



## The Influence Of Stress On The Progression Of Periodontal Disease

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### Abstract

Periodontal disease is a multifactorial disease influenced by various etiological factors such as local, systemic, environmental, and psychologic factors. Stress influenced periodontal diseases modifies host immune response and leads to severe periodontal destruction. Stress affects periodontal health by producing behavioural changes leading to an imbalanced inflammatory reaction. The two major pathways involved in stress are the hypothalamic-pituitary-adrenal axis [HPA] and the adrenomedullary sympathetic nervous system. Thus, coping skills and strategies are essential for effective management of stress and it provides the course for successful periodontal therapy. Various stress biomarkers in saliva and blood and many stress scales are available which aids in early detection of periodontal disease. Thus, proper diagnosis includes evaluation of psychosocial factors and treatment should focus on effective management of the etiology. This review article gives a knowledge and understanding about the influence of stress on periodontal diseases.

**Keywords:** coping, periodontitis, stress

### Introduction

Oral health is the mirror of general health and wellness of an individual. Periodontitis is a chronic inflammatory multifactorial disease in which dental plaque is the primary etiological factor <sup>[1,2]</sup>. Several other risk factors are also associated with periodontitis including smoking, genetic polymorphisms, systemic diseases, socioeconomic status and psychological stress <sup>[3,4]</sup>. The damage occurs directly from the bacterial products and indirectly by the bacterial induction of host immune response. A strong possible relationship has been proved to exist between the etiology, progression and treatment outcome of periodontal disease and stress <sup>[5,6]</sup>. When stress is present for a longer duration it exerts a negative effect on the efficacy of immune system , modifies salivary flow , produces an imbalance between host and bacteria leading to periodontal breakdown and

immunosuppression <sup>[7,8]</sup>. Stress has an indirect effect on periodontal health through lifestyle modifications , unhealthy diet and oral hygiene neglect which further increases the risk for periodontal disease <sup>[9]</sup>. Various studies has shown that circumstances such as financial strain , domestic and health problems increases bacterial invasion due to poor immune response leading to periodontal damage. Due to the presence of many confounding factors the exact mechanism between stress and periodontal disease is still unknown <sup>[10]</sup>. Stress operates at various levels as it is dynamic <sup>[11]</sup>.

### What Is Stress?

Hungarian Hans Selye was the first person to coin the word 'stress'. Stress is derived from a Latin word 'stringere' meaning tight /strained. Later Canon found out that stress influences sympathetic system and occurs as a result of homeostasis <sup>[12]</sup>. Selye

defined stress as a response state of the organism to forces acting on the body which, if occurs beyond the limits leads to diseases of adaptation and eventually to exhaustion and death<sup>[13]</sup>. Now stress is defined as physiological and metabological perturbations caused by many aggressive agents and the psycho-physiological response of an organism to that particular challenge or a threat. Stress occurs as a result of imbalance between the demands applied to the subject versus the potential to face them. The modifications appear in three levels namely somatic, hormonal and metabolic. Coping is the rescue response of the individual to stress. It reduces the severity of stress and helps to overcome the situation.

### Types Of Stress

Stress is of two types namely acute and chronic. The acute stress lasts only for minutes to hours while chronic stress lasts for several hours to months<sup>[14]</sup>. The acute stress prepares the immune system to face challenges like infections, but chronic stress leads to development of systemic / local diseases like diabetes and periodontal diseases<sup>[14, 15,16]</sup>

### Stressor

A stressor is any event/experience which manifests stress in an individual. The positive stressor is called 'EUSTRESS'. The negative stressor is called 'DISTRESS'. It is of three categories namely,

Crises/catastrophes- This kind of stress is unpredictable and totally out of control of the individual.

Eg- Natural disasters

Major life events – These can bring positive/negative effects and are only minor causes of stress due to its rare occurrence.

Eg- Marriage, birth of a child

Daily hassles/microstressors

This is the most common type occurring in day-to-day life.

