Efficacy of scaling and root planing on serum cortisol levels in COVID-19 recovered patients with periodontitis: A clinical & biochemical study.

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Abstract— Periodontitis is characterized by microbially-associated, host-mediated inflammation that results in loss of periodontal attachment.Numerous risk factors are involved for progression of periodontal disease like uncontrolled diabetes, smoking, age, psychosocial stress and certain psychosomatic conditions like anxiety and depression.

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. Stress has a direct effect on the hypothalamus-pituitary adrenal cortex axis. Many studies have demonstrated a correlation between stress and an increased risk of developing periodontal disease and clinical attachment loss.Release of stress hormones (cortisol) impairs host defense which helps in the growth of opportunistic organisms in the gingival sulcus.

Corona Virus Disease-2019 (COVID-19) is a disease caused by novel coronavirus named Severe Acute Respiratory Syndrome Corona Virus-2 (SARS-CoV-2) that triggers damage to the lungs and other organs. The COVID-19 pandemic has caused a tremendous amount of stress for the average individual, both financially and psychologically. A study showed that levels of cortisol in patients with COVID- 19 were significantly high and had increased as the severity of the disease increased.

However, there is paucity of literature regarding the effect of scaling and root planing on serum cortisol levels in COVID-19 recovered patients and whether any association can be established between periodontal status and serum cortisol levels post periodontal therapy. Thus this study was undertaken to assess the effect and association of scaling and root planing on serum cortisol levels in COVID-19 recovered patients with periodontitis.

Keywords: Periodontitis, Stress, COVID-19, Serum cortisol

I. INTRODUCTION

Periodontitis is characterized by microbially-associated, host-mediated inflammation that results in loss of periodontal attachment.[1] The etiology and pathogenesis of periodontal disease are multifactorial. Numerous risk factors are involved for progression of periodontal disease like uncontrolled diabetes, smoking, age, psychosocial stress and certain psychosomatic conditions like anxiety and depression.[2,3,4] 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 the organism naturally desires to avoid.[5] Stress has a direct effect on the hypothalamus-pituitary adrenal cortex axis[6,7]. It is hypothesized that prolonged activation of this axis can be detrimental to health and may provide a link between mental stress and physical illness.[8,9,10] Many studies have demonstrated a correlation between stress and an increased risk of developing periodontal disease and clinical attachment loss.[11,12,13] Both financial stress and psychological stress have been shown to double and even quadruple the risk of developing periodontal attachment loss.[11] Release of stress hormones (cortisol) impairs host defense which helps in the growth of opportunistic organisms in the gingival sulcus. Studies have shown that higher levels of serum cortisol are found in patients with periodontal disease. [14]

Corona Virus Disease-2019 (COVID-19) is a disease caused by novel coronavirus named Severe Acute Respiratory Syndrome Corona Virus-2 (SARS-CoV-2) that triggers damage to the lungs and other organs[15]. Most COVID-19 patients present mild symptoms; however, a few could develop severe illness having pneumonia, pulmonary edema, acute respiratory distress syndrome, venous thromboembolism,

multiple organ dysfunction syndrome, or may even result in death.[16] The COVID-19 pandemic has caused a tremendous amount of stress for the average individual, both financially and psychologically. In one survey, 70% of respondents stated that the months during this pandemic have been the most stressful time in their entire lives[16]. Ramezani M (2020) in a study showed that levels of cortisol in patients with COVID- 19 were significantly high and had increased as the severity of the disease increased[17]. Periodontal therapy can play a major role in avoiding tissue breakdown.[18] Study by Omer Cakmak (2019) have concluded that non-surgical periodontal treatment has significantly reduced gingival crevicular fluid cortisol levels.[19] However, there is paucity of literature regarding the effect of scaling and root planing on serum cortisol levels in COVID-19 recovered patients and whether any association can be established between periodontal status and serum cortisol levels post periodontal therapy. Thus the study was undertaken to assess the effect and association of scaling and root planing on serum cortisol levels in COVID-19 recovered patients with periodontitis.

