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RESEARCH ARTICLE

ASSOCIATION OF STRESS AND CHRONIC PERIODONTITIS BY ESTIMATION OF SERUM CORTISOL LEVELS

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ABSTRACT

Background-The relationship of stress and chronic periodontitis was assessed using serum cortisol levels.
Aim – To evaluate the relationship between stress and chronic periodontitis by estimation of serum cortisol levels.
Settings and design- A case control study having 30 cases of chronic periodontitis and 30 age and sex matched healthy controls.
Methods and materials- stress analysis was performed using standardized questionnaire method, social readjustment rating scale (SRRS). Clinical assessment of plaque, gingival inflammation, probing pocket depth and clinical attatchment level was performed. Serum cortisol level was estimated using ELISA.
Statistical analysis- Pearson correlation coefficient was used for evaluating the relationship between different variables and its statistical significance was determined using students't' test.
Results-The SRRS scores and serum cortisol levels were higher in group I when compared to group II. There was a statistically significant correlation of plaque and probing depth with serum cortisol levels in chronic periodontitis patients.
Conclusion- The present study revealed a significant correlation between serum cortisol levels and chronic periodontitis.

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INTRODUCTION

Psychological stress refers to the emotional and physiological reactions experienced when a person confronts a life event that exceeds his or her ability to cope effectively with the situation. Stress evokes emotional and physiologic reactions and is an important modifiable risk factor for both mental and physical illnesses (Hammen, 2005; Kessler, 1997). In recent years the traditional view of physical illness as a pure biological phenomenon has changed to a bio-psychosocial model of illness. According to this bio-psychosocial model, physical illness is the result of a complex interaction of biological, psychological and socio-cultural factors (Weiten, 1995). Periodontitis is an inflammatory response of the periodontium which involves the destruction of the investing tissues around the teeth, resulting in loss of tooth support, ultimately leading to the tooth loss.

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The etiology and pathogenesis of periodontal disease are multifactorial and there are several studies that have demonstrated that psychosocial stress, physiological stress, anxiety, and depression were associated with significant amount of periodontal disease progression and wound healing (Monteiro da Silva *et al*., 1996; Genco, 1996; Boyapati, 2000). Hans Selye (1936) coined the term stress and postulated the possible mechanism of activation of the adrenocortico-pituitary axis (Weiten, 1995). The stress-induced responses either result in change in behavior or are transmitted to the hypothalamic—pituitary—adrenal (HPA) axis to release corticotrophic releasing hormone (CRH) from the hypothalamus. CRH activates the pituitary gland to release adrenocorticotropic hormone (ACTH), which in turn induces the release of glucocorticosteroids like cortisol from the adrenal cortex (Miller, 1947; Moulton *et al*., 1952; Belting and Gupta, 1961; Green *et al*., 1986) (Figure 1) Cortisol is most potent and responsible for 95% of total glucocorticoid activity.

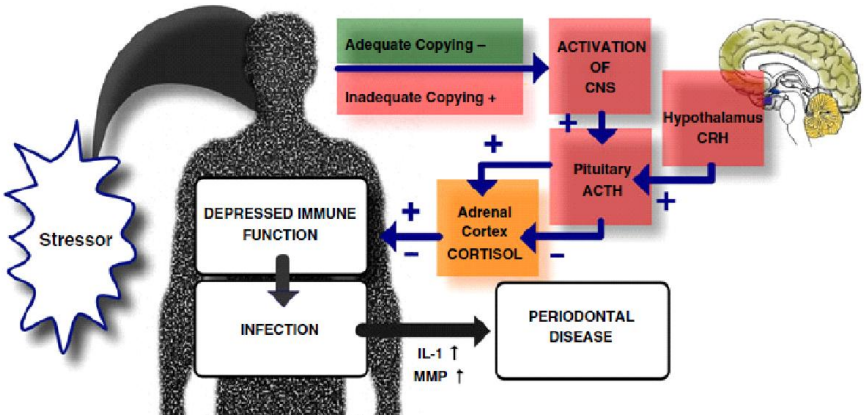

Figure 1. Model of the effects of chronic stress on the immune system and periodontal disease, ACTH, adrenocorticotropichormone; CNS, central nervous system; CRH, corticotropic-releasing hormone; IL-1, interleukin-1; MMP, matrix metalloproteinase Adapted from Kimberly *et al.* (2000)

