

## THE EFFECT OF NON SURGICAL PERIODONTAL THERAPY ON THE SERUM C REACTIVE PROTEIN LEVELS IN GENERALIZED CHRONIC PERIODONTITIS PATIENTS : A CLINICAL STUDY.

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### ABSTRACT

**Background:** Although many studies have compared circulating IL-6 and CRP concentrations in periodontal patients and controls, a limited number of studies have compared systemic inflammatory markers at baseline and follow-up and also Data on whether periodontal therapy affects serum CRP levels are inconclusive. **Aims and Objective:** By the virtue of this study, an attempt was made to evaluate and compare the effect of non surgical periodontal therapy on serum C-Reactive Protein levels in Generalized chronic periodontitis patients. **Material and Method:** A total of thirty patients with Generalised chronic periodontitis, within the age range of 30-70 years, were selected and underwent non surgical periodontal therapy. Further, they were put on a two month follow up after post operative phase for evaluation and comparison of pre and post values. **Results and Conclusion:** The results of our study showed that non surgical periodontal therapy significantly reduces the serum levels of C-reactive protein along with other clinical parameters in patients with generalised chronic periodontitis.

**Keywords :** C-reactive protein, Periodontitis, CRP, Inflammatory marker, Periodontal therapy

### INTRODUCTION

In recent years, periodontal disease has been implicated in the onset and development of cardiovascular diseases, including atherosclerosis, cerebrovascular and coronary artery diseases, rheumatoid arthritis, diabetes mellitus, occlusive respiratory diseases and preterm low birth weight.

Chronic low-grade inflammation is emerging as a conceivable etiologic mechanism linking periodontal disease and the conditions cited above, as well as other systemic diseases. IL-6 is the main procoagulant cytokine (Willerson et al; 2004).<sup>1</sup> It can increase plasma concentrations of fibrinogen and plasminogen activator inhibitor type-1, as well as induce the expression of CRP, which amplifies inflammatory and pro-coagulant

responses.<sup>2-3</sup>

CRP is associated with endothelial cell damage and it has been viewed as a marker of low-grade vascular inflammation.<sup>4</sup> CRP has received a great deal of attention because it is now considered a risk factor for cardiovascular events when its levels are > 0.21 mg/dl and Serum CRP level closely reflects the extent and activity of diseases.

Recent investigations suggested that even a moderate increase in C-reactive protein (CRP) levels (Range of 0.1- 0.3 mg/dl), such as those found in periodontitis patients, may predict a risk for atherosclerosis and coronary vascular diseases.

Although many studies<sup>5-6</sup> have compared circulating IL-6 and CRP concentrations in periodontal patients and

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controls, a limited number of studies<sup>7-10</sup> have compared systemic inflammatory markers at baseline and follow-up.

Data on whether periodontal therapy affects serum CRP levels are inconclusive. Ide et al<sup>7</sup> found no clinically significant effect, whereas Mattila et al<sup>10</sup> and D'Aiuto et al<sup>8</sup> found that periodontal therapy resulted in decreased serum CRP values. So, by the virtue of this study, an attempt was made to evaluate and compare the effect of non-surgical periodontal therapy on serum C reactive protein levels in generalized chronic periodontitis patients.

### **C reactive protein (CRP)**

The CRP was discovered in 1930 by Tillet and Francis.<sup>11</sup> They were investigating serological reactions in pneumonia with various extracts of pneumococci and observed that a non-specific somatic polysaccharide fraction, which they designated fraction C, was precipitated by the sera of acutely ill patients. After the crisis was over, the capacity of the patients sera to precipitate C polysaccharide (CPS) rapidly disappeared, and the C-reactive material was not found in sera from normal healthy individuals.

Avery (1941)<sup>12</sup> and his collaborators characterized the C-reactive material as a protein which required calcium ions for its reaction with CPS (C-polysaccharide) and introduced the term “**acute phase**” to refer to serum from patients acutely ill with infectious disease and containing the C-reactive protein.

CRP was the first protein to be discovered which behaves as an acute phase reactant, and was named for its calcium dependent interaction with the somatic C-polysaccharide of pneumococci, in which CRP recognizes phosphocholine residues. CRP also binds to other substances which contain phosphocholine, including phospholipids, some plasma lipoproteins and the plasma membranes of damaged or apoptotic but not intact cells. In addition, CRP binds specifically to small nuclear ribonucleoprotein particles when these are exposed in dead or damaged cells.<sup>12</sup>

C-reactive protein is normally present in minute quantities but may increase dramatically within 72 hours following tissue injury. CRP is a trace protein in overtly normal, healthy individuals.