II. MATERIALS & METHODS

The patients were recruited from outpatient department, Department of Periodontology, School of Dental Sciences, Sharda University, Greater Noida. The nature and outcome of the study was explained to the patients following which a written consent form was obtained. The study was approved by Institutional Ethics Committee. A total number of 30 patients which included both males and females in the age group of 18-60 years with periodontitis were included in the study who had Localized /Generalized Stage I and II, Periodontitis having Interdental CAL which is detectable at ≥ 2 non- adjacent teeth, or Buccal or oral CAL ≥ 3mm with pocketing > 3 mm detectable at ≥ 2 teeth. Patients who had ≥ 20 natural teeth & systemically healthy patients recovered from mild COVID-19 who were symptomatic but without evidence of viral pneumonia or hypoxia and who were not hospitalized for treatment. The patients were recruited within one month of SARS-CoV-2 RT PCR negative report. Patients who had undergone periodontal therapy in last 6 months or with history of any steroidal, antipsychotic drug therapy, oral contraceptives & hormonal replacement therapy were excluded. Pregnant, lactating women, users of tobacco in any form, and patients not willing to give a written consent form were also excluded from the study. The study was carried out between August 2021 to November 2022.

30 volunteers were divided into the test and control groups using a coin toss as the randomizer. Each patient was presented over the course of three visits in this single blind randomised controlled clinical

research. According to the inclusion and exclusion criteria, patients were chosen for recruitment. Periodontal parameters were measured during the baseline visit, including the Community Periodontal Index of Treatment Needs (CPITN) and serum cortisol levels. For the control group, 0.12% Chlorhexidine mouthwash was administered along with general oral hygiene instructions, and for the test group, full mouth scaling and root planing was carried out in addition to the prescription of 0.12% Chlorhexidine mouthwash and general oral hygiene guidelines.

III. STATISTICAL ANALYSIS

Version 21 of the Statistical Package for Social Sciences (SPSS) was used to analyse the data. Frequencies will be used to summarise categorical variables, whereas Means & Standard Deviations were used to summarise continuous variables. The significance of differences in serum cortisol levels and other clinical parameters before and after scaling and root planing among COVID-19 recovered patients was examined using repeated measures of the ANOVA/Friedman test.The cutoff point for statistical significance was 0.05. The software GPower 3.0 was used to estimate the sample size. For the F test and ANOVA, the sample size was calculated using repeated measures within factors for 3 related measurements. For an alpha of 0.05, power of 80%, and effect size of 0.25 (measured for difference in serum cortisol levels at 3 different follow-ups), a minimum total sample size of 28 was found to be adequate. ANOVA and F tests: Measures taken repeatedly within factors Analysis: A priori: Compute required sample size. Input: Effect size f = 0.25 α err prob = 0.05, Power (1-β err prob) = 0.80 Number of groups = 1, Number of measurements = 3, Corr among rep measures = 0.5, Non sphericity correction ε = 1, Output: Non centrality parameter λ = 10.5000000, critical F = 3.1682460, Numerator df= 2.0000000, Denominator df= 54.0000000, Total sample size = 28, Actual power= 0.8124546.

IV. RESULTS

A total number of 30 patients which included both males and females in the age group of 18-60 years with periodontitis were included in the study who had localized /Generalized Stage I and II and fulfilled the inclusion & exclusion criteria. The distribution of males and females was not found to be significantly different among two study groups, i.e., test group and control group ($p>0.466$). The mean age of study participants among both the study groups was not found to be significantly different as ($p>0.05$).

Intragroup comparison of mean levels of serum cortisol at baseline, 1 month and 3 months follow ups among control group showed that the mean level of serum cortisol did not show any significant

difference from baseline to 1 month and also from 1 month to 3 months follow up. Overall, no significant difference could be found in the mean serum cortisol levels among control group at baseline, 1 month & 3 months follow up.(Table 1) Intragroup comparison of CPI scores at baseline, 1 month & 3 months follow up among control group showed a statistically significant difference from baseline to 1 month, baseline to 3 months & from 1 month to 3 months. The frequency of CPI score 4 increased significantly from baseline to 3 months while, the frequency of score CPI score 1 decreased significantly from baseline to 1 month and from baseline to 3 months. Intragroup comparison of TN scores at baseline, 1 month & 3 months follow up among control group showed a statistically significant difference from baseline to 1 month, baseline to 3 months & from 1 month to 3 months. The frequency of TN score 3 increased significantly from baseline to 3 months while, the frequency of score TN score 2 decreased significantly from baseline to 1 month and from baseline to 3 months. (Table 1)

