Al-Azhar Journal of Dentistry

Volume 10 | Issue 1 Article 26

Oral Medicine and Surgical Sciences Issue (Oral Medicine, Oral and Maxillofacial Surgery, Oral Pathology, Oral Biology)

1-1-2023

# The Effect of Psychological Stress on Periodontal Disease during COVID-19 Virus Threat: Relation to Salivary Prostaglandin (PGE2)

Samah Helmy
*Dentist at Al -Azhar medical administration Girls branch.*, samahmohamedhelmy92@gmail.com

Hamdy Nassar
*Professor of Oral medicine, periodontology, Oral Diagnosis and Radiology Faculty of Dentistry for Girls, Al-Azhar University, Cairo, Egypt.*, hnassar2004@yahoo.com

Omnia Ahmed
*Lecturer of Oral medicine, periodontology, Oral Diagnosis and Radiology Faculty Dentistry for Girls, Al Azhar University, Cairo, Egypt.*, omneyaemam611@gmail.com



## How to Cite This Article

Helmy, Samah; Nassar, Hamdy; and Ahmed, Omnia (2023) "The Effect of Psychological Stress on Periodontal Disease during COVID-19 Virus Threat: Relation to Salivary Prostaglandin (PGE2)," *Al-Azhar Journal of Dentistry*: Vol. 10: Iss. 1, Article 26.
DOI: https://doi.org/10.58675/2974-4164.1482

AL-AZHAR
Dental Journal
For Girls

The Official Publication
of The Faculty of Dental
Medicine For Girls,
Al-Azhar University
Cairo, Egypt.

Print ISSN 2537-0308 • Online ISSN 2537-0316

ADJ-for Girls, Vol. 10, No. 1, January (2023) — PP. 139:150

# The Effect of Psychological Stress on Periodontal Disease during COVID-19 Virus Threat: Relation to Salivary Prostaglandin (PGE2)

**Samah M. Helmy[1*], Hamdy A.Nassar[2], Omnia E. Ahmed[3].**

Codex : 2-04/23.01

azhardentj@azhar.edu.eg

http://adjg.journals.ekb.eg

https://doi.org/10.58675/2974-4164.1482

Oral Medicine & Surgical Sciences
*(Oral Medicine, Oral & Maxillofacial Surgery, Oral Pathology, Oral Biology)*

## *ABSTRACT*

**Purpose:** The current study aimed to evaluate the impact of the stress on the periodontium and its clinical features present in the oral cavity, also to measure the $PGE_2$present in saliva and its effect on the periodontal disease. **Subjects and Methods:** A total number of thirty health care providers were involved in the study. They were passing through heavy physiological issues during theCOVID-19 pandemic threats. The study consisted of three phases. First phase the clinical periodontal evaluation which included assessment of Gingival index (GI), probing depth (PD) and clinical attachment level (CAL).Second phase the psychological stress was assessed via the PSS questionnaire. Third phase included the biochemical quantification of serum cortisol concentration and S-PGE2 levels using the enzyme-linked immunosorbent assays method (ELIZA) atthe beginning of the lockdown period then following up 3, 6 months later.**Results:** A statistically significant positive correlation was found between stress and cortisol (P0.05<), while a weak positive correlation was found between stress, PGE2 and periodontal readings through different time intervals. **Conclusion:** The novel pandemic of (COVID-19) and its consequences of lockdown period, acted as a stress inducing model in this study which in turns affected clinical parameters, serum cortisol level and PGE2 level as well.

***KEYWORDS***

*COVID-19, Stress, Cortisol, PGE2.*

- A paper extracted from Master Thesis titled ''The Effect of Psychological Stress on Periodontal Disease during COVID-19 Virus Threat: Relation to Salivary Prostaglandin (PGE2)''

1. Dentist at Al -Azhar medical administration Girls branch.
2. Professor of Oral medicine, periodontology, Oral Diagnosis and Radiology Faculty of Dentistry for Girls, Al-Azhar University, Cairo, Egypt.
3. Lecturer of Oral medicine, periodontology, Oral Diagnosis and Radiology Faculty Dentistry for Girls, Al Azhar University, Cairo, Egypt.

* Corresponding author email: samahmohamedhelmy92@gmail.com

## INTRODUCTION

Human population is expecting the most critical phase of the century because of the severe acute respiratory syndrome (SARS-COV-2), outbreak over the whole world. On January 30, 2020, the WHO announced the COVID-19virus as an international public health emergency. The first case was reported in December 2019 originating from China then it continued to spread through the continents to affect different countries from Europe, America, Asia and Africa all over the world [(1)].

