared with the other groups. They hypothesized that overgrowth of *T. forsythia* may occur in periodontally healthy individuals who are obese, putting them at risk for the initiation and progression of periodontitis.

Metabolic syndrome as a risk factor for periodontal disease

Metabolic syndrome is a cluster of disorders, including increased blood pressure, elevated plasma glucose, excess body fat around the waist and abdominal area, and altered cholesterol levels, which occur in certain individuals. Metabolic syndrome increases the risk of heart disease, stroke, and diabetes. Having metabolic syndrome is defined as having three or more of these disorders related to an individual's metabolism at the same time.

The cause of metabolic syndrome, although not completely known, appears to be associated with insulin resistance. Risk factors for metabolic syndrome include age, race, obesity, a history of diabetes and other diseases, including hypertension, cardiovascular disease and polycystic ovary syndrome.

Evidence for the association of metabolic syndrome with periodontal disease.

One of the first studies by Shimazaki and coworkers⁶⁵, of 984 Japanese women, showed that metabolic syndrome increases the risk of periodontitis. They examined the relationship between periodontitis and five components of metabolic syndrome, including abdominal obesity, triglyceride level, high-density lipoprotein cholesterol level, blood pressure, and fasting plasma glucose. The odds ratio for subjects who had four or five of these components was 6.6 (95% confidence interval: 2.6–16.4) for greater pocket depth. Isterol and fasting plasma glucose had the highest effects of the five components. High-density lipoprotein cholesterol and fasting plasma glucose had the highest effects of the five components.

Mechanisms to explain the association between periodontal disease and metabolic syndrome.

The cytokines elevated in these conditions include interleukin-6, interleukin-1 β and the acute-phase proteins, C-reactive protein, and fibrinogen. It may be, as suggested for patients with diabetes, that the elevated systemic inflammatory response seen in individuals who are obese increases the destructive immunopathologic

response of these individuals to the periodontal microflora, resulting in greater tissue destruction⁶⁶.

OSTEOPOROSIS, DIETRY CALCIUM & VITAMIN D

Osteoporosis as a risk factors for periodontal disease

Osteoporosis is a systemic disorder characterized by reduced bone-mineral density throughout the skeletal system, including the jaws. Osteoporosis increases the risk for fracture, particularly hip fractures, which in the elderly doubles the risk of death in the first 12 years after fracture⁶⁷. The main risk factor for osteoporosis in women is menopause, which is associated with reduced estrogen production that results in increased bone resorption⁶⁸. In addition, there is also a decrease in calcium absorption and an increase in calcium excretion, which increases the calcium requirement⁶⁹. This process has a significant impact on mortality and morbidity. Also, because menopause is associated with increased bone resorption, other disease processes that involve bone loss, including periodontal disease and tooth loss, are probably affected.

Dietary calcium and vitamin D as risk factors for periodontal disease

The role of dietary calcium in periodontal disease has also been studied and an inverse relationship was found. Nishida et al.⁶⁴ reported from the NHANES III data that individuals, especially women, with a low intake of dietary calcium (less than half of the recommended dietary allowance, for example) had more severe periodontal disease. The same was true for men, but it was a more modest effect. Several studies show that calcium and vitamin D supplements used to prevent or treat osteoporosis also appear to have beneficial effects on tooth retention⁶⁵. Miley et al.⁶⁶ showed, in a randomized controlled trial over 5 years, that subjects taking calcium and vitamin D lost fewer teeth than subjects in the control group.

The effects of bisphosphonates, which are commonly used to treat osteoporosis, have been studied for their ability to inhibit periodontal bone loss. In one study⁶⁷, bisphosphonates were effective in reducing alveolar bone loss in those patients who had low baseline bone mineral density. Other studies also show an effect of bisphosphonates in reducing alveolar bone loss^{68,69}. Knowledge of the dental patient's systemic bone health, as well as intake of calcium and vitamin D, may be important in understanding their periodontal status and provide direction for modification of these factors.

STRESS

Stress, distress, and coping skills as risk factors for periodontal disease

The association of psychological stress with periodontal disease was postulated in early studies of acute necrotizing ulcerative gingivitis⁷⁰. More recently, many studies have addressed the role of psychological stress,

distress and coping as they affect the more common adult chronic periodontal disease^{71,72}

Hugoson et al.⁷³ stated that traumatic life events, such as loss of a spouse, increased

the risk of periodontal disease, but individuals with the ability to cope with this stressful stimulus had reduced the role of the traumatic life event in the progression of periodontal disease.