Intragroup comparison of mean levels of serum cortisol at baseline, 1 month and 3 months follow ups among test group showed that the mean level of serum cortisol did not show any significant difference from baseline to 1 month and also from 1 month to 3months follow up. Overall, no significant difference could be found in the mean serum cortisol levels among test group at baseline, 1 month & 3 months follow up.(Table 2) Intragroup comparison of CPI scores at baseline, 1 month & 3 months follow up among test group showed a statistically significant difference from baseline to 1 month, baseline to 3 months & from 1 month to 3 months. The frequency of CPI score 0 increased significantly from baseline to 3 months while, the frequency of score CPI score 2, 3 & 4 decreased significantly from baseline to 1 month and from baseline to 3 months. Intragroup comparison of TN scores at baseline, 1 month & 3 months follow up among test group showed a statistically significant difference from baseline to 1 month, baseline to 3 months & from 1 month to 3 months. The frequency of TN score 0 & score 1 increased significantly from baseline to 3 months while, the frequency of score TN score 2 & 3 decreased significantly from baseline to 1 month and from baseline to 3 months. Intergroup comparison of mean levels of serum cortisol at baseline, 1 month and 3 months follow ups showed that the mean levels of serum cortisol were comparable among the test group and control group at baseline, 1 month & 3 months follow up (Table 2).

Intergroup comparison of changes in mean levels of Serum cortisol from baseline to 1 month and 3 months follow ups showed no statistically significant difference among test group & control group (Table 3). Intergroup comparison of CPI score at baseline among test group and control group showed that the distribution of different CPI scores at baseline among test group & control group was not significantly different. Intergroup comparison of CPI score at 1 month among test group

and control group showed that the distribution of different CPI scores at 1 month among test gr & control gr was significantly different. The frequency of CPI score 4 was found to be significantly high among control group, while the frequency of CPI score 0, 1 & 2 were found to be significantly high among test group. Intergroup comparison of CPI score at 3 month among test group and control group showed that the distribution of different CPI scores at 3 month among test group & control group was significantly different. The frequency of CPI score 3 & 4 were found to be significantly high among control group, while the frequency of CPI score 0, 1 were found to be significantly high among test group. Intergroup comparison of TN score at 1 month among test group and control group showed that the distribution of different TN scores at 1 month among test gr & control group was significantly different. The frequency of TN score 3 was found to be significantly high among control group, while the frequency of TN score 1 & 2 were found to be significantly high among test group. Intergroup comparison of TN score at 3 months among test group and control group showed that the distribution of different TN scores at 3 month among test goupr & control group was significantly different. The frequency of TN score 2 & 3 were found to be significantly high among control group, while the frequency of TN score 1 was found to be significantly high among test group. (Table 3)

Table 1: Intragroup comparison of mean levels of Serum cortisol, CPI & TN scores, at baseline, 1month and 3 months follow ups among Control group.

Cortisol among Control group										
	Mean		Std. Deviation		N	Pvalue	**P value of pair wise comparison**			
At baseline	18.4140		7.58571		15	0.137, NS	Baseline*1m – 0.054,NS			
At 1 month	19.3327		7.89071		15		Baseline*3m– 0.411,NS			
At 3 months	22.3493		4.80949		15		1m*3m – 0.787,NS			
Control Group										
	CPIScore 0		CPIScore 1		CPIScore 2		CPIScore 3		CPIscore4	
	n	%	n	%	n	%	n	%	n	%
Baselin	0	0	2	13.3%	4	26.7 %	6	40%	3	20%

e		%								
At 1m	0	0 %	1	6.7%	3	20%	6	40%	5	33.3%
At 3m	0	0 %	1	6.7%	1	6.7%	6	40%	7	46.7%
P value	Baseline v/s1 month– 0.017,S Baseline v/s 2 month– 0.005, S1month v/s 2month–0.001,S									
Control Group										
	TN0		TN1		TN2		TN3			
	n	%	n	%	n	%	n	%		
Baseline	0	0%	0	0%	6	40 %	9	60%		
At1 month	0	0%	1	6.7%	4	26.7%	10	66.7%		
At 3 month	0	0%	1	6.7%	3	20%	11	73.3%		
P value	Baseline v/s 1month–0.004, S Baseline v/s 2month–0.209, NS 1month v/s 2 month –0.001, S									

Table 2: Intragroup comparison of mean levels of Serum cortisol, CPI & TN scores, at baseline, 1month and 3 months follow ups among Test group.

Cortisol among Test group										
	Mean		Std. Deviation		N	P value	**P value of Pair wise comparison**			
At baseline	16.7840		8.40184		15	0.385 ,NS	Baseline*1m –0.999, NS			
At1 month	17.3427		8.97630		15		Baseline*3m– 0.999, NS			
At3 months	17.8760		8.36864		15		1m*3m – 0.999, NS			
Test Group										
	PI Score 0		CPI Score 1		CPI Score 2		CPI Score 3		CPIscore4	
	n	%	n	%	n	%	n	%	n	%
Baseline	0	0 %	0	0%	7	46.7 %	7	46.7 %	1	6.7 %

