ORIGINAL RESEARCH

Exploration of Association between Chronic Periodontitis and Sleep Deprivation and Evaluation of this Interrelationship with Stress Hormone (Cortisol) Levels: A Clinico-immunological Study

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ABSTRACT

Background: Sleep deprivation and stress has become a global phenomenon, and various epidemiologic data indicates that short sleep duration and high level of stress adversely impacts human physical health. Underlying mechanisms involves the modulation of immuneinflammatory mechanisms of the body. These changes in the host might contribute to potentiation of destructive periodontal disease. Therefore, the present study aimed to assess the exploration of association between chronic periodontitis and sleep deprivation and to evaluate this Inter- Relationship With Stress Hormone (Cortisol) Levels.

Materials and Methods: Hundred subjects who were diagnosed as chronic periodontitis patients were taken in to the study. Periodontal status of subjects was assessed by pocket probing depth. All the study subjects were administered Pittsburgh Sleep Quality Index (PSQI) questionnaire for the assessment of sleep deprivation and the ones who had score as =5 were further evaluated for their corresponding serum cortisol levels.

Results: Present investigation revealed that in 80% of the chronic periodontitis cases where the PSQI Value was 5 or more than 5 (evaluated as sleep deprived patients) there was a corresponding increase in the serum cortisol levels and the results were statistically significant.

Conclusion: The present study with its results is suggestive of the association of sleep deprivation and stress with the severity of periodontal disease.

Keywords: Chronic periodontitis, Cortisol, Pittsburgh Sleep Quality Index, Sleep deprivation, Stress.

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INTRODUCTION

Periodontitis is a chronic inflammatory disease of infectious origin that leads to the destruction of the supporting structures of the teeth, including the periodontal ligament and alveolar bone, and in the severe cases, may lead to tooth loss.[1] Periodontal pathogenic bacteria and their products are the primary etiological agents for the initiation of periodontitis; however, it has become evident that their presence alone is not sufficient to cause the tissue destruction that can lead to periodontal disease.[2,3]

A number of risk factors contribute to the susceptibility of individuals to periodontal diseases and to the pathogenesis and severity of the disease. Various epidemiological evidences indicate that the initiation of periodontal disease is highly multifactorial with a complex interaction between bacterial infection and host responses which is often modified by behavioral factors. Several risk factors that include bad oral hygiene, smoking, age, and some systemic diseases can contribute to periodontal destruction. Stress can also be considered as a contributing factor in periodontal disease. Moreover, there is a reasonable amount of research, indicating that periodontitis may be associated with sleep deprivation, psychosocial stress, financial stress, distress, and depression.[4]

The word sleep means relaxation or rest in a lighter term, but it is a complex and essential biological process that is required on a daily basis for all humans regardless of age, sex, or ethnic origin. In addition to maintaining normal brain functioning and activity, sleep plays an important role in controlling the functions of many body systems which are vital to health and well-being.[5] Sleep deprivation is very common in today's society. If we compare it to a few decades ago, major changes in sleep culture have been observed globally because there has been a trend toward adopting a 24 × 7 lifestyle with longer working hours and work shifts. Various

medical conditions along with many social and domestic responsibilities further contribute to sleep restriction. This has led to a marked reduction in total sleeping hours in both adults and children. Epidemiologic data indicate that sleep disturbance and short sleep duration adversely impact human physical health and mortality risk.[6-14] Underlying mechanisms include decrease in overall immunity, a state of systemic inflammation with increased inflammatory markers ensues, and upregulation of hormones.[15-18] Thus, in recent years, there has been an increasing body of research investigating the role of sleep deprivation in the pathogenesis of various chronic inflammatory and infectious diseases such as chronic periodontitis.

Stress is a state of physiological or psychological strain caused by adverse stimuli, physical, mental, or emotional, internal or external, that tend to disturb the functioning of an organism and which an organism normally desires to avoid.[19] Socioeconomic condition, type of occupation, daily schedule, competitive workload, emotional disturbances, lifestyle factors, inadequate rest, and sleep deprivation have led to increased stress levels in the modern lifestyle.[20]

Psychosocial stress can affect the periodontal tissues directly through biological mechanism and indirectly through the changes in lifestyle such as ignoring oral hygiene measures, smoking more heavily, and consuming more fat and sugar in diet.[21] Hence, there are two proposed mechanistic links: One biological and the other behavioral.[22]

However, the role of sleep deprivation in chronic periodontal disease and its relation with stress hormone level has not been investigated extensively. Hence, the aim of the study was to explore the association between chronic periodontitis and sleep deprivation and evaluation of this interrelationship with stress hormone (cortisol [CORT]) levels.