Living under current circumstances of COVID-19 pandemic is a huge challenge especially for health care providers constituting heavy stressful conditions. The pandemic with its consequences of lockdown period is considered the stress inducing model for most of the common psychological risk factors such as stress, anxiety, depression and self-harm [(2,3)].

Stress develops a modulation in the immune response where it reduces the defense mechanism turning the body more likely to develop inflammatory diseases. Changes in modulation favors the progression of the periodontal disease through aggravating damage to the supporting tooth structure[(4)].

The adrenal gland produces a steroid hormone called cortisol. It is the hormone that controls stress and fight responses. It is a well-known stress biomarker regulated by the pituitary gland's adrenocorticotropic hormone. Both Physical and mental stress can affect its level, where the level of serum cortisol increases under high level of stress thus it is considered to be a reliable indicator for stress especially for patients subjected to heavy stressful conditions[(5)].

Stress and high cortisol level present a role of modulation on the immune response by decreasing the natural killer cell activity, the number of lymphocytes, the ratio of T helper cells to suppressor T cells, the antibody production and subsequently, decreasing the body response to infection. Thus, psychological stress is considered the potential factor for the pathogenesis of chronic diseases such as periodontal diseases. It also may favors the progression of periodontitis since stressors can aggravate damage to the supporting tooth structures[(6)].

Prostaglandin is one of the important biomarkers, it is derived from arachidonic acid metabolism of osteoclast and it is found in abundance at sites of inflammation. It is responsible for most of the periodontal changes occurring in the inflammatory process of periodontal diseases. In addition, it increases the vasodilatation and capillary permeability responsible for the clinical signs of redness and edema. High levels of $PGE_2$ in the gingival crevicular fluid are found at destructive sites of inflammation [(7)].

Literature deducted the effect of psychological stress on the inflammatory responses and the immune system of the body. The potentiality of psychological stress to affect the incidence and progression of chronic diseases such as periodontal diseases is questioned. Thus, the current study aimed to investigate the psychological stress levels during COVID-19 virus threats affecting serum cortisol concentrations and S-PGE2 concentrations and its relationship to the periodontal health.

## SUBJECTS AND METHODS

### Patient's selection:

A cross- sectional study conducted according to sample size calculation on 30 patients particularly those having high scores on the Perceived Stress Scale. Patients were selected from Al-Azhar university hospitals clinics. The whole procedure was explained to all participants and informed consent was signed by patients. Approval number **REC-PD-21-08** from the Research Ethic Committee of the Faculty of Dental Medicine for Girls, Al-Azhar University, was received.

All patients were selected according to the following inclusion criteria [(8)];Patients aging from25

up to 60 years old, with minimum 20 teeth present in the whole mouth, were recruited for this study. Health care providers under stress due to the novel pandemic COVID-19.Patientswithmoderately good oral hygiene habits such as tooth brushing and usage of mouthwashes. Asymptomatic free patients from any systemic disease. Excluded patients [8]; patients using corticosteroid drugs chronically. immunosuppressive patients, patients using anti-inflammatory drugs at least2 months prior the study and finally those who had a periodontal treatment six months prior to selection .

**Sample size calculation:**

A total sample size of 26 patients was sufficient to detect an effect size ranging from 1.66 to 2.05 with a power (1-error) of 0.99[9], regarding a prior study in 2012 [8].

**Study Design:**

The study consisted of three components:-

1. Clinical examination using the following clinical parameters [10]: Gingival Index, Probing Depth (PD) as shown in Figure (1) and Clinical Attachment Level (CAL). Measurements were recorded at base line, 3 months and 6 months follow-ups.

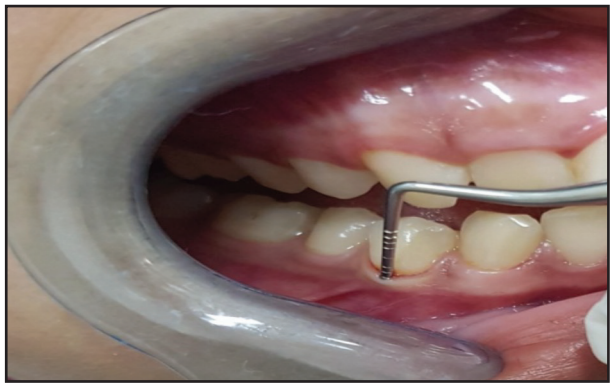
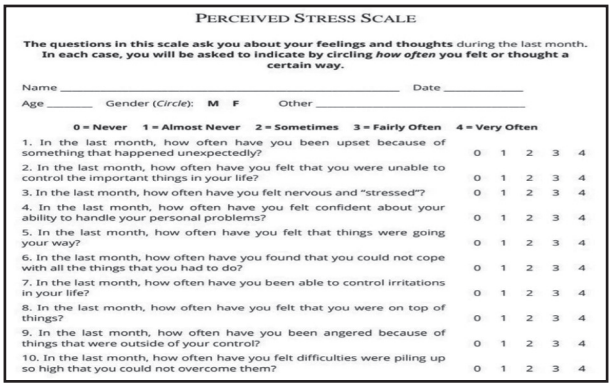