At 1 month	1	6.7 %	6	40%	6	40%	2	13.3 %	0	0%
At 3 months	6	40 %	7	46.7 %	1	6.7 %	1	6.7 %	0	0%
Pvalue	Baseline v/s 1 month– 0.002, S Baseline v/s 3 month– <0.001, S 1month v/s 3month–0.00, S									

Test Group								
	TN0		TN1		TN2		TN3	
	n	%	n	%	n	%	n	%
Baseline	0	0%	0	0%	7	46.7%	8	53.3%
At 1 month	1	6.7%	7	46.7%	7	46.7%	0	0%
At 3 months	5	33.3 %	8	53.3%	2	13.3%	0	0%
Pvalue	Baseline v/s 1month–0.003, Baseline v/s 2month–0.119, NS 1month v/s 2month– 0.083, NS							

Table 3: Intergroup comparison of mean levels of Serum cortisol, CPI & TN scores, at baseline, 1month and 3 months follow ups among control & test group.

Cortisol					
	Group	N	Mean	Std.Deviation	Pvalue
At baseline	Control group	15	18.4140	7.58571	0.58, NS
	Test group	15	16.7840	8.40184	
At 1 month	Control group	15	19.3327	7.89071	0.524, NS
	Test group	15	17.3427	8.97630	
At 3 months	Control group	15	22.3493	4.80949	0.083, NS
	Test group	15	17.8760	8.36864	

Change in the level of Serum cortisol					
	Group	N	Mean	Std.Deviation	Pvalue
From baseline to 1 month	Control group	15	-.9187	1.32871	0.631, NS
	Test group	15	-.5587	2.54700	
From baseline to 3 months	Control group	15	-3.9353	9.66287	0.315, NS
	Test group	15	-1.0920	4.71857	

			Intergroup comparison of CPI at baseline				Total
			CPI1	CPI2	CPI3	CPI4	
Group	Control group	n	2	4	6	3	15
		%	13.3%	26.7%	40.0%	20.0%	100.0%
	Test group	n	0	7	7	1	15
		%	0.0%	46.7%	46.7%	6.7%	100.0%
Total		n	2	11	13	4	30
		%	6.7%	36.7%	43.3%	13.3%	100.0%
P value			0.273, NS				

			Intergroup comparison of CPI at 1 month					Total
			CPI0	CPI1	CPI2	CPI3	CPI4	
Group	Control group	n	0	1	3	6	5	15
		%	0.0%	6.7%	20.0%	40.0%	33.3%	100.0 %

	Testgroup	n	1	6	6	2	0	15
		%	6.7%	40.0%	40.0%	13.3%	0.0%	100.0 %
Total		n	1	7	9	8	5	30
		%	3.3%	23.3%	30.0%	26.7%	16.7%	100.0 %
P value			0.014, S					

			Intergroup comparison of CPI at 3 months					Total
			CPI0	CPI1	CPI2	CPI3	CPI4	
Group	Control group	n	0	1	1	6	7	15
		%	0.0%	6.7%	6.7%	40.0%	46.7%	100.0 %
	Test group	n	6	7	1	1	0	15
		%	40.0%	46.7%	6.7%	6.7%	0.0%	100.0 %
Total		n	6	8	2	7	7	30
		%	20.0%	26.7%	6.7%	23.3%	23.3%	100.0 %
P value			<0.001, S					

			Intergroup comparison of TN at baseline		Total
			TN2	TN3	
Group	Control group	n	6	9	15
		%	40.0%	60.0%	100.0%
	Test group	n	7	8	15
		%	46.7%	53.3%	100.0%
Total		n	13	17	30
		%	43.3%	56.7%	100.0%
Pvalue			0.999, NS		

			Intergroup comparison of TN at 1month				Total
			TN0	TN1	TN2	TN3	
Group	Control group	n	0	1	4	10	15
		%	0.0%	6.7%	26.7%	66.7%	100.0%
	Test group	n	1	7	7	0	15
		%	6.7%	46.7%	46.7%	0.0%	100.0%
Total		n	1	8	11	10	30
		%	3.3%	26.7%	36.7%	33.3%	100.0%
Pvalue			0.001, S				
			Intergroup comparison of TN at 3months				

			TN0	TN1	TN2	TN3	Total
Group	Control group	n	0	1	3	11	15
		%	0.0%	6.7%	20.0%	73.3%	100.0%
	Test group	n	5	8	2	0	15
		%	33.3%	53.3%	13.3%	0.0%	100.0%
Total		n	5	9	5	11	30
		%	16.7%	30.0%	16.7%	36.7%	100.0%
Pvalue			<0.001, S				

v. DISCUSSION

An infection-related, host-mediated inflammation known as periodontitis causes the loss of periodontal attachment. Periodontal disease has a complex etiology and pathophysiology. Numerous risk factors, including uncontrolled diabetes, smoking, aging, psychosocial stress, and some psychosomatic diseases like anxiety and depression, contribute to the evolution of periodontal disease.[19]