MATERIALS AND METHODS

Patient Selection and Study Design

The study was conducted at the Department of Periodontology, Faculty of Dental Sciences, SGT University, Gurgaon, Delhi NCR, after the approval from the Ethical Committee of the University.

Present Study was divided into Two Phases: Phase I and Phase II

The study sample consisted of 100 patients who were diagnosed as chronic periodontitis patients according to the criteria of the 1999 International Workshop on the Classification of Periodontal Diseases conducted by the American Academy of Periodontology. All subjects participating in the study signed a consent form to willingly participate in the study. Appropriate medical and dental history was evaluated for each subject. All data were collected in the presence of the trained examiner in the local language or language suitable for the participant.

Inclusion criteria had the subjects who had pocket probing depth of ≥5 mm in more than 30% of the sites present in the mouth, subjects who had not undergone any periodontal treatment within the previous 6 months, subjects who had not used anti-inflammatory drugs within the past 3 months, and subjects who had not used antibiotics within the previous 6 months.

All the participants who were systemically unhealthy were excluded from the study.

Phase-I of the Study

The patients who were diagnosed as chronic periodontitis patients according to the criteria of the 1999 International Workshop on the Classification of Periodontal Diseases conducted by the American Academy of Periodontology were included in Phase-I of the study. Probing pocket depth (PPD) was measured with UNC-15 probe for the diagnosis of chronic periodontitis.

They were asked to fill Pittsburgh Sleep Quality Index (PSQI)for the estimation of sleep deprivation.

Estimation of Sleep Deprivation

The PSQI[23] is an effective instrument used to measure the quality and patterns of sleep in the older adult. It differentiates "poor" from "good" sleep by measuring seven domains: Subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep medication, and daytime dysfunction over the last month. The client self-rates each of these seven areas of sleep. Scoring of the answers is based on a 0–3 scale, whereby 3 reflects the negative extreme on the Likert scale. A global sum of "5" or greater indicates a "poor" sleeper. The index will be explained to the patient in the local language. The index will be recorded in the presence of trained examiner and collected data will be entered in the spreadsheets.

Of 500 chronic periodontitis patients screened initially, 100 patients who only qualified PSQI and were willing for further surgical treatment of chronic periodontitis were randomly selected for Phase II of the study.

Phase-II of the Study

Phase II was the estimation of serum CORT levels using the same blood sample in which the patient had submitted for routine hematological investigations deemed necessary for surgical treatment of periodontitis.

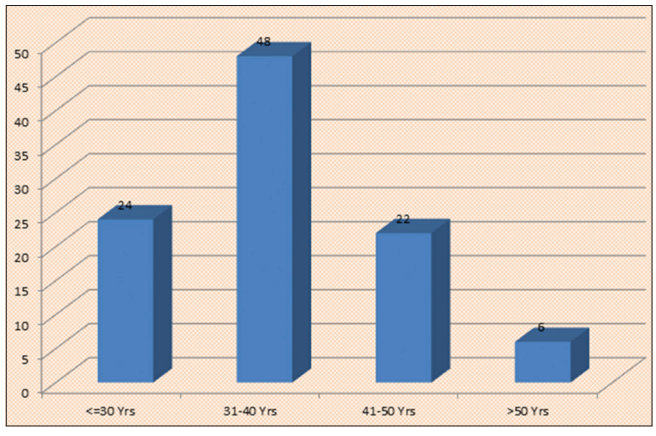
Table 1: The frequency distribution of participants in various age groups

Age group	Frequency	Percentage	Valid percentage	Cumulative percentage
≤30	24	24	24	24
31–40 years	48	48	48	72
41–50 years	22	22	22	94
>50 years	6	6	6	100
Total	100	100	100	

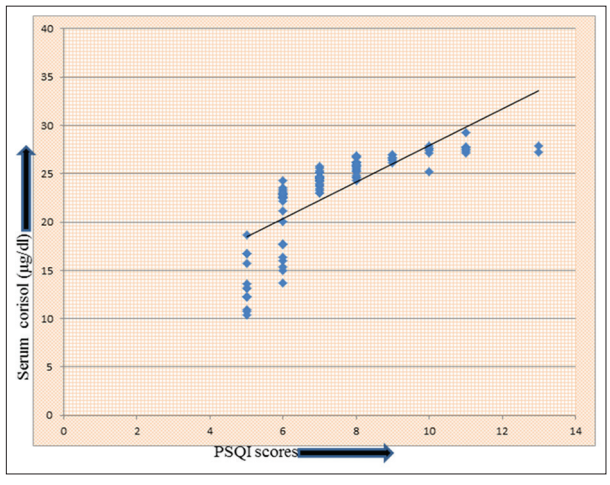
Table 2: The mean values and standard deviation of age, PSQI value, and serum cortisol levels

