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Original Research

Evaluation of CRP levels in patients with periodontitis- A cross-sectional study

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ABSTRACT:
Background: CRP levels have a significant role as a biomarker for confirmation of role of inflammation in chronic periodontitis which may pose as a risk factor for other systemic diseases. **Aim**: The aim of the study was to evaluate serum C-reactive protein levels in chronic periodontitis. **Materials and methods**: This prospective cross-sectional study was comprised of 200 subjects suffering from various grades of periodontitis and normal controls (n=100). Oral prophylaxis and root scaling was performed 3 months prior to blood collection. Samples were collected at three spaced visits and clinical parameters of plaque index, gingival index, clinical loss of attachment and pocket depths were recorded. Statistical analysis was performed by using the Analysis of Variance (ANOVA) tool. **Results**: A significant reduction in serum CRP levels was seen concomitantly with improvement in clinical parameters- CAL and pocket depths. **Conclusion**: It can be concluded from the study that serum CRP levels may act as a biomarker of improvement in periodontal health.
Keywords: Serum, CRP, periodontitis, Pocket depth, Clinical loss of attachment.

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INTRODUCTION

Periodontitis is a chronic inflammatory disease which begins due to biofilm development. Diseases of periodontium are among the most common chronic infections as well as inflammatory disease which is prevalent around the globe. It is found to affect 10 % to 15 % of population and is the most common reason for loss of teeth. Complex interactive mechanisms existing between oral microbial biofilm and host immunological system are main factors responsible for both initiation as well as disease progression. [1, 2]

Periodontal diseases are inflammatory in etiology affecting both soft as well as hard tissues supporting teeth. In gingivitis, the inflammatory process is confined within the supra-crestal periodontal tissues. This causes an ulceration of junctional epithelium leading to loss of clinical attachment. Sites affected with periodontitis demonstrate inflammation of gingiva and loss of connective tissue attachment. The loss of connective tissue attachment is referred to as a pathological detachment of collagen fiber bundles from surface of cementum along with apically migrating junctional epithelium. [3, 4]

The C-reactive protein is an 'acute phase' protein molecule produced as a result of acute inflammatory response. It is synthesized within liver and from major proteinaceous component in plasma. An elevated level of this protein has been observed within 24 to 72 hours of onset of an inflammatory process or damage to tissues. The sharp decline in CRP levels has been seen following the resolution of the inflammatory and disease conditions. [4] The synthesis of C-reactive protein occurs in presence of interleukin-1 (IL-1) and interleukin-6 (IL-6). CRP levels rise rapidly for up to 100 to 1000 times the normal limits following 72 hours of injury to tissues. Its usefulness as an analytical

biomarker is reinforced due to its long half-life and an absence of a circardian rhythm thus, it can be assessed easily using blood testing. [5] It was initially recognized due to its capability to undergo precipitation with the C-polysaccharide Streptococcus pneumonia extract. Its level rises when compared to other serum biomarkers and can be used as an effective tool of damage to periodontal tissues. [6]

Severing of clinical attachment loss or CAL is graded as follows- a) Slight clinical loss of attachment- 1 to 2 mm; b) Moderate clinical loss of attachment- 3 to 4 mm and c) Severe clinical loss of attachment- 5 mm. The C Reactive protein or CRP is synthesized as a response to trauma, infection, hypoxic conditions or periodontitis. Its levels have demonstrated association with obesity, smoking habit, diabetes, triglyceride levels, diabetes and periodontal inflammatory conditions. A positive correlation between CRP levels and severity of periodontal disorders has been proven by many investigators. [3, 4]

The serum levels of C-reactive proteins have also been observed to decline following non-surgical therapy of periodontitis. [7, 8, 9] it is equally efficacious as a biochemical assay even in stored and frozen plasma samples. [10] The normal range of serum CRP level is 0 to 10 mg/l. [10] Performing CRP level assays is important in periodontitis as an elevated levels have been closely associated with numerous systemic conditions. For example, cardiovascular diseases, atherosclerosis etc. [11, 12] It should be born in mind that C-reactive Protein (CRP) levels demonstrate variations among various racial groups. For example, the CRP levels are higher among Black people when compared to the Asian-origin population. [13]

Thus, the aim of this study was to evaluate C-reactive protein (CRP) levels in periodontitis.