**Figure (1)** A clinical photograph showing the mesio-buccal aspect of the lower right first premolar with PD 1mm.

2. Data collection via a questionnaire to assess psychological stress using the Perceived Stress Scale. PSS consists of 10 questions on a 5-point scale, with a value range from (0-4). Each patient was given a score. Only patients with high scores were enrolled in this study (Fig. 2).



PERCEIVED STRESS SCALE

**The questions in this scale ask you about your feelings and thoughts** during the last month. **In each case, you will be asked to indicate by circling *how often* you felt or thought a certain way.**

Name _____ Date _____

Age _____ Gender (*Circle*): **M F** Other _____

| | 0 = Never | 1 = Almost Never | 2 = Sometimes | 3 = Fairly Often | 4 = Very Often |
|---|---|---|---|---|---|
| 1. In the last month, how often have you been upset because of something that happened unexpectedly? | 0 | 1 | 2 | 3 | 4 |
| 2. In the last month, how often have you felt that you were unable to control the important things in your life? | 0 | 1 | 2 | 3 | 4 |
| 3. In the last month, how often have you felt nervous and "stressed"? | 0 | 1 | 2 | 3 | 4 |
| 4. In the last month, how often have you felt confident about your ability to handle your personal problems? | 0 | 1 | 2 | 3 | 4 |
| 5. In the last month, how often have you felt that things were going your way? | 0 | 1 | 2 | 3 | 4 |
| 6. In the last month, how often have you found that you could not cope with all the things that you had to do? | 0 | 1 | 2 | 3 | 4 |
| 7. In the last month, how often have you been able to control irritations in your life? | 0 | 1 | 2 | 3 | 4 |
| 8. In the last month, how often have you felt that you were on top of things? | 0 | 1 | 2 | 3 | 4 |
| 9. In the last month, how often have you been angered because of things that were outside of your control? | 0 | 1 | 2 | 3 | 4 |
| 10. In the last month, how often have you felt difficulties were piling up so high that you could not overcome them? | 0 | 1 | 2 | 3 | 4 |

**Figure (2):** The perceived stress scale PSS questionnaire.

3. Samples collection:

a- Blood samples collection: About 1.5 ml of blood sample was collected from all participants in the early morning between 9 and 11 am from all individuals after 20 minutes of rest to reduce the impact of circadian fluctuation [11]. Samples were centrifuged for 20 minutes by using an Ependo type centrifuge at 2000-3000 RPM to obtain serum (fig. 3).

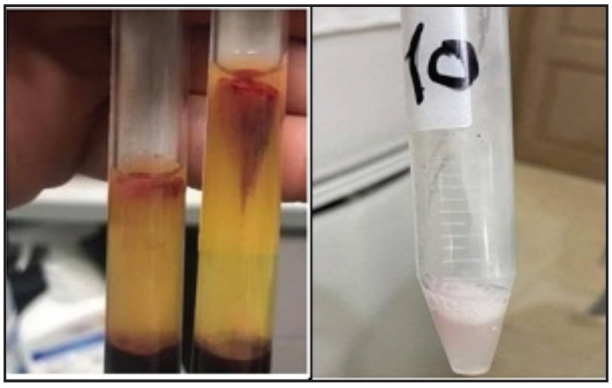


**Figure (3):** Serum blood and saliva samples

b- Saliva samples collection: Participants were scheduled early and were instructed to eat breakfast early and to stop eating and drinking

before the start of the collection process. Whole saliva samples were collected by spitting method[12] and then stored frozen at -20°C within 10 minutes of collection (fig. 3).

**Lab investigations:**

Serum Cortisol and Salivary Prostaglandin were assessed at the base line, 3 and 6 months follow ups using ELISA kit.

***A-Serum Cortisol ELISA kit:***

All reagents were prepared, all standard solutions and samples as explained by the instructions. The whole procedure was performed at room temperature.

1. Number of the strips needed for the assay was determined then inserted in the frames for usage.
2. 50µl of biotin reagent was added to all wells.
3. 100µl of Cortisol Enzyme Conjugate was added to all wells, mixed for 10 seconds then incubated for 60 minutes at 20-25°C.
4. Liquid was removed then the wells were washed 3 times with the wash buffer. The plate was plotted onto absorbent towels.
5. 100µl of TMB substrate was added to all wells, and then the plate was incubated for 15 minutes at 20-25°C (Fig. 4).