It reduces the number of circulating lymphocytes, monocytes, and other proinflammatory cells resulting in decrease in functions such as chemotaxis and proliferation of effector lymphocytes to differentiate into helper lymphocytes, cytotoxic lymphocytes, natural killer cells, IgG and IgA antibody forming B cells. Decreased functioning of neutrophils and secretory IgA, and IgG antibodies leads to increased susceptibility to periodontal infections, which results in increased production of inflammatory cytokines like IL-1 and matrix metalloproteinases by periodontal pathogens causing rapid periodontal tissue destruction (Cupps, 1982; Williams, 1990; Genco *et al*., 1998; Kimberly *et al*., 2000). Even though investigators have studied the impact of the immune response and psychological components on the extent and severity of periodontitis by assesement of salivary cortisol (Mannem and Chava, 2012), very few studies have demonstrated the impact of stress on the status of the well being of the immune system and health of the periodontium by assessment and comparison of serum cortisol in periodontally diseased and healthy patients (Rohini *et al*., 2015; Katuri *et al*., 2016)

Aim of the study

The aim of the present study was to evaluate the relationship between stress and chronic periodontitis by estimation of serum cortisol levels.

MATERIALS AND METHODS

A total of sixty study participants in the age group of 35-50 years from the Out Patient Department of Periodontology, Yashwantrao Chavan Dental College, Ahmednagar were recruited for this case control study. Ethical clearance was obtained from the Institutional Ethical Committee. Written informed consent for participation in the experimental protocol was obtained from all the study participants. Subjects excluded from the study were patients with psychiatric disorder, systemic diseases that affects the periodontium, pregnant or lactating females, patients who received any anti-inflammatory drugs, antibiotics or corticosteroids within previous 3 months, patients who were smokers , had received scaling and root planing (SRP) or subgingival instrumentation <2 months before the study.

The 60 study participants were divided as follows:

Group I: Thirty patients (13 females and 17 males) with chronic periodontitis were allocated as Test group

Group-II Thirty periodontally healthy age and sex matched study participants were selected as controls.

Group I participants were diagnosed with chronic periodontitis clinically and radiographically (Armitage, 1999; Schätzle *et al*., 2003). They were patients with untreated moderate to severe chronic periodontitis, having at least 4 sites with probing pocket depth (PPD) of >5 mm and clinical attachment loss >4 mm (Armitage, 1999; Schätzle *et al*., 2003).

Stress Analysis

A standardized questionnaire method, Social Readjustment Rating Scale (SRRS) was used to measure a number of stressful life events and their impacts that had occurred in the last 12 months. The instrument contains 43 life events and respondents were given opportunity to report any other events not included in the list that had happened in the previous year. The impact of each event was scored as an attempt to evaluate how the individual has coped with it. Thus an event with a positive score (+1) was considered good or fortunate and an event with a negative score (-1) was evaluated as unpleasant and not welcome. A neutral score (0) indicated that an event was seen as indifferent or without importance (Holmes, 1967).

Clinical parameters

Clinical examination was conducted immediately after stress analysis, before disclosing the stress analysis report. Two independent examiners performed the clinical examinations. The periodontal health status of the patients and controls was evaluated using

- Plaque index (PI) (Silness, 1964)
- Gingival Index (GI) (Loe and Silness, 1963)
- Probing Pocket depth (PPD)
- Clinical attachment level (CAL).