Eg- Traffic jams, encountering people with irritating behaviours

### Stress Scale

A scale is given by Holmes and Rahe which lists out all possible stressors with the values as shown in Table 1.

### Stages Of Stress

There are three stages of stress namely alarm phase, stage of resistance, and a stage of exhaustion. In 'alarm stage', increase in blood hypertension, and hyper-function of the sympathetic and corticotropic systems occur. Inhibition of sexual and thyroid growth hormones is observed but the brain and the muscles are activated. An anxiety and panic state with lapse of memory is seen. In 'resistance stage' the patient will be in a state of stress and increasing activity of the noradrenergic and corticotropic systems is observed. The cardio-vascular disease, digestive and immune disorders also starts to develop during this stage. In the 'exhaustion stage/ burn out stage' the patient will be in a depressed state as all the resources are exhausted.

### Stress Pathway

There are two pathways majorly involved during stress. The hypothalamic-pituitary- adrenal axis [HPA] and the adrenomedullary sympathetic nervous system. When stress occurs the HPA axis is stimulated by the anterior hypothalamus leading to secretion of corticotropin-releasing hormone and vasopressin. This gland increases the release of cortisol, that stimulates immune responses<sup>[17]</sup>. This glucocorticoid hormone modifies cytokine profile and at the molecular level it inhibits the important functions of inflammatory cells and their functions such as chemotaxis, secretion and degranulation. The ANS is stimulated by adrenergic receptors leading to secretion of catecholamines and chromogranin A[CgA]. Catecholamines regulate the immune response by stimulation of immune cell proliferation while CgA has antimicrobial effects. Autonomous nervous system moderates the HPA axis by stimulating central nervous system leading to secretion of neuropeptides such as substance P<sup>[18]</sup>. The release of substance P causes modulation of immune system activity and leads to an imbalanced inflammatory reaction. Neuropeptides regulate Th1 and Th2 cytokine secretions which are involved in the regulation of the immune response; thus, stress may disturb a regulated immune response, resulting in reduced effectiveness of the response[Figure 1].

### Coping

The effort done to decrease, control or tolerate the state of stress is called coping. Adjustment,

adaptation and confrontation strategies are to be applied to tackle stress. The different coping strategies include,

Resigned coping : avoidance, escape and contemplation.

Active coping : situation and response control with positive self-affirmation.

Distractive coping : substitute gratification, search for self-affirmation and seeking for social support.

Defensive coping : self-blame with denial of guilt

Coping with aggression and drug use.

### **Stress And The Immune System**

Relationship has been established between HPA axis, autonomic nervous system and the immune system [19]. The balance between pro-inflammatory and anti-inflammatory cytokines has been altered by stress. Changes in GCF IL-1, IL-6 levels and altered chemotaxis and phagocytosis of leukocytes is observed. Stress produces changes in the immune system by two pathways.

1. Changes in the autonomic nervous system leading to the production of increased prostaglandins and proteases.
2. The hypothalamo-pituitary-adrenal axis (HPA) leads to a production of glucocorticoids (cortisol) which decreases the production of IgA and IgG thus depressing the immune system.

The cortisol levels upregulated the expression of matrix metalloproteinases and tissue inhibitor of matrix metalloproteinases (TIMP)-1 in human gingival fibroblasts [20].

### **Stress And Behavioural Changes**

Mental stress has an impact on life-style and dental hygiene habits [21]. It was observed that during stress, usage of tobacco and alcohol consumption has increased and a change in food pattern was seen which led to the diminution of overall health. As a result, the quality of oral hygiene is compromised which facilitates the bacterial invasion [22].

### **Stress And Gingivitis**

Emotional stress produces changes in salivary pH and decreases the salivary flow and increases dental plaque formation leading to the development of

gingivitis [23]. Increase in gingival inflammation was observed in people with academic stress. Axtelius confirmed the presence of cortisol in gingival crevicular fluid in persons showing depression signs.