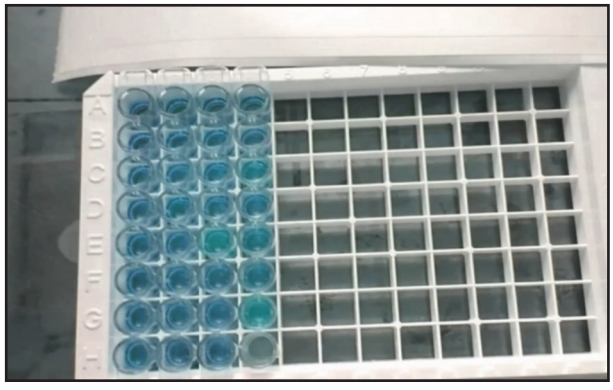


**Figure (4):** Wells after placement of substrate.

6. 50µl of Stop Solution was then added, the color changed immediately into yellow (Fig. 5).
7. Absorbance was read by ELISA reader at 450 nm within 20 minutes after adding the stop solution.

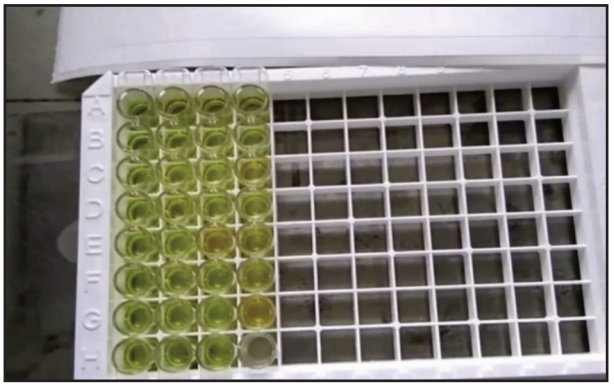


**Figure (5):** Wells after placement of stop solution.

***B- Salivary Prostaglandin ELISA kit:***

1. 50µl standard was added to standard well.
2. 50µl sample was added to sample wells, 10µl anti PG-E2 antibody was also added then 50µl streptavidin-HRP was finally added to sample &standard wells. The plate was covered then incubation was done at 37°Cfor 1 hour.
3. The sealer was removed; the whole plate was washed successively. Wells were soaked for about 1 minute with at least 0.35 ml wash buffer for each wash.
4. 50µl substrate of solution A together with 50µl substrate of solution B were added to each well. The plate was incubated and then was covered by a new sealer at37°C for 10 minutes in the dark (Fig. 6).
5. 50µl of Stop Solution was then added, the color changed immediately into yellow (Fig. 7).
6. Using a micro plate reader set to 450 nm, the optical density of each well was determined immediately within 10 minutes after adding the stop solution.

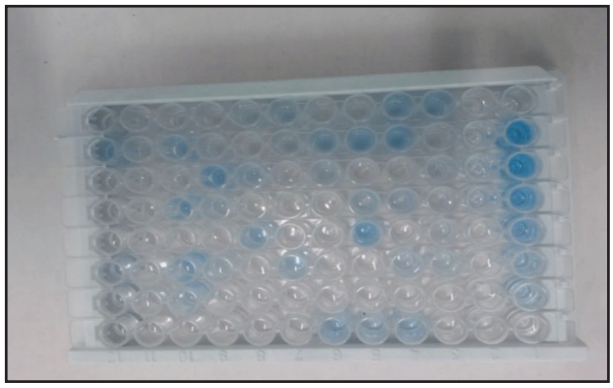


**Figure (6):** Wells after placement of substrate.

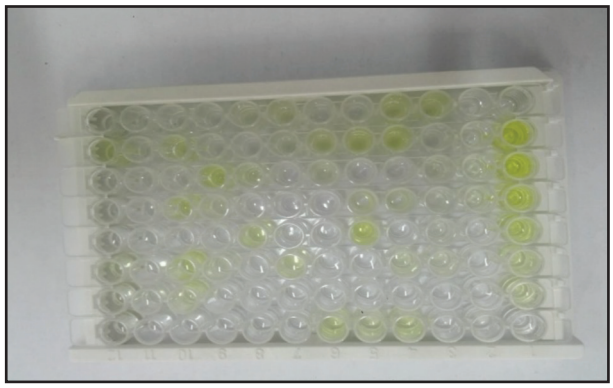


**Figure (7):** Wells after placement of Stop Solution

**Statistical analysis:**

Statistical analysis of the results was performed by applying the paired t-test and one way ANOVA to show the effect of time within each variable. Pearson Correlation coefficient test was applied to study the effect of stress on each variable. It is a test used to measure the strength and direction of linear relationship between two variables statically. (P< 0.05) was considered statistically significant (95% significance level). In addition, Shapiro Wilk test was used for testing the normality of data. Statistical evaluation was done using the SPSS statistical package (version 25, IBM Co. USA).