## **MATERIALS AND METHODS**

### **Subjects:**

The present study was conducted in the Department of Periodontology & Oral Implantology, M.M. College of Dental Sciences & Research, Mullana, Ambala. The patients were selected from amongst the outpatient department of the Department of Periodontology & Oral Implantology and were explained the whole study protocol.

A written informed willingness to participate was taken in the consent form duly signed by the patient. The study was carried out as per the Declaration of Helsinki (1964) and was also approved by the Institutional Ethical board.

### **Inclusion criteria:**

Patients of either sex, aged between 30 to 70 years, with a minimum of 20 teeth were selected randomly and each subject had probing pocket depth equal to or more than 5 mm accompanied with loss of attachment and/or radiographic evidence of alveolar bone loss.

### **Exclusion criteria:**

Patients were not included in the study if they were pregnant or lactating women; if they had undergone any periodontal treatment or tooth extraction in the last 6 months or taken any anti inflammatory drug therapy, antibiotics, steroids in the last 6 months. Patients with adverse habits such as tobacco and alcohol abuse were also excluded from the study.

### **Clinical assessment :**

All the selected subjects were evaluated clinically to assess the following periodontal measurements: number of teeth, probing pocket depth, clinical attachment levels, plaque index (PI) by Silness & Loe, and gingival index (GI) by Loe & Silness. Four sites were examined on each tooth: facial or buccal, mesial, distal and lingual/palatal. One trained examiner took all measurements and recorded the results. All the patients were evaluated clinically after two months of non-surgical periodontal therapy to reassess the periodontal measurements described previously.

### **Laboratory analysis (Serum C-reactive protein assessment)**

The serum C reactive protein level assessment was carried out by drawing 5ml of fasting venous blood

sample from selected patients pre-operatively and post-operatively. The collected blood sample was allowed to coagulate for 30 minutes at 37°C to get the serum sample by centrifugation using a tabletop centrifuge (REMY Laboratories) at 2000 rpm for 15 minutes. The serum C reactive protein level of each patient was quantified using Turbidimetric Immunoassay for Ultrasensitive Determination (By Quantia- US).

#### Scoring criteria:

MILD	< 0.1 mg / dl
MODERATE	0.1 – 0.3 mg / dl
HIGH	> 0.3 mg / dl

#### Non-surgical periodontal therapy:

The selected patients were treated with non-surgical periodontal therapy which included scaling, root planing and subgingival irrigation with normal saline. Coronoplasty was done in patients where indicated. Oral hygiene measures included the demonstration of manual tooth brushing techniques and patients were instructed and motivated to brush their teeth twice daily and rinse their mouth after every meal. Also, dental floss and interdental brush were advised where indicated. Patients were then periodically monitored after the periodontal therapy at one month for reinforcement of the oral hygiene instructions and then at two months for assessment of clinical parameters and laboratory investigations.

#### Statistical Analysis :

The pre-operative and post-operative values of all the clinical parameters and serum C reactive protein levels, so obtained, were subjected to the statistical analysis. The descriptive statistical analysis was carried out in the study. Results on continuous

measurements are presented on Mean SD (Min-Max). Student's paired 't' Test was used to find the significance of study parameters on continuous scale pre-operatively and post-operatively after two months.

## RESULTS

#### Study Population characteristics

Thirty patients with generalized chronic periodontitis were enrolled in the study with the age range between 32 to 67 years of which 16 were males and 14 were females. All the patients were inhabitants of Haryana state in India and the socio-economic status ranged from fair to poor.

The mean pre-operative serum C- reactive protein level was  $0.65 \pm 0.379$  and the mean post-operative level after two months of non-surgical therapy was  $0.40 \pm 0.341$  which was highly significant ( $P$  value  $< 0.001$ ).

Table 1 shows the mean pre-operative and post-operative values for plaque index, gingival index, probing pocket depth, clinical attachment level and serum C- reactive protein level along with standard deviation and standard error.

Table 2 shows the mean reduction and the percentage reduction in the plaque index, gingival index, probing pocket depth, clinical attachment level and serum C reactive protein level after two months of non-surgical periodontal therapy.