### **Stress And Acute Necrotizing Ulcerative Gingivitis**

Acute necrotizing ulcerative gingivitis [ANUG] occurs mainly due to the impaired host response to the pathogenic microorganisms. Stress produces changes in the immune system of an individual predisposing to development of necrotic periodontitis. The stress induced inadequate maintenance of oral hygiene, poor eating habits, smoking and alcohol are the other aggravating factors for the rapid progression of the disease. In a study by Pindborg [24], increased cases of necrotic periodontitis was seen in individuals in military service and Giddon observed increased incidence of necrotic periodontitis among college students during examination period [25]. These results clearly indicate that stress plays a vital role as a risk factor for ANUG.

### **Stress And Chronic Periodontitis**

Chronic periodontitis is an inflammatory disease of the supporting tissues of the teeth leading to progressive attachment loss and bone loss. Though plaque is considered to be the primary etiological factor, psychosocial stress with financial constraints are considered to be the risk indicators for periodontal diseases. Linden et al. has proposed that the future attachment loss depends on the following criteria such as age, socio-economic status, professional life and a passive and dependent character [26]. Axtelius has observed that patients with less stressful psychosocial situation and with a rigid personality responds well to periodontal treatment than patients with psychosocial strain and passive dependent traits [27].

### **Stress And Aggressive Periodontitis**

Aggressive periodontitis differs from chronic periodontitis by the age onset, the disease progression rate, the type of the subgingival microflora. It is mainly attributed to the host immunity alteration and a strong racial influence is also observed. Page et al. observed that psycho-social factors and loss of appetite influences aggressive periodontitis [28]. Monteiro da Silva showed aggressive periodontitis

patients were more depressed and more socially isolated than the control group [29].

### **Stress And Wound Healing**

Stress influences the early stages of wound healing. Proinflammatory cytokines protects against infection and prepares the tissue for repair and remodeling by increasing the recruitment of phagocytes. They also play a role in fibroblast chemotaxis and collagen production. Thus, wound healing is impaired due to stress induced defective production of the pro-inflammatory cytokines. Stress also increases glucocorticoid levels and decreases growth hormone levels thus further delaying wound healing.

### **Stress And Herpes Infection**

This infection is caused by herpes simplex virus and affects most commonly the genitals and mouth. When the stress levels gets increased more amount of catecholamines are released. The IL-12 production is suppressed while the IL-10 production is increased. Cell shift from Th1 cells involved in cell mediated immunity to Th2 cells involved in antibody mediated immunity occurs. As a result, increased susceptibility to viral infections is noted.

### **Stress And Bruxism**

It is the clenching of teeth while awake [awake bruxism] and sleep [sleep bruxism]. Bruxism can be frequent and severe enough which leads to jaw disorders, headaches, damaged teeth. A positive correlation exists between physiological stress and bruxism. Studies have reported that bruxism habit was found to be more prevalent among students with academic stress and people with financial problems. There are also other problems like difficulty in chewing; dry mouth was observed.

### **Stress And Its Influence On Periodontal Treatment**

It has been observed from several studies that emotional stress influences the outcome of periodontal therapy in a significant way. Kamma and Baehni found that in aggressive periodontitis patients harboring less stress, better supportive periodontal care was established. It was also noted that persons with poor adaptative coping strategies have more progressive disease and poor response to the periodontal treatment. Thus, coping strategies are positively correlated with the treatment outcomes [30].

Gamboa et al. showed that the emotional intelligence influences the initial response to periodontal treatment in patients with chronic periodontitis.

### **Stress And Its Role On Pathogens**

Stress-related hormones favors the infection by increasing bacterial growth, thereby inducing a breakdown in oral biofilms. In 1993, the concept of Microbial endocrinology has been proposed and it investigated effects of catecholamines such as noradrenaline on periodontal pathogen [35]. It was found that noradrenaline reduces growth of *P. gingivalis* and *A. actinomycetemcomitans* but increases the growth of *Eikenella corrodens*. It also increases expression of virulence factors like gingipains. Cell culture studies were performed to investigate the role of stress on progression of periodontal diseases and results demonstrated that stress modulates the response of macrophages by upregulating nitric oxide secretion.