**RESULTS**

A total number of thirty participants were recruited in the study to evaluate their clinical periodontal parameters, serum cortisol concentrations and salivary PGE2 concentrations at baseline during the lockdown, 3months and 6 months after the lockdown period. The results were correlated to their stress levels detected throughout the study period.

1. **The Gingival Index (GI):** the mean was recorded the lowest value at baseline during lockdown (0.93±0.37), then showed some increase at 3 months after lockdown (1.03±0.39), and the maximum increase was at 6 months after lockdown (1.18±0.37).A statistically significant difference was reported in the mean of GI between baseline during the lockdown and all follow-ups as well as between the 3 months after lockdown&6 months after lockdown ($P < 0.05$).
2. **The Probing Depth (PD):** the mean was recorded the lowest value at baseline during lockdown (1.16±0.27), then showed some increase at 3 months after lockdown (1.23±0.28), and the maximum increase was at 6 months after lockdown (1.31±0.283).A statistically significant difference was reported in the mean of PD between baseline during the lockdown and all follow-ups as well as between the 3 months after lockdown&6 months after lockdown ($P < 0.05$).
3. **The Clinical attachment loss (CAL):** the mean was recorded the lowest value at baseline during lockdown (0.41±0.38), then showed some increase at 3 months after lockdown (0.56±0.43), and the maximum increase was at 6 months after lockdown (0.68±0.49).A statistically significant difference was reported in the mean of CAL between baseline during the lockdown and all follow-ups as well as between the 3 months after lockdown&6 months after lockdown ($P < 0.05$).

**Table (1)** *The mean for the clinical periodontal parameters recorded at different experimental periods.*

| Periodontal Parameter | During lockdown | 3 M after lockdown | 6 M after lockdown | P-value |
|---|---|---|---|---|
| **Gingival Index (GI)** | 0.93±0.37[a] | 1.03±0.39[b] | 1.18±0.37[c] | 0.00 |
| **Probing depth(PD)** | 1.16±0.27[a] | 1.23±0.28[b] | 1.31±0.28[c] | 0.013 |
| **Clinical attachment loss (CAL)** | 0.41±0.38[a] | 0.56±0.43[b] | 0.68±0.49[c] | 0.00 |

*--Means with different superscripts are statistically significantly different at P ≤ 0.05.-*

**4- The perceived stress scale (PSS):** the mean of PSS scores was recorded the lowest value at baseline during lockdown(18.29±3.62), then showed a slight increase3 months after lockdown (22.00±4.53) and finally increased to (23.91±3.99) 6 months after lockdown. The mean was recorded at different experimental periods (Fig. 8), denoting a barely statistically significant increase in PSS levels among all intervals (p value=0.02).

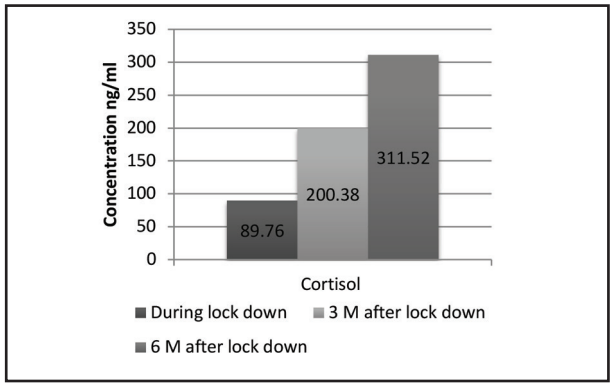



**Figure (8)** Bar chart showing mean of Perceived Stress Scale at different experimental periods.

**5- The serum cortisol concentrations:** the mean of serum cortisol concentrations was recorded the lowest value at baseline during lockdown (89.76±43.43), then it showed some increase at 3 months after lockdown (200.38±117.66), and the maximum increase was at 6 months after lockdown(311.52±62.69). The mean was presented at different times (Fig. 9), donating a statistically significant increase in serum cortisol concentrations among all intervals (p-value < 0.05).