Stress is a condition of physiological or psychological pressure brought on by unfavorable external or internal stimuli that try to disrupt an organism's normal functioning and that the organism naturally tries to avoid. The hypothalamus-pituitary adrenal cortex axis responds directly to stress. Long-term stimulation of this axis is thought to be harmful to health and to establish a relationship between mental stress and physical sickness.[20] Periodontitis and stress-related hormones have a well-established link. Stress and periodontal disease are positively correlated, according to studies. Cortisol is a crucial glucocorticoid hormone that is generated when the HPA axis is activated because of its capacity to control immune cell recruitment into inflamed tissues and to tip the TH1/TH2 balance in favour of a TH2 dominant response that is responsible for the progression of periodontal disease.[21] Around the world, Covid-19 has caused enormous distress. In addition to the obvious physical signs of infection, it has seriously harmed public mental health. Like other nations, India enacted a nationwide shutdown to stop and restrict the spread of the virus. Research has indicated that people who did not have enough supplies to sustain the lockdown were most affected and family affluence was found to be negatively correlated with stress, anxiety, and depression. Among different professions, students and healthcare professionals were found to experience stress, anxiety, and depression more than others.[22] We hypothesized that periodontal therapy could play vital role in reducing stress in COVID-19 patients. Hence this study was undertaken to evaluate the effect of scaling and root planing on serum cortisol levels in COVID-19 recovered patients. However, no significant difference was seen in serum cortisol levels in both control and study group after periodontal treatment at one and three months. COVID-19 infections lead to higher morbidity and mortality in medically compromised patients. This led to higher psychosocial issues among patients and their family members for longer duration of time, thus reflecting no changes in serum cortisol levels in individuals in our study. The periodontium can serve as the source of bacteria inducing inflammatory responses as well as mediators of inflammation. Those factors could infiltrate saliva through gingival crevicular fluid and further can be aspirated/ swallowed to cause inflammation or infection within the respiratory and gastrointestinal tracts, promoting Covid-19. The periodontal bacteria, such as *Veillonella, Prevotella, Treponema* and *Fusobacterium* were recovered from the bronchoalveolar lavage fluid of patients with Covid-19. Likewise, cytokines (e.g. IL-1β and TNF-α) from periodontally diseased tissues can infiltrate

saliva and be aspirated, and thus cause inflammation or infection within the lungs. Periodontal pathologies, apart from direct effects on SARS-CoV-2 local infection and its consequences, may also produce systemic responses affecting Covid-19. Clinical study documented a higher risk of mortality in Covid-19 individuals who presented bleeding gums, and thus periodontal disease. Periodontal bacteria, as demonstrated for *Fusobacterium nucleatum*, were able to stimulate local production of pro-inflammatory cytokines (e.g. IL-1β, IL-6, IL-8, IL-17, TNF-α) by epithelial cells.[23]

A periodontal intervention can lower the number of bacterial infections and regulate local inflammation, both of which have a good impact on overall health. The normalization/improvement of blood indicators of systemic inflammation (CRP, IL-6, and IL-17), systemic metabolic regulation, as well as a decrease in pneumonia mortality and a reduction in influenza morbidity, have all been linked to effective periodontitis treatment. Such a causal relationship between periodontitis and Covid has not yet been proven. However, maintaining good periodontal health may help people with Covid-19 have a better prognosis.[2]

Implementing periodontal health control and treatment may slow the progression of Covid-19 and stop the virus' attachment, internalisation, and local reproduction in the periodontium. More work needs to be put into validating and establishing a local pharmacotherapeutic strategy that targets SARS-CoV-2 in the oral cavity. It has been shown that vaccination lowers the risk of SARS-CoV-2 infection among local residents and healthcare personnel. The impact of SARSCoV-2 immunisation on periodontal health and disease, however, remains unknown. It can be assumed that vaccinations set off immune system reactions that better regulate viral infections, lessen localised inflammatory reactions in gingival tissues, and help avoid periodontal disease.[25,26] Small sample size, incomplete understanding of COVID-19 disease, weak link between periodontal disease and COVID-19 infection, and lack of proof that antibodies play a role in COVID-19 infection are all drawbacks of our work. To establish a connection between the effects of periodontal treatments and COVID-19 infection, additional well-designed studies should be carried out.

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