The radiographic examination of all patients and controls was performed using intraoral radiographs. Periodontal probing depth and Clinical attachment level were measured at six sites per tooth (mesio-buccal, buccal, distobuccal, mesiolingual, lingual and distolingual) of all erupted teeth excluding third molars. All the clinical measurements were carried out by a single examiner using graduated Williams probe (Hu-Friedy, Chicago, IL, USA.) The clinical parameters were measured by a single examiner and the stress scale ratings by the other.

Estimation of Serum Cortisol

All the participants were instructed to abstain from unusual physical activity and were refrained from oral intake for at least 2 hours before blood collection. They were called between 9.00am to 11.00am for blood samples collection and 2 ml of venous blood sample was drawn from median cubital vein after 20 min of rest, under strict aseptic conditions. Blood samples were then centrifuged to separate the serum and the serum was then stored at -80 degree C for cortisol estimation. The serum cortisol levels were measured using enzyme-linked immuno-sorbent assay (ELISA) (VIDAS® Cortisol, Biomerieux, Marcy I'Etoile, France) in accordance with manufacturer's instructions.

RESULTS

The collected data were analyzed by using minitab software (17.0 version).In descriptive statistics, median, mean, and standard deviation of all the clinical periodontal parameters, SRRS values and serum cortisol were determined. Pearsons correlation coefficient was used to assess the correlation between different variables and t–test was used for testing the significance of correlation. The mean cortisol values were higher in Group I (16.94 ± 4.29) compared to Group II [Table 1]. Group-I showed no correlation between cortisol levels and GI and a statistically significant correlation between cortisol levels and PI and PPD [Table 2]. In group 1, plaque index was 1.73 ±0.27, gingival index was 1.65± 0.28, probing depth was 4.17± 0.66 and clinical attachment level was 5.81± 0,69. In group 2 plaque index was 0.87 ± 0.13.

Table 1. Mean serum cortisol levels and SRRS scores in Group I and Group II

	Serum Cortisol((∝g/mL)	SRRS scores
Group I	16.94±4.29	189.81±82.49
Group II	13.18±1.56	128.60±27.63

Table 2. Pearson's correlation co-efficient values in chronic periodontitis patients

	SRRS	Serum cortisol
PI	r=0.106, p=0.28*	r=0.338 p= 0.033**
GI	r= 0.004 p=0.489*	r=0.129 p=0.247*
PPD	r=0.160 p=0.198*	r=0.310 p=0.047**
CAL	r= -0.21 p= 0.26*	r= 0.05 p=0.75*

*- non significant
**-significant

DISCUSSION

An association between chronic periodontitis and stress was hypothesized by many authors over the years, but the role of stress hormones and the psycho-neuro-immunologic mechanism behind it was not very well understood because of limited data. In the present study, the relationship between stress and periodontal disease was investigated using serum cortisol, Social Readjustment Rating Scale and different periodontal parameters. Serum, saliva, and gingival crevicular fluid are the three different media considered for examining cortisol levels. Very few studies have explored the relationship between serum cortisol and periodontal disease (Rohini *et al*., 2015; Katuri *et al*., 2016) and since serum cortisol level is routinely investigated in psychiatric and endocrinal disorders, serum cortisol assessment was considered. The results of statistical analysis showed that the mean SRRS scores and serum cortisol levels were higher in chronic periodontitis group compared to healthy controls. This result is in agreement with the study done by Genco *et al*. (1998) and other investigators (Kessler *et al*., 1997; Kimberly *et al*., 2000) in which the mean cortisol levels were higher in group of patients with the disease. This could be due to deregulation of the immune system, mediated through the hypothalamic–pituitary–adrenal and sympathetic–adrenal medullary axis (Cury *et al*., 2007). The activation of this by means of stress might result in the release of an increased concentration of the corticotropin-releasing hormone from the hypothalamus, which in turn, may act on the anterior pituitary, resulting in the release of the corticotrophin. The corticotropin may then act on the adrenal cortex enhancing the production and release of cortisol into the circulation, leading to unwanted effects throughout the body, such as suppression of the inflammatory response, modifying cytokine profiles, elevation of blood glucose levels, and alteration of certain growth factor levels (Buckingham *et al*., 1996; Yang and Glaser, 2002).