MATERIALS AND METHODS

Study design: This was a prospective, cross-sectional study comprised of 300 subjects (age-range between 30 to 65 years) who were diagnosed with periodontal disease. Periodontitis was defined as "probing depths measuring greater than and equal to 5 millimeters and within greater than 2 mm of loss of clinical attachment. Mean age of subjects was found to be 35.9 ± 1.5 years. Ethical clearance was obtained from Institutional Ethical Committee. Informed consent was obtained as per the 'Declaration of Helsinki's guidelines.

Each patient visit was planned at following intervals: a) 1st visit; b) 2nd visit (at a duration of six months) and c) 3rd visit (12 months following 1st visit).

Scaling and/or root planning procedures were done three months before doing first collection of serum samples for C-reactive protein evaluation. Periodontal health examination and serum CRP levels measurements were performed regularly at six month intervals i.e., 2nd and 3rd visits. Inclusion criteria for subject selection were- a) No systemic diseases; b) Patients who were not on any type of medication; c) Those patients who provided their informed consent. Exclusion criteria of the study were- a) Those subjects who were diagnosed with systemic diseases; b) Pregnant or lactating females; c) Subjects suffering from disorders of sleep; e) Patients consuming alcohol; f) Patients with Smoking habit and g) Those suffering from depression.

Periodontal parameters were assessed using the following indices: a) Plaque index by Silness and Loe; b) Gingival index by Loe and Silness), c) Pocket Depths and clinical loss of attachment as per Glavind and Loe. All indices were assessed by s single investigator using a standard Williams's periodontal probe.

Periodontal health assessment:

Subjects with periodontal pockets were evaluated using the following parameters- a) clinical attachment loss measuring greater than 2 millimeters; b) bleeding on probing observed in ≥ 35 % examined sites; c) minimum of one site in four different teeth with pocket depths which measured greater than 4 millimeters. Radiographic examination was done by using either a panoramic or an intra-oral peri-apical (IOPA) radiograph.

Pocket depth evaluation at each visit was done by using the William's periodontal probe along side clinical loss of attachment by walking the probe at six sites around index teeth- a) mesio-buccal, b) middle, c) disto-buccal, d) mesio-lingual, e) lingual and f) disto-lingual. Probing depth measurement was done from margin of gingiva to periodontal pocket base (milli-meters). The losses in levels of clinical attachment were measured from gingival recession till probing depth (millimeters).

Subjects were divided into three categories depending clinical assessment:

a. Group 1- Control subjects with a clinically healthy periodontium with probing depth measuring ≤2 mm with no loss of attachment (n=100);
b. Group 2- Subjects with probing depths which measured ≥5 mm and a clinical attachment loss at greater than 30% sites with varying diseases severity(n=100);
c. Group 3- Subjects with probing depths which measured ≥5 mm and a loss of clinical attachment on 8 or greater numbers of teeth which includes- 1st permanent molars and incisors(n=100).

Procedure for collection of blood samples:

a) Collection and storage method of blood sample [14]

10 ml of blood sample was withdrawn from branchial vein and transferred into a test tube. The test tube containing the blood sample was centrifuged at 3000 rpm for 10 minutes. Separated serum was then, stored at -80 degrees celsius up to further laboratory analysis.

b) Quantification of C-reactive protein levels

Serum CRP levels were assessed using the commercially available ELISA kit (Beckman Coulter Immunotech Company, Mersaiiles, France).

Statistical analysis: Mean ± SD levels were calculated for periodontitis as well as control groups. Inter-group comparisons were done by using ANOVA (Analysis of Variance) test for statistical significance. P value below 0.05 was of statistical significance.

RESULTS AND OBSERVATIONS

Serum C-reactive protein levels were found to decrease during the period of treatment with a mean values of 1.6 ± 1.4mg/dl (males) and 1.3 ± 1.2 mg/dl (females); 2.0±1.8 mg/dl (males) and 1.9 ± 1.6 mg/dl (females); 0.9 ± 0.7 mg/dl (males) and 0.8 ± 2.3 mg/dl (females) during first, second and third visits, respectively in periodontitis while in the control group, mean values were found to be 1.0 ± 2.5 mg/dl (males) and 0.8 ± 0.6 mg/dl (females) (table 1 and graphs 1 and 2). Statistical significance (P= 0.03) was obtained between the study and control groups (table 1). Although, comparison of serum CRP levels with gender-distribution (n= 130 and 170 males in case and control groups, respectively and n= 155 and 145 females in case and control groups, respectively) demonstrated no statistically significant difference (P=0.3) (table 1).