Descriptive statistics	Mean±SD	*N*
Age	37.76±8.87	100
PSQI value	7.43±1.85	100
Serum cortisol in μg/dl	23.07±4.60	100

PSQI: Pittsburg Sleep Quality Index, SD: Standard deviation



Graph 1: The frequency distribution of participants in various age groups



Graph 2: The correlation between Pittsburg Sleep Quality Index and serum cortisol levels

Estimation of Serum CORT

Collection of blood sample

About 3 ml of blood was collected by venipuncture, using sterile disposable syringe and needle, from the median cubital vein, on the anterior forearm between 9:00 and 11:00 a.m.[24]

Analysis of serum CORT

Analysis of serum CORT level was done using ADVIA Centaur® CP Immunoassay System by Siemens from an authorized laboratory (the National Accreditation Board for Testing and Calibration Laboratories [NABL] approved).

Statistical Analysis

The statistical evaluation was performed using Pearson correlation to see the relationship between two variables. $P < 0.05$ is considered statistically significant at 95% confidence interval. SPSS version 16.0 was used to analyze the data.

RESULTS

A total of 100 patients (age range 35–65 years and mean age 50 years) were enrolled on the basis of the screening criteria in the study. The number of males was 49 (age range 30–65 years and mean age 47.5 years) and females were 51 (age range 35–55 years and mean age 45 years). Based on the parameters recorded, the comparison was done between the PSQI and serum CORT values, and the correlation was calculated. Results showed that, in 80% of the chronic periodontitis cases where the PSQI value was 5 or more than 5 (evaluated as sleep deprived patients), there was a corresponding increase in the serum CORT levels.

Table 1 shows that the maximum age group that is affected by sleep deprivation and high-stress levels is between 31 and 40 years of age [Graph 1],whereas Table 2 represents the mean values and standard deviation of age, PSQI value, and serum CORT levels. In a total sample of 100 patients, it shows a mean of 37.76 years in age including 7.43 as the mean of PSQI values and 23.07 μg/dL as the mean of serum CORT levels. The correlation between the PSQI values and serum CORT levels is shown in Table 3. Pearson correlation is used to see the relationship between two variables. $P < 0.05$ is considered statistically significant at 95% confidence interval. $P < 0.001$ shows a highly significant result [Graph 2].

DISCUSSION

Chronic periodontitis is a multifactorial disease characterized by a bacterially induced progressive loss of

Table 3: The correlation between PSQI and serum cortisol levels

Correlations	Age	PSQI value	Serum cortisol in μg/dL
PSQI value			
Pearson correlation	−0.125	1	0.758**
Significant (two-tailed)	0.213		<0.001
N	100	100	100
Serum cortisol in μg/dL			
Pearson correlation	−0.115	0.758**	1
Significant (two-tailed)	0.254	<0.001	
N	100	100	100

PSQI: Pittsburg Sleep Quality Index. **Correlation is significant at the 0.01 level (two-tailed)

clinical attachment, including destruction of periodontal ligament and adjacent supporting bone. Gingivitis and periodontitis are found to result from an imbalance which is caused between those oral microorganisms which normally colonize tooth surfaces in close contact with the gingival margin and the nature and efficiency of the host response. The bacteria are seen to be the triggering factors, but the host defense mechanisms within the gingival/periodontal tissues are seen to be responsible for most of the tissue damage and also for the outcome and progression of the various diseases. It has been shown recently that emotional or psychological load (stress) may influence immune activities directly through nerve messenger substances (neurotransmitters and neuropeptides) and/or indirectly through neuroendocrine (hormone) substances.[25]

Sleep deprivation can be called as the condition of not having enough sleep; it can be either chronic or acute. In case of a chronic sleep-restricted state, certain signs and symptoms such as fatigue, daytime sleepiness, clumsiness, and weight loss or weight gain can be seen.[26] It can adversely affect the brain and cognitive function. However, in a few cases, sleep deprivation can be seen paradoxically leading to increased energy, alertness, and enhanced mood.

In general, sleep deprivation may result in:

- Aching muscles
- Confusion, memory lapses, or loss
- Depression.[27]

Sleep deprivation can adversely affect various activities of the brain as well as the cognitive function.