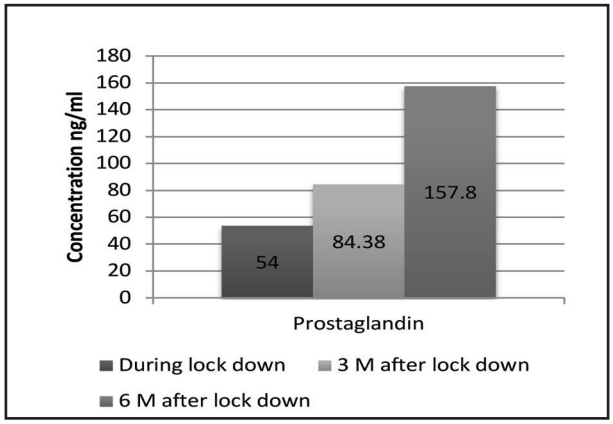



**Figure (9):** Bar chart showing mean of serum cortisol concentrations at different experimental periods.

6- **The salivary prostaglandin concentration (S-PGE2):** the mean of salivary PGE2 concentrations was recorded the lowest value at baseline during lockdown (54.00±28.64), then it showed some increase at 3 months after lockdown (84.83±55.08), and the maximum increase was at 6 months after lockdown (15780±64.65). The mean was presented at different times (Fig. 10), donating a statistically significant increase in salivary PGE2 concentrations among all intervals (p-value < 0.05).

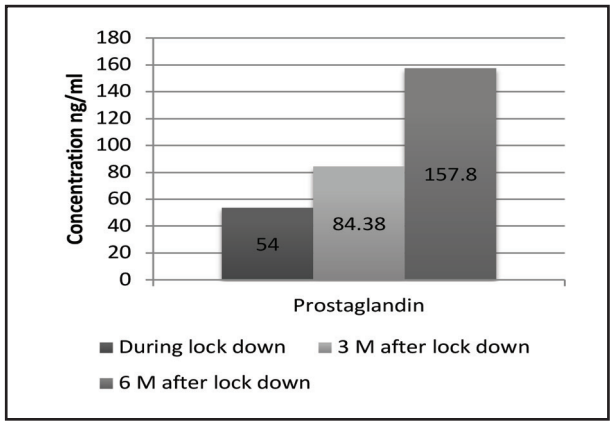



**Figure (10):** Bar chart showing mean of salivary PGE2 concentrations at different experimental periods.

**Effect of Stress on clinical parameters:**

***A) Effect of stress on gingival index (GI)***

We can briefly say that there was a weak positive correlation between stress and Gingival Index and this correlation was not statistically significant as presented in Table (2).

**Table (2):** *Correlation between stress and all clinical parameters at different time intervals*

| G I | R | P-Value | Correlation type |
|---|---|---|---|
| During lock down | 0.012 | 0.955 | Weak positive |
| 3 M after lock down | 0.12 | 0.577 | Weak positive |
| 6 M after lock down | 0.24 | 0197 | Weak positive |
| **PD** | **r** | **P-Value** | **Correlation type** |
| During lock down | 0.031 | 0.886 | Weak positive |
| 3 M after lock down | 0.127 | 0.619 | Weak positive |
| 6 M after lock down | 0.005 | 0.980 | Weak positive |
| **C A L** | **r** | **P-Value** | **Correlation type** |
| During lock down | 0.23 | 0.112 | Weak positive |
| 3 M after lock down | 0.20 | 0.154 | Weak positive |
| 6 M after lock down | 0.19 | 0.516 | Weak positive |

*P – Value significant at p ≤ 0.05*

***B) Effect of stress on probing depth (PD)***

We can briefly say that there was a weak positive correlation between stress and Probing Depth and this correlation was not statistically significant as presented in Table (2).

**C) Effect of stress on clinical attachment loss (CAL)**

We can briefly say that there was a weak positive correlation between stress and Clinical attachment loss and this correlation was not statistically significant as presented in Table (2).

**2- Effect of stress on Cortisol concentration**

There was a moderate positive correlation between stress and cortisol at 6 M after lock down (r = 0.656), this correlation was highly statistically significant (P)0.001<.Therefore, we can briefly say that there was a clear moderate positive correlation between stress and cortisol and this correlation was statistically significant as presented in Table (3).

**Table (3)** *Correlation between Perceived stress scale and Cortisol at different time*

| Cortisol | r | P-Value | Correlation type |
|---|---|---|---|
| **During lock down** | 0.478 | 0.014 | **Moderate positive** |
| **3 M after lock down** | 0.421 | 0.032 | **Moderate positive** |
| **6 M after lock down** | 0.656 | 0.000 | **Moderate positive** |

*P – Value significant at p ≤ 0.05*

**3- Effect of stress on Salivary Prostaglandin level**

There was a weak positive correlation between stress and S-PGE2 at 6 M after lock down(r = 0.098), and the correlation was not statistically significant (P0.05>).

Therefore, we can briefly say that there is a weak positive correlation between stress and S-PGE2 and this correlation is not statistically significant as presented in Table (4).