Brevik *et al* in their study of experimental periodontitis in rats, illustrated a positive feedback loop between HPA axis and periodontal disease. They mentioned that periodontal disease activates HPA axis and a genetically determined high HPA responsivity further increases disease susceptibility (Brevik *et al*., 2001). In present study, serum cortisol levels showed no correlation with the GI which can be explained by the anti-inflammatory effect of cortisol. Furthermore, a positive correlation was found between serum cortisol levels and other clinical parameters in group 1 except clinical attachment level. Peruzzo *et al*. conducted a systematic review of the evidence on the influence of stress and psychological factors on periodontal disease. and concluded that 57% reported a positive relationship between stress and periodontal disease. Another 28.5% of the studies observed a positive relationship between some characteristics of stress and periodontal disease, demonstrating that the majority of the works published to date examining this relationship have indeed found significant associations (Peruzzo *et al*., 2007) Brief stressors appear to suppress cellular immunity whilst preserving measures of humoral immunity; in contrast, chronic stressors generally result in dysregulation of the immune system involving both cellular and humoral pathways (Segerstrom *et al*., 2004). Therefore, chronic stress and depression have been resulting in a higher rate of infection with pathogenic organisms and a greater degree of periodontal tissue destruction. In general, the evidence is consistent with the hypothesis that stress can modify the host immune defense and permit the progression of periodontal infections in patients susceptible to periodontitis (Doyle and Bartold, 2012).

The influence of stress on the periodontium can also be explained by the behavioral model which explains the importance of health impairing behaviors including poor oral hygiene, increased consumption of cigarettes, alcohol consumption, disturbed sleeping patterns, poor nutritional intake etc (Hilgert *et al*., 2006). Venous blood samples were collected early in the morning from study participants since cortisol levels in the peripheral blood and saliva follow a circadian rhythm, showing highest titers in the early morning during the final hours of sleep, followed by a gradual decline over the course of the day, with minimum minimum titer reached near midnight. External factors such as inflammatory, physical, and psychosocial stress are known to increase cortisol release (Cury *et al*., 2007; Buckingham *et al*., 1996). It must be

emphasized that for group I a baseline score of 189.81 was the threshold of stress factor, which was assessed through a standard questionnaire [social readjustment rating scale (SRRS)] contemplated for the study. It measures the psychological impact of different life changes such as changes in personal relationships, changes at work, changes in finances etc. which can be stressful even when the changes are welcomed. A SRRS score of 150 or less indicates a low level of stress and low probability of developing stress related diseases, about 30% and increase in this score increases this probability. The stress caused by a particular stressor varies from one person to the next because of variability in the circumstances, interpretation, goals, personality, values coping strategy and resources from one person to the next. Therefore although this scale is well researched, the values are only a rough approximation at best (Holmes *et al*., 1967). Another limitation of the study was the small sample size.

One of the advantage of the study was, the patients age group selected for the study (35 to 50 with mean age 37.19 years) since patients above 40 years may come across many negative life events which could probably cause an increase in serum cortisol levels persistently for a long time and ultimately leading to various systemic diseases including periodontal disease (Mannem and Chava 2012). However, many epidemiological studies and studies with larger sample size are necessary to assess the role of social support and stress coping strategies together with the psychological stress on the development, course and progression of chronic periodontitis. Within the limits of the study, it can be concluded that serum cortisol levels were higher in the chronic periodontitis group compared to the healthy controls and a statistically significant correlation was found between the cortisol levels and Other periodontal parameters like PI and PPD.

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