The t value and p value are shown in table 2. P value is significant for all the above mentioned clinical parameters and serum C- reactive protein level which shows that non-surgical periodontal therapy has a positive effect on lowering the levels of serum C- reactive protein.

Table 1: Pre-operative and post-operative mean values

		Mean	N	Std. Deviation	Std. Error Mean
CRP	CRP (mg / dl ) pre	.6500	30	.37959	.06930
	CRP (mg / dl ) post	.4013	30	.34125	.06230
Plaque Index	Plaque Index pre	1.68	30	.387	.071
	Plaque Index post	1.03	30	.409	.075
Gingival Index	Gingival Index pre	2.02	30	.424	.077
	Gingival Index post	1.55	30	.370	.068
Clinical attachment level (mm.)	Clin Attach levels pre	4.21	30	.600	.109
	Clin Attach levels post	3.63	30	.672	.123
Probing pocket depth (mm.)	Probing Depth pre	3.81	30	.425	.078
	Probing Depth post	3.22	30	.538	.098

Table 2: Mean reduction of clinical and laboratory parameters

	Mean	Percentage Reduction	Std. Deviation	t	df	Significance
CRP	.24867	38.46 %	.16055	8.483	29	<.001**
PI	.650	38.69 %	.148	24.059	29	<.001**
GI	.467	23.26 %	.173	14.786	29	<.001**
CAL (gain)(mm.)	.578	13.77 %	.237	13.371	29	<.001**
PPD (mm.)	.583	15.48 %	.258	12.379	29	<.001**

## DISCUSSION

The results of this study shows that non-surgical periodontal therapy significantly lowers the serum levels of C- reactive protein along with other clinical parameters like plaque index, gingival index, probing pocket depth and causes gain in clinical attachment level in patients with generalized chronic periodontitis.

The results of the present study shows a reduction in C reactive protein level which is in line with other studies.<sup>13-16</sup> Conversely, Ide et al<sup>7</sup> and Yamazaki et al<sup>17</sup> did not show significant reductions in CRP levels. The interval between blood collection varied between 1 and 6 months, which may have affected the results for the different studies. CRP was not reduced 6 weeks after periodontal therapy in the study by Ide et al<sup>7</sup> although Mattila et al<sup>10</sup> reported a reduction in CRP levels in this same interval. Iwamoto et al<sup>18</sup> collected blood 1 month after periodontal therapy and observed significant reductions in CRP, whereas Elter et al<sup>19</sup> reported a trend in the reduction of serum levels of CRP during this interval. D'Aiuto et al<sup>8</sup> observed reductions in CRP only after 6 months. In the present study, the blood samples were collected two months after the periodontal therapy because this is considered as an ideal time period to evaluate periodontal healing after non-surgical periodontal treatment.<sup>20</sup>

The baseline values of inflammatory marker, susceptibility of the patients, selection criteria of the studied population, and differences in the severity of periodontal disease may explain some of the discrepancies in the results compared to previous studies. All clinical parameters improved after non-surgical periodontal therapy probably because oral hygiene instructions were given to the patients which were reinforced at one month interval. Oral hygiene measures included the demonstration of manual tooth

brushing techniques and patients were instructed and motivated to brush their teeth twice daily and rinse their mouth after every meal. Also, dental floss and interdental brush were advised where indicated.

Limitations of this study includes a relatively small sample size, which may affect the reproducibility of the results, and the short observation period (2 months). Prospective studies with a larger sample size and longer observation periods are required to evaluate the benefits of reducing serum C reactive protein levels which can be further used as a way of decreasing the global cardiovascular risk for patients.

## CONCLUSION

The observations made by the serum C- reactive protein levels and various other clinical parameters suggest that non-surgical periodontal therapy can be effectively used in significantly lowering the serum levels of C- reactive protein in all the patients with generalized chronic periodontitis. Hence, serum C-reactive protein assessment may be used as a diagnostic and prognostic marker of inflammation and tissue injury which may benefit the medically compromised patients in reducing the risk of various cardiovascular events like – coronary artery diseases, chronic heart diseases, myocardial infarction etc.