Stress/psychological factors are risk factors for periodontal disease, and that the effects can be modified or abrogated by adequate coping behaviors. To date, there is one randomized controlled trial that addresses the important issue of the effects of modification of stress in modifying periodontal disease⁷⁴. In this trial, the influence of coping behavior was assessed over a 24-month period. It was found that passive coping strategies resulted in more pronounced periodontal disease, whereas patients with active coping strategies (presumably a more effective form of coping) had a milder disease level and more favorable course of treatment. . Dysregulation of the host immune response can be brought about by psychologic stress in several ways. Exposure to stress can induce the release of noradrenaline through the sympathetic nervous system by activation of the adrenal medulla, which can have immunosuppressive effects⁷⁵. Such immunosuppressive effect can enhance periodontal tissue destruction⁷⁶. Stress can promote the production of corticotropin-releasing hormone by the pituitary gland and the production of glucocorticoid hormones from the adrenal cortex^{77,78,79,80}.

Stress can also result in a decrease in the production of proinflammatory cytokines as a result of the release of neuropeptides from sensory nerve fibers. These neuropeptides can modulate the activity of the immune system, leading to more tissue destruction⁸⁰.

Another effect of stress is on behavior. Stress may modify behaviors that are harmful to periodontal health, such as poor oral hygiene, increased smoking, fewer dental visits, and changes in eating habits. These behaviors may have effects on periodontal disease, by affecting plaque control, increasing the adverse effects of smoking on periodontal disease, and also may result in suppression of the immunologic system⁸¹. Hilgert et al.⁸² showed that cortisol levels were positively associated with the extent and severity of periodontitis; that is, higher levels were indicative of stress and were associated with higher levels of periodontal disease. A more recent, but smaller, study showed that salivary cortisol and beta-endorphins were statistically significantly associated with tooth loss and clinical parameters of periodontal disease⁸³. There is emerging evidence that stress and inadequate coping skills may explain some of the risk for periodontal disease in some patients. Therefore, recognizing that patients suffer from stress suggests that more definitive management of their periodontal disease may be necessary.

GENETICS

Genetic factors as risk factors for periodontal disease

Periodontal disease is initiated by microorganisms in the subgingival biofilm, and lifestyle risk factors, as well as

systemic diseases, play a role in modifying the disease. In addition, it has been hypothesized that some genes may also modify periodontal disease. It also is clear that other genetic factors, such as gene–gene interactions and gene–environmental interactions (epigenetic factors) may be important in the development of periodontal disease.

Familial aggregation and twin studies.

Familial aggregation studies carried out by Marazita and co-workers⁸⁴ suggest that early-onset, or aggressive, periodontitis is inherited as an autosomal-dominant trait in Black families. Genetic studies of families affected with aggressive periodontitis were reviewed by Meng and co-workers⁸⁵. Their review of the literature shows that the familial aggregation of aggressive periodontitis is often very high among certain families, with the percentage of affected siblings and affected pedigree members reaching 40–50%, suggesting that genetic factors may be important in susceptibility to aggressive periodontitis. In fact, subtypes of aggressive periodontitis have been proposed to be inherited in a Mendelian manner as X-linked-dominant, autosomal-recessive or autosomal-dominant characteristics; however, this is controversial. It should be pointed out that it is commonly reported that the underlying cause of localized aggressive periodontitis is related to leukocyte dysfunction in certain races, and the basis of this dysfunction may be genetic.

Familial aggregation studies in chronic periodontitis are less common. However, a study by Shearer et al.⁸⁶, of a proband–parent group of 625 individuals, concluded that parents with poor periodontal health tend to have offspring with poor periodontal health. They also found that family history^{87,88} is a valid representation of shared genetic and also shared environmental factors that contribute to an individual's periodontal status.

Michalowicz and co-workers estimate that a substantial portion of the expression of periodontitis in adult chronic periodontitis in twins could be attributed to genetic factors. However, a recent study comparing monozygotic and dizygotic twins^{89,90} found a lack of concordance between both monozygotic and dizygotic twin pairs regarding the severity of attachment loss or alveolar bone loss. In the dizygotic twins, 45.6% of the discordance could be explained by smoking. The familial aggregation phenomenon of periodontal disease is more apparent among young individuals with periodontitis and therefore, it may be that this form of periodontitis (aggressive periodontitis) has a stronger genetic background than does adult chronic periodontitis.