**Table (4)** *Correlation between Perceived stress scale and Prostaglandin at different time*

| Prostaglandin | r | P-Value | Correlation type |
|---|---|---|---|
| **During lock down** | 0.005 | 0.982 | **Weak positive** |
| **3 M after lock down** | 0.016 | 0.506 | **Weak positive** |
| **6 M after lock down** | 0.098 | 0.611 | **Weak positive** |

*P – Value significant at p ≤ 0.05*

## DISCUSSION

During the outbreak of COVID-19, pandemic, healthcare providers are considered to beat a great risk of virus transmission. They experienced massive psychological issues with the feeling of stress, anxiety, incompatibility, depression and fear of transmitting diseases and infection to their families[13].

Mental stress or physical stress is considered an important trigger for most of the major psychiatric disorders. However, in case of exaggerated stressful conditions, it leads to "stress-induced hypercortisolaemia" which is considered the main phase of the adaptive process which results in chronic distress. This is manifested in different body organs in the form of peptic ulcer, arthritis, asthma, and other pathological conditions mediated by inflammation[14].

Periodontal disease affects the supporting structures of the teeth, which may lead to tooth loss and may contribute to systemic inflammation. Periodontal disease initiation and propagation occurs through commensals of oral microbes, interacting with the immune defense of the host and finally lead to inflammation of the tissues [15].

Severity of the periodontal disease depends on both the environmental factors and the host risk factors. Some of them are modifiable such as smoking, alcohol consumption and neglecting oral hygiene measures and others are non-modifiable such as genetic susceptibility, ageing, diabetes mellitus and metabolic diseases. These risk factors affect the propagation, severity and the progression of periodontal disease [16].

Accordingly, there is a correlation between the psychological status of the patient and the progressive course of the periodontal disease. Both stress and periodontitis are inflammatory diseases with a complex etiology and pathogenesis, comprising many interactions between the host genetic factors and infectious agents.It has been demonstrated that psychological stress can elicit immunological responses, which causes exacerbation and progression of the periodontal diseases [17].

Therefore, this study was performed to investigate serum Cortisol concentrations and salivary Prostaglandin levels under psychological stress during COVID-19 pandemic threats and its effect on periodontal status.

Concerning the methodology, patients chronically using corticosteroid drugs were excluded because this increases serum cortisol level and this increase will not be related to stressful conditions of the pandemic. Samples were assessed at baseline then follow-ups at 3&6 months were done to study the effect of stress on the periodontium through the measurement of the periodontal parameters during corresponding time interval [8].

Psychological stress was assessed via a questionnaire using the Perceived Stress Scale. PSS is one of the most widely used instruments to measure psychological stress in the world. It is valid in more than 20 countries and is considered the best instrument to assess the perception of stress. The scale has been demonstrated to predict mental and physical health outcomes and enables for the analysis of stress pathology relationships [18].

In this study, serum blood samples were taken to measure cortisol level in blood. Measurement of serum cortisol level is one of the most accurate

methods to configure the stress [19]. Cortisol is the main glucocorticoids in humans. It is a reliable stress biomarker regulated by the pituitary gland's adrenocorticotropic hormone. Physical stress, mental stress, and disease can all affect its levels. The value of serum cortisol is bound to rise in the presence of a high level of stress, making it a reliable marker in individuals experiencing stressful life events [20].

Saliva samples were taken as it contains a highly complex mixture of substances, and are considered to be diagnostic tool containing many biomarkers specific for diagnosis of periodontal diseases as PGE2,IL-1, IL-6, and tumor necrosis factor (TNF-α) [21].PGE2 was selected as it is a potent inflammatory mediator. It induces vasodilatation and increases the capillary permeability, expressed in redness and edema the early clinical signs of gingival inflammation. In addition, it stimulates fibroblasts and osteoclasts acting on the degradation of connective tissue collagen and alveolar bone resorption and finally the clinical expression of periodontal disease [22].

On correlating the results of clinical parameters with PSS value to show the effect of stress on clinical parameters, a positive correlation between GI, PD,CAL at the baseline and on following up 3 & 6 months later was found. Yet it was not of high significance statistically (P>0.05).

The biological possibility for this association is based on the fact that glucocorticoids, including cortisol inhibit the production of secretory IgA, IgG and neutrophil function. Inhibition of these antibodies allows the proliferation of bacteria and affect the defense mechanism against infection, leading to destructive periodontal disease. On autonomic nervous system activation, it stimulates the production of many neuroendocrine hormones such as catecholamine's and glucocorticoids. Upon activation of these hormones lymphocytes and natural killer cell, activity is decreased, resulting in infection, which accelerates the periodontal degradation [23].