Significant reduction in mean pocket depths in male subjects with periodontitis at three subsequent visits- 2.5 ± 0.5 mm ; 1.4 ± 0.6 mm and 1.8 ± 0.7 mm when compared to normal controls with mean pocket depth of 0.7 ± 0.4 mm was seen. Similarly, decrease in pocket depths was seen among female subjects with periodontitis- 2.6 ± 0.8 mm, 2.3 ± 0.8 mm and 1.5 ± 0.4 mm at the planned visits. On comparison with control subjects, mean pocket depths were noted as 1.0 ± 0.6 in males and 0.8 ± 0.5 mm in females. Statistically significant P values of 0.4 and 0.3 were observed on gender-wise comparisons.

On comparison of clinical loss of attachment, improvement in mean values were noted in both genders, i.e., 6.12 ± 0.78 mm, 2.78 ± 0.6 mm and 1.07 ± 0.9 mm in males and 4.09 ± 0.7 mm, 3.07 ± 0.47 mm and 1.87 ± 0.6 mm, respectively in females. On gender comparisons, significant P values of 0.44 and 0.25 were noted (table 2).

On applying ANOVA, a statistically significant P value of 0.35 was obtained (table 3).

However, no statistically significant value (P=0.56) was obtained between plaque and gingival indices (table 4).

Table 1: Table showing comparisons of serum CRP levels within in study groups

	Periodontitis						Controls	
Visit	First visit		Second visit		Third visit		Baseline levels	
Gender	Males	Females	Males	Females	Males	Females	Males	Females
Mean C-reactive protein concentration	1.6±1.4 mg/dl	1.3±1.2 mg/dl	2.0±1.8 mg/dl	1.9±1.6 mg/dl	0.9±0.7 mg/dl	0.8±2.3 mg/dl	1.0±2.5 mg/dl	0.8 ±0.6 mg/dl

Table 2: Table showing pocket depths at follow-up visits

	Periodontitis						Controls		P value	
No. of visit	First visit		Second visit		Third visit					
Gender	Males	Females	Males	Females	Males	Females	Males	Females	Males	Females
Pocket depth (mm)	2.5± 0.5	2.6± 0.8	1.4± 0.6	2.3± 0.8	1.8±0.7	1.5± 0.4	1.0 ± 0.6	0.8 ± 0.5	0.4	0. 3
Clinical loss of attachment (mm)	6.12 ± 0.78	4.09 ± 0.7	2.78 ±0.6	3.07 ± 0.47	1.07±0.9	1.87±0.6	N.A.		0.44	0.25

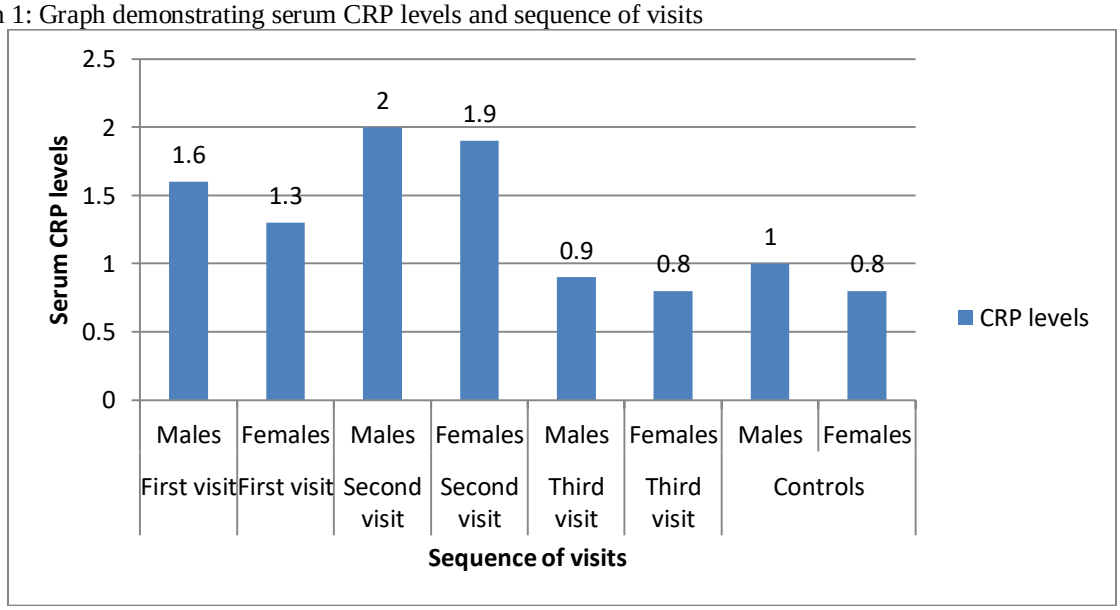
Table 3: Table demonstrating intra-group comparisons in pocket depths, clinical loss of attachment and serum CRP levels