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## REFERENCES

- 1) Willerson JT, Ridker PM. Inflammation as a cardiovascular risk factor. *Circulation* 2004; 109 (21, Suppl 1) II 2- II 10.
- 2) Pasceri V, Willerson JT, Yeh ET. Direct pro-inflammatory effect of C-reactive protein on human endothelial cells. *Circulation* 2000; 102: 2165-2168.
- 3) Yeh ET, Anderson HV, Pasceri V, Willerson JT. C-reactive protein: Linking inflammation to cardiovascular complications. *Circulation* 2001; 104: 974-975.
- 4) Blake GJ, Ridker PM. C-reactive protein: A surrogate risk marker or mediator of atherothrombosis. *Am J Physiol Regul Integr Comp Physiol* 2003; 285: R1250- R1252.
- 5) Buhlin K, Gustafsson A, Pockley AG, Frostegard J, Klinge B. Risk factors for cardiovascular disease in patients with periodontitis. *Eur Heart J* 2003; 24: 2099- 2107.
- 6) Craig RG, Yip JK, So MK, Boylan RJ, Socransky SS, Haffajee AD. Relationship of destructive periodontal disease to the acute-phase response. *J Periodontol* 2003; 74: 1007-1016.
- 7) Ide M, McPartlin D, Coward PY, Crook M, Lumb P, Wilson RF. Effect of treatment of chronic periodontitis on levels of serum markers of acute-phase inflammatory and vascular responses. *J Clin Periodontol* 2003 ; 30: 334-340.
- 8) D'Aiuto F, Parkar M, Nibali L, Suvan J, Lessem J, Tonetti MS. Periodontal infections cause changes in traditional and novel cardiovascular risk factors: Results from a randomized controlled clinical trial. *Am Heart J* 2006; 151: 977-984.
- 9) Linden GJ, McClean K, Young I, Evans A, Kee F. Persistently raised C-reactive protein levels are associated with advanced periodontal disease. *J Clin Periodontol*. 2008 Sep;35(9):741-747.
- 10) Mattila K, Vesanen M, Valtonen V et al. Effects of treating periodontitis on C-reactive protein levels: A pilot study. *BMC Infect Dis* 2002; 2: 30-33.
- 11) Tillett WS, Francis Jr T. Serological reactions in pneumonia with a non protein somatic fraction of pneumococcus. *J Exp Med* 1930; 52: 561-585.
- 12) Avery OT, Abernethy TJ. The occurrence during acute infections of a protein not normally present in the blood. - Distribution of the reactive protein in patients' sera and the effect of calcium on the flocculation reaction with C polysaccharide of pneumococcus. *J Exp Med* 1941; 73:173-82.
- 13) Tonetti MS, D'Aiuto F, Nibali L, et al. Treatment of periodontitis and endothelial function. *N Engl J Med* 2007; 356: 911-920.
- 14) Slade GD, Offenbacher S, Beck JD, Heiss G, Pankow JS. Acute-phase inflammatory response to periodontal disease in the US population. *J Dent Res*. 2000 Jan ; 79 (1): 49-57.
- 15) Noack B, Genco RJ, Trevisan M et al. Periodontal infections contribute to elevated systemic C-Reactive protein level. *J Periodontol* 2001; 72 : 1221 – 1227.
- 16) Pederson ED, Stanke SR, Whitener SJ, Sebastiani PT, Lamberts BL, Turner DW. Salivary levels of  $\alpha_2$ -macroglobulin,  $\alpha_1$ -antitrypsin, C-reactive protein, cathepsin G and elastase in humans with or without destructive periodontal disease. *Archives of Oral Biology* 1995; 40: 1151-1155.
- 17) Yamazaki K, Honda T, Oda T et al. Effect of periodontal treatment on the C-reactive protein and proinflammatory cytokine levels in Japanese periodontitis patients. *J Periodont Res* 2005; 40: 53-58.
- 18) Iwamoto Y, Nishimura Y, Soga Y et al. Antimicrobial periodontal treatment decreases serum C reactive protein, Tumor Necrosis factor  $\alpha$  but not adiponectin levels in patients with chronic periodontitis. *J Periodontol* 2003: 74: 1231 – 1236.
- 19) Elter JR, Hinderliter AL, Offenbacher S, Beck JD, Caughey M, Brodala N. The effects of periodontal therapy on vascular endothelial function: a pilot trial. *Am Heart J*. 2006 Jan;151(1):47.
- 20) Nanri A, Moore MA, Kono S. Impact of C-reactive protein on disease risk and its relation to dietary factors. *Asian Pac J Cancer Prev* 2007; 8(2):167-177.

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