In agreement with these results, in 2019, [24] a cross-sectional study was conducted to estimate the association between stress and periodontitis. Results showed that those patients exposed to stress was 15–36% higher than those without experiencing such stressful conditions regardless age, sex, schooling level, and health status. Results showed that 48.47% of the participants were classified with high stress, 23.92% of them were diagnosed with periodontitis.

On the contrary, another study was conducted in 2016, [25] to evaluate the link between stress and periodontal disease. It included 50 periodontitis patients. Clinical parameters as Plaque index (PI), probing depth (PD), and clinical attachment level (CAL) were assessed. Stress assessment was performed by Zung's self-rating anxiety scale. The clinical parameters did not show any differences among patients with different levels of stress with no association found between stress and periodontal disease.

In the present study, on correlating the cortisol results with PSS value to show the effect of stress on cortisol level, a moderate positive correlation was found and it was statistically significant(P>0.05).

Several theories explained the link between stress and periodontitis through two main models. Two mechanisms are included in the first model, in which the stress-induce immunosuppressive effects through the activation of the central nervous system and autonomic central system. Second model explains the stress-induce behavioral changes [26].

The stress-induced response is a well-known physiological response system, which transfers to the hypothalamic pituitary adrenal (HPA) axis and is triggered by the acute stressful situations. Stimulation of the HPA axis stimulates the hypothalamus to produce corticotrophin releasing hormone (CRH). That in turn results in the secretion of adrenocorticotropic hormone from the pituitary and cortisol from the adrenals. Altering the host's immune response, may predispose periodontal disease [27].

These results are in accordance with a study performed in 2012,[8] to evaluate the effect of psychological stress and salivary cortisol level on periodontitis, where it showed a significant association between cortisol level and stress level. In this study, a moderate positive correlation between stress and cortisol level during lock down is found (r = 0.478), then it continues to increase(r = 0.656) on following-up 6 months later. This correlation was statistically significant (P)0.05<.

This disagrees with a study conducted in 2020,[28] where it showed no relation between cortisol and psychological stress. This result could be due to the participant's response and the small size of the sample.

Regarding the results of PGE2 level, it was found that prostaglandin level increased upon exposure to high levels of stress. On correlating these results with PSS value to show the effect of stress on Pge2,a positive correlation was found at baseline and on following up 3 & 6 months later, yet it was not of high significance statistically (P>0.05).

High psychological stress elicits responses that are transmitted to the autonomic nervous system, which in turns stimulate the secretion of catecholamines, epinephrine and norepinephrine. Catecholamines affect PGE2 that favors the periodontal breakdown .This can be explained due to the stress role of regulation of the immune response as the result of reduction in their defense capacity. PGE2 elicit pro-inflammatory effects such as increasing vasodilatation, and activation of osteoclast, thereby causing bone resorption increasing the body susceptibly to develop inflammation [29].

These results were in line with a previous study conducted in 2020,[30]which showed that PGE2 level in GCF in periodontitis patient under stressful conditions, increases way more than its level in periodontitis patient not subjected to current stressful conditions and may indicate the risk of progression of periodontal disease**.** PGE2 is a major mediator in the inflammatory response. Inflammatory mediators in GCF have been proposed as indicators for periodontitis progression and severity, that may increases alveolar bone resorption.

Additionally, the study conducted in 2017[31], had shown a positive correlation between PGE2 concentrations in gingival crevicular fluid and the severity of periodontal disease.$PGE_2$ concentration shows a gradual increase by increasing the severity of periodontitis with a strong correlation with gingival inflammation and clinical parameters.

## CONCLUSION

The Pandemic of COVID-19 and its consequences of quarantine and lock down period, acted as a stress inducing model with high level of stress recorded on " PSS". High Cortisol levels might have an indirect effect on the periodontal condition as there was an apparent reflection of Prostaglandin on the periodontal condition and the worst clinical parameters were recorded at the end of the study. Time factor was very detrimental in this study as it was evident that the longer time the subject was stressed, the more exaggerated was the effect on the periodontal condition.

## ACKNOWLEDGMENTS

I would like to pay my deep gratitude for many people whose names may not all be enumerated for their support and guidance but specially, I would like to acknowledge Sigma Aldrich company for importing the ELISA kits needed for this study.

## RECOMMENDATIONS

1. Following up for a longer duration is needed to show whether the cortisol level, PGE2 level and clinical parameters will continue to increase or remain constant, because of the general adaption syndrome.
2. Further studies can be made at the end of COVID-19 pandemic on the same patients in comparison with another control group not experiencing such stressful conditions to study the effect of stress on cortisol and PGE2 levels then, correlate it with the periodontal condition.

## CONFLICT OF INTEREST

The authors declared that there is no conflict of interest.

## FUND RECEIVED FOR THE STUDY

None.

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