### **Stress Markers**

The oral health status can be monitored by the analysis of blood and saliva in which stress associated markers are present. These markers indicate the severity of the disease.

### **Cortisol**

It is used as a biological marker as it rightly reflects the HPA axis activity [31]. Cortisol can be seen in free bioactive form and also bound to plasma protein as cortico-steroid binding globulin. Cortisol acts as an anti-inflammatory and immune-suppressive hormone and acts by inhibiting the formation of T lymphocytes.

### **Catecholamines**

These are obtained from the spillover of synaptic noradrenaline from the sympathetic nervous system. It serves as a useful index of sympathetic adrenomedullary system activity. The functions are antibody production, immune functions and cytolytic activity [32].

### **Chromogranin A**

It is released during exocytosis from adrenal medulla sympathetic nerve endings. It is a secretory acidic phosphorylated glycoprotein and serves as an index of sympathetic adrenomedullary system activity. [33].

### **Salivary alpha amylase**

It is secreted in response to sympathetic stimuli and is one of the major salivary enzymes. It shows inhibition against pathogens and is an indirect indicator of autonomic nervous system activity<sup>[34]</sup>.

### Neuropeptides

These are generated in central nervous system and its functions includes vasodilatation, plasma extravasation and immune cells recruitment.

### Stress Measuring Scales

Psychometric instruments are used to record the reports of patients in an organized way. There are two scales namely rating and self-reporting. The rating scale records observer's experience and the self-reporting records the subject's experience [Gorenstein et al 2000]. Most of the scales were idealized for western countries and should undergo a trans-cultural adaptation in order to be used for other countries (Gorenstein et al. 2000)

### Self reporting questionnaire -20

This scale detects mental disorders and primary health care attendance and is scored by para-professionals. It consists of 20 statements concerned with psychotic and non- psychotic disorders. Patients with mental disorder were found to have higher values.

### Beck depression inventory

This comprises of 21 statements including symptoms and attitudes. Scoring is given from 0 to 3. These questions are related to sadness, pessimism, lack of satisfaction, irritability etc (Beck et al. 1961). A score of 10 or greater is considered to be a sign of depression symptoms.

### State-trait anxiety inventory

It has 20 statements and measures the state and trait of anxiety (Spielberger et al. 1970). The scores range from 1 to 4. Minimum score of 20 and maximum of 80 is attained.

### Life events scale modified by Savoia

Given by Holmes & Rahe (1967) to assess psychological stress. Initially it had 43 life- events occurred in the last 12 months later modified by Savoia[1995 and contains 26 life-events. The events are related to work, family, environmental changes and financial strain.

### Beck hopelessness scale

This scale consists of 20 statements and assess the extent of negative expectancies about the immediate and long-term future (Beck et al. 1974). The statements are scored either 1 or 0. Higher scores indicates greater hopelessness.

### Conclusion

Various studies indicates clearly that stress has an influence on the periodontal diseases and considered to be a risk factor but the exact mechanism is still unknown and further studies are needed. Thus, it is important to understand the patient's emotional condition to help them to maintain a healthy periodontium. Thus, the role of dentists should not only be focused on treating patients but also help patients to cope up stress. The dentists should understand psychological attitude of the patients in a broader concept than just oral hygiene and should provide methods to de-stress. Helping the patients to quit smoking is a part of the periodontal treatment. Thus, molecular and cellular basis of stress should be understood clearly, which may lead to effective intervention strategies that can reduce the impact of psychological factors as risk factors for periodontal disease.

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**TABLE 1: Stress scale values given by Holmes and Rahe**

Change in sleeping habits	16
Change in work hours	20
Trouble with professional work	23
Financial crisis	31
Pregnancy	40
Marriage	50
Personal injury	53
Divorce	73
Death of spouse	100

FIGURE 1 : STRESS PATHWAY