The psychophysiological response of the organism to a certain perceived challenge or threat can be referred to as stress. The presence or absence of the stress response and its intensity is determined by the organism's perception of its situation and its perceived ability to master it. The function of the stress response is to prepare the organism to meet the challenge or threat appropriately and is therefore homeostatic in its function. The stress response is essential for the survival of the organism and should not be regarded as undesirable in itself. Stress becomes a danger for the organism only when it is sustained or when one or more aspects of the neuroendocrine response act on organ systems which for some reason are already predisposed to pathology.

Thus, stressful life events cause negative affective states such as fear, anxiety, hostility, and aspects of depression, for example, sadness and loneliness. They may all be regarded as risk factors for a variety of diseases, including infectious diseases such as chronic periodontitis.[25]

Focusing on the first aim of present study, the study sample consisted of 500 patients who were diagnosed as chronic periodontitis patients according to the criteria of the 1999 International Workshop on the Classification of Periodontal Diseases conducted by the American Academy of Periodontology. Subjects who had pocket probing depth of ≥5 mm in more than 30% of the sites present in the mouth were diagnosed as generalized chronic periodontitis cases. Of 500 patients, 100 patients were selected for the study who showed the PSQI value as 5 or more than 5 qualifying as "poor sleepers" on the evaluation of the questionnaire which they filled.

Results of the present study were in accordance with the results of the study done by Grover *et al*.,[23] in which 60 systemically healthy subjects (34 females and 26 males) in age group of 25–50 years were assessed for the association of sleep deprivation with chronic periodontal disease and the results showed a positive correlation of PSQI and PPD in periodontitis groups. In the present study, PSQI was used as a tool to assess sleep deprivation which was in accordance to the study performed by Grover *et al*.,[23] thus concluding that the chronic periodontitis has direct association with sleep deprivation.

The present study showed that the condition was more commonly affecting females which was in accordance with the work of Utomo[28] which concluded that the females were more affected by sleep deprivation and chronic periodontitis as it showed the findings about the connection of the luteal phase or the high progesterone phase, with sleep disturbances; the female patient in the reviewed case report suffered from headache and sleep

disturbances every day and was a patient of chronic periodontitis.

Sleep deprivation is most commonly seen in young adults. In the present study age group affected, the most was 30–40 years which was in accordance with the results of the study done by Knutson *et al*.[29] who found that adult men and women between the ages of 30 and 64 years reported sleeping <6 h per night which led to sleep deprivation.

Sleep deprivation has been associated with multiple physiological changes, including increased CORT levels. In the work done by Aldabal *et al*.,[5] they found that certain experimental studies have also shown an increase in inflammatory and pro-inflammatory markers, which are indicators of body stress, under sleep deprivation which was in positive correlation with the second objective of the present study which showed the increased serum CORT levels in patients with sleep deprivation.

Much research has not been done on this correlation, so there is a limitation on the literature availability.

The second objective of the present study was to evaluate the relationship of the stress hormone (CORT) levels to the patients diagnosed with chronic periodontitis and sleep deprivation. The present study showed elevated CORT levels in the patients who were sleep deprived and had higher PSQI values correspondingly, and with the increased PSQI values, there was a corresponding increase in the serum CORT levels. In 80% of cases, there was an elevation in the serum CORT levels.

According to a study done by Mahendra *et al*.,[30] on police personnel, results showed a positive correlation between stress, serum CORT level, and chronic periodontitis. They examined 110 police personnel and grouped into test (Group 1 and Group 2) and controls depending on their PPD: Control group (PPD ≤ 3 mm, n = 30), test Group 1 (at least four sites with PPD ≥ 4 mm and ≤ 6 mm, n = 40), and test Group 2 (at least four sites with PPD > 6 mm, n = 40). The clinical parameters such as Silness-Löe plaque index, sulcus bleeding index, PPD, and clinical attachment level were recorded. Stress was measured using a stress questionnaire. Blood samples were collected and serum CORT level was evaluated using ELISA. The results showed elevated serum CORT levels which was in accordance with the results of the present study.

The methodology used in the present study was similar to the study done by Goyal *et al*.,[24] in which the clinical parameters were measured by a single examiner and venous blood sample was drawn in the morning between 9:00 and 11:00 am after 20 min of rest for the subject. The serum CORT levels were measured using enzyme-linked assays. The results showed that high-stress strung patients had higher CORT levels and they concluded psychosocial stress to be contributing factor in the pathogenesis of periodontal disease and increased serum CORT level. The results of this study were in positive correlation with the present study. In the present study, venous blood was drawn and serum analysis for CORT was done after centrifugation of the blood sample, and the serum sample was evaluated using ELISA.