Variable	Sum of squares		F	P value
	Within groups	Between groups		
Pocket depth	22.243	55.346	98.6	0.35
Clinical loss of attachment	18.59	85.67	194.04	
Serum CRP levels	24.56	108.66	376.98	

Table 4: Table showing plaque and gingival indices

Variables	Periodontitis group (mean ± SD)			Control group (mean ± SD)	P value
	First visit	Second visit	Third visit		
Plaque index	1.86 ± 0.25	1.64 ± 0.13	1.76 ± 0.23	1.41 ± 0.10	0.56
Gingival index	1.08 ± 0.06	1.87 ± 0.29	1.63 ± 0.46	1.57 ± 0.34	

Graph 1: Graph demonstrating serum CRP levels and sequence of visits



DISCUSSION

In current study, a statistically significant association between periodontitis and serum C-reactive protein levels was observed in subsequent visits. Similarly, significant gains in clinical attachments were observed in pocket depth when comparisons were made gander-wise. However, no significant difference was noted between plaque and gingival indices.

Esteva-Lima et al in 2020 showed that individuals suffering from periodontitis demonstrated statistically significant (p=0.008) changes in serum levels of C-reactive protein. Also, on performing regression analysis, it was seen that individuals suffering from obesity presented with significantly elevated C reactive protein levels when compared with normal or under-weight persons. An association between obesity and periodontal health has been demonstrated. The adipocytic cells secrete CRP which causes a heightened inflammatory reaction with significant influence of pathogenetic mechanism of periodontitis. [15]

Alade et al in 2018 in their study reported statistically significant P value (P=0.006) on comparing serum levels of CRP and diseases severity in periodontal involvement. [16]

Podzimek et al (2015) in their study on subjects diagnosed with chronic, aggressive form of periodontitis showed an increase in levels of CRP which was concomitant with an increase in disease severity. [17]

Jayaprakash et al (2014) reported higher mean levels of CRP in gingival crevicular fluid (GCF) obtained from patients with periodontitis (2.42 ± 0.47 ng/ml) with comparison to those diagnosed with gingivitis (mean CRP levels= 1.40 ± 0.32 ng/ml) along with healthy subjects (mean CRP levels= 0.56 ± 0.20 ng/ml). [18]

Leite et al (2014) in their study reported that the pre-operative CRP levels in subjects suffering from periodontitis was significantly greater than when assessed in post-operative samples (P <0.0339). [19]
Shoajee et al (2013) reported statistically significant difference between serum CRP levels diagnosed with periodontitis (53332.62 ± 50501.63 pg/ml); gingivitis (3545.41 ± 3061.38 pg/ml) and in healthy controls (3108.51 ± 3574.47 pg/ml). A P value of 0.045 was observed on comparing the mean CRP values in all three study groups. [20]

CONCLUSION

Periodontitis is a multi-etiological inflammatory disease caused by numerous mediators like-CRP, interleukin-6 and tumor necrosis factor-α. These mediators are activated by bacteria which cause inflammatory changes within periodontal tissues or by systemic spreading of bacteria or toxic by-products. These can modify process of athero-genesis and various thromboembolic events which cause stimulation of coagulation pathway and increase blood coagulation. Hence, the assessment of CRP levels in body fluids may pose as a biomarker of risk of cardiovascular disease risk which may be caused by periodontitis.

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