Polymorphisms in chronic periodontitis

Studies attempting to differentiate aggressive periodontitis from chronic periodontitis based upon gene polymorphisms were reviewed by Stabholz et al.⁹⁰. Patients with aggressive periodontitis do show a positive association with human leukocyte antigen-A9, and a negative association with human leukocyte antigen-A2 and human leukocyte antigen-A5⁹¹. An extensive review

of gene polymorphisms in chronic periodontitis has been carried out by Laine et al.⁹². They present a comprehensive literature search up to 2009 and have analyzed studies looking at polymorphisms in the following: the interleukin-1 gene cluster; the tumor necrosis factor- α gene cluster; the interleukin-4 and interleukin-4RA genes; the interleukin-6 and interleukin-6R genes; the interleukin-10 genes; the FcR genes; the vitamin D receptor genes; pattern recognition receptor genes such as CD-14; and a series of miscellaneous genes. The evidence points to polymorphisms in the interleukin-1, interleukin-6, interleukin-10, vitamin D receptor, and CD-14 genes as playing a role in chronic periodontitis, but most find that these associations are restricted to certain populations. A particularly active area of investigation deals with interleukin-1 polymorphisms. These studies were reviewed by Karimbux and co-workers⁹³. They found significant effects for two individual gene variations – interleukin-1A (odds ratio = 1.48) and interleukin-1B (odds ratio = 1.54) – and for a composite genotype that combines minor alleles at each locus (odds ratio = 1.51). Significant heterogeneity was found that could not be explained. They conclude that interleukin-1A and interleukin-1B genetic variations are significant contributors to chronic periodontitis; however, like other polymorphisms, the association is found mainly in Caucasians. There is presently a commercially available test to assess interleukin-1 genetic polymorphisms in periodontal disease

Epigenetics in periodontal disease

Evidence is emerging for a role of epigenetic phenomena, including post-translational methylation of genes, in periodontal disease. It is therefore reasonable to expect that these effects will have significance, especially in contributing to the chronicity of periodontal disease. For example, the methylation status of genes affecting levels of prostaglandins was changed in tissues from periodontal disease, suggesting an epigenetic contribution to the periodontal disease inflammatory response⁹⁴. The evidence in other diseases suggests that epigenetic regulatory mechanisms can modulate inflammatory responses, and the finding that periodontal pathogens can promote DNA hypermethylation⁹⁵ suggests that this may occur in periodontal disease.

Sharing genetic risk factors between periodontal disease and other associated chronic diseases

Genetic risk factors may increase susceptibility not only to periodontal disease, but also to other associated chronic diseases such as cancer, heart disease and diabetes. A study of shared genetic risk factors between periodontal disease and cancer, based upon twin studies, is described to illustrate the potential of this approach to understand not only the risk for periodontal disease, but also for associated systemic conditions⁹⁶. In another study⁹⁷, co-twin analysis using dizygotic twins with baseline periodontal disease showed a 50% increase in total cancer risk, but in monozygotic twins this

association was markedly attenuated. The association of periodontal disease with total as well as digestive tract cancers was stronger in dizygotic twins than in monozygotic twins and this supports the hypothesis of shared genetic factors that may affect the association between periodontal disease and cancer. It is hypothesized that inflammation may underlie this association and that interleukin-1 gene polymorphisms associated with increased levels of periodontal disease may also be associated with the increased risk of gastric cancer. Genetic studies of periodontal disease have the potential to lead to a better understanding of the etiopathogenesis of periodontal disease and its association with other chronic diseases of humans. Periodontal disease risk is clearly associated with genetic factors; however, the genes involved, and their mechanisms of action, are as yet unclear.

SUMMARY & CONCLUSION

Risk factors work to change the susceptibility or resistance of individuals to the disease.

Risk factors for periodontal disease can be systemic or local, and those that are systemic include behaviors, such as smoking; medical conditions, such as poorly controlled diabetes, possibly obesity, stress, osteopenia, and inadequate dietary consumption of calcium and vitamin D. It is reasonable to talk of "eliminating" or modifying these risk factors as part of the management of periodontal disease. Other risk factors, such as race or genetic factors, cannot be changed; however, identifying people at risk for adverse outcomes by race or genetic make-up provides a means for targeting interventions.

In conclusion, it is imperative that the clinician looks beyond the oral cavity for factors of which to potentially recommend modification in order to help their patients reach their common goal of prevention or management of periodontal disease -- and thereby possibly improve general health as well.

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How to cite this article: Avasthy P, Govila V, Verma S, Pant VA, Sharma M. Risk Factors for Periodontal Disease. *J App. Dent. Med. Sci.* 2015; 1(1):44-54.

Source of Support: Nil, Conflict of Interest: None declared.

TABLES AND FIGURES**Table 1: the periodontal risk factors for which modification is possible**

<u>Risk factor</u>	<u>Modification</u>
<u>Smoking</u>	<u>Smoking cessation</u>
<u>Poorly controlled diabetes</u>	<u>Improved glyceemic control</u>
<u>Obesity</u>	<u>Diet and exercise</u>
<u>Osteoporosis</u>	<u>Bone-sparing agents, calcium and vitamin D supplementation</u>
<u>Low dietary calcium and vitamin D</u>	<u>Calcium and vitamin D supplementation</u>
<u>Stress and inadequate coping</u>	<u>Stress-reduction measures</u>