Genco *et al*.[31] conducted a study to evaluate the association of stress, distress, and coping behavior with periodontal disease. The subjects were asked to fill five psychosocial questionnaires which measure psychological traits and attitudes including discrete life events and their impact. They found that psychosocial stress manifests as depression and are significant risk indicators for periodontal disease. Questionnaire was used to assess the patients which was in accordance with the methodology of the present study.

Hugo *et al*.[32] evaluated the effects of stress, depression, and CORT levels in dental plaque accumulation and gingivitis in a population of individuals aged ±50 years. In the cross-sectional study, 230 subjects, selected from caregivers of demented patient groups and from social activities groups of Porto Alegre, Brazil, were evaluated. Stress was evaluated with the Lipp stress inventory, whereas depressive symptoms were assessed using the Beck Depression Inventory. CORT analysis by means of radioimmunoassay was done. CORT levels were expressed as the area under the curve of the three samples for each patient. Multivariate logistic regression was performed with the visible plaque index and gingival bleeding index as outcomes. They concluded that stress was a significant risk indicator of elevated levels of plaque and gingivitis, whereas CORT was a risk indicator of plaque in the sample. The results showed were similar to the results of the present study.

Another study by Rosania[22] evaluated 45 periodontal patients referred by three dentists. Participants completed composite health, chronic stress, depression, and demographic questions, and salivary CORT was measured. A hygienist assessed the magnitude of periodontal disease. Stress, depression, and CORT were correlated with measures of periodontal disease. In addition, oral care neglecting during periods of stress and depression was associated with attachment loss and missing teeth. After controlling for age, family history, and brushing frequency, depression and CORT were significant predictors of the number of missing teeth. What they concluded was similar to the conclusions of the present study.

Rai *et al*.[33] explored the associations among periodontal disease, psychological factors, and salivary markers of stress, psychoneuroimmunologic variables, and health behaviors. 100 periodontitis patients were

selected, and participants provided information on general health, chronic stress, and demographics. Stress markers (chromogranin A, CORT, a-amylase, and b-endorphin) were measured from saliva. A dentist assessed the presence of dental plaque on lingual and buccal surfaces, the gingival index, and the number of remaining teeth with periodontal disease. They found that stress and salivary stress markers were significantly correlated with clinical parameters of periodontal disease (ranging from 0.19 to 0.59; $P < 0.001$). Neglecting to brush teeth during stress was associated with missing teeth. The study suggested that stress might be associated with periodontal disease through physiologic and behavioral mechanisms. The present study also suggests a similar result and conclusion.

Recently, in 2016, Jaiswal *et al*.[34] investigated the association between psychological stress and serum CORT levels in patients with chronic periodontitis in their study. 40 subjects were recruited from the outpatient department at the Department of Periodontics, from a college in Mangalore, divided into two groups, i.e., 20 as healthy controls and 20 as stressed subjects with chronic periodontitis. The clinical examination included the assessment of PPD, clinical attachment level, and oral hygiene index simplified. Serum CORT levels were estimated biochemically using the enzyme-linked immunosorbent assay method, and the estimation of psychological stress was done by a questionnaire. They concluded that high serum CORT levels and psychological stress are positively linked with chronic periodontitis establishing a risk profile showing a significant correlation, and thus, stress in periodontitis patients should be considered as an imperative risk factor for periodontal disease. The conclusions of the study were quite similar to the present study showing a positive correlation between stress and chronic periodontitis.

The numerous studies already performed on the objectives of the present study show a positive correlation with the results obtained in the present study, thus concluding that there is a significant association between chronic periodontitis and sleep deprivation and a positive inter-relationship with the stress hormone (CORT) levels.

CONCLUSION

In this today's world, where the lifestyle is too hectic to even concentrate on one's health, sleep and stress levels play a very important role in the complete well-being of an individual. Proper sleep and stress-free life have become a rare entity in an individual's life in this era. Sleep deprivation and stress not only cause various diseases but also affect day-to-day life leading to depression and other psychosocial conditions. Hence, keeping in mind these two major upcoming issues of this century, this study was performed showing its correlation with its effect on periodontal structures leading to periodontitis.

Thus summarizing the whole thing, it can be concluded that today's stressful life with severe sleep deprivation can lead to direct effect on periodontal structures causing periodontitis. Thus, the lifestyle should be taken into consideration for an overall health and a healthy periodontium.

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