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Original Article

Evaluation of Association between CRP Levels in Chronic Periodontitis patients and Chronic Periodontitis with Cardiovascular Diseases

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ABSTRACT

Background: C-reactive protein (CRP) levels increases to hundreds of mg/L within hours following infection. Studies have shown that serum CRP levels were elevated in periodontal disease. Numerous cross-sectional studies have suggested that chronic periodontitis is a risk factor for cardiovascular diseases (CVD). There is evidence that periodontitis and cardiovascular diseases are linked by inflammatory factors including C-reactive protein. The purpose of the study was to investigate the levels of CRP as a marker of inflammatory host response in the serum of chronic periodontitis patients and in patients with CVD. **Materials and Methods:** Study population included 75 patients; both male and female above 40 years of age were included for the study. Based on clinical (probing depth (PD) ≥5 mm) and radiolographical findings (bone loss more than 5mm from CEJ (cemento-enamel junction) and presence or absence of CVD. The study population were divided into three groups of 25 each, Group I: Chronic periodontitis patients with CVD, Group II: Chronic periodontitis patients without CVD and Group III: Control (without chronic periodontitis and CVD). The control group had PD ≤ 3 mm and no CVD. Venous blood was collected from the patients and C-reactive protein levels were analyzed by latex slide agglutination method using commercially available kit with lower detection limit of 10 mg/L. **Results:** On comparison, CRP values showed significant difference from Group I to III. CRP level was highly significant in Group I when compared with Group II and Group III. **Conclusion:** From this study we can conclude that chronic periodontitis patients, with increased CRP levels are more prone to CVD.

Keywords: Periodontitis, C-reactive protein, Cardiovascular disease, Reactant proteins, Atherosclerosis, Inflammatory cytokines.

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INTRODUCTION

The association between oral diseases and systemic diseases has been extensively discussed in many scientific communities and this association was suspected from centuries, as early as the 7th century, Assyrians proposed the effect of oral health on rest of the body.[1]The main exposure measurement in most studies, associated periodontal disease with systemic diseases. Periodontitis plays a major etiological or modulating role in cardiovascular and cerebrovascular diseases, diabetes, and respiratory diseases.[2] Periodontal disease is a chronic inflammatory process of multifactorial nature that occurs in the tooth supporting tissues in response to accumulation of bacteria, predominantly gram-negative.[3]

Patients suffering from severe periodontitis show increased local production of inflammatory cytokines (IL−7b, TNF and IL−6) and moderate systemic inflammatory response (raised concentration of CRP, fibrinogen and moderate leukocytosis).[4] C−reactive proteins (CRP) is a strong, type−I acute phase protein, which is synthesized by hepatocytes and other cell types like monocytes, endothelial cells, fibroblast and adipocytes which reflects a measure of acute phase response. But chronic periodontitis show the rise of CRP levels in the blood, which is a risk indicator of cardiovascular disease.[5,6]

MATERIALS AND METHODS

The study was designed and conducted on 75 patients (both males & females above 40 years of age) in the Department of Oral Medicine and Radiology at Mamata Dental College and Hospital, Khammam after the institutional ethical committee clearance and patients consent was obtained. The patients were divided into three groups of 25 each – Group I: Chronic periodontitis with CVD, Group II: Chronic periodontitis without CVD and Group III: Controls. The patients with or without CVD (based on electrocardiogram (ECG) changes) were selected based on clinical (probing depth ≥5 mm) and radiolographical findings (bone loss more than 5mm from CEJ) and were included in the study. The patients with PD ≤ 3 mm with no cardiovascular diseases (CVDs) were taken as controls.

Patients having any systemic diseases except cardiovascular diseases, history of any periodontal surgery in past 6 months, any antibiotic or anti-inflammatory medication in past 6 months, any history of trauma and recent tooth extractions or any other infections and uncooperative patients were excluded from the study.

PROCEDURE

Venous blood samples were obtained from the antecubital vein by venipuncture using a standard 2-ml syringe from each patient and transferred to a sterilized test tube. Samples were allowed to centrifuge. Then Serum was separated by using micropipette. Serum levels of CRP were determined by using a latex slide agglutination method with commercially available RHELAX -CRP kit (Sensitivity: 100% & Specificity: 100%), as it has the advantage of rapid performance (within 2 minutes) in comparison to other methods for detection of CRP. Since the lower detection limit of CRP was 10 mg/L, and patients with CRP values <10 mg/L were regarded sero-negative.

RESULTS

The result of the study shows, the mean ± standard deviation in Group I, Group II and Group III, was 151.20±29.20, 115.20±24.85 and 6.16±1.93 respectively. In pair wise comparision of three groups by Tukeys multiple posthoc procedures in comparing Group I versus Group II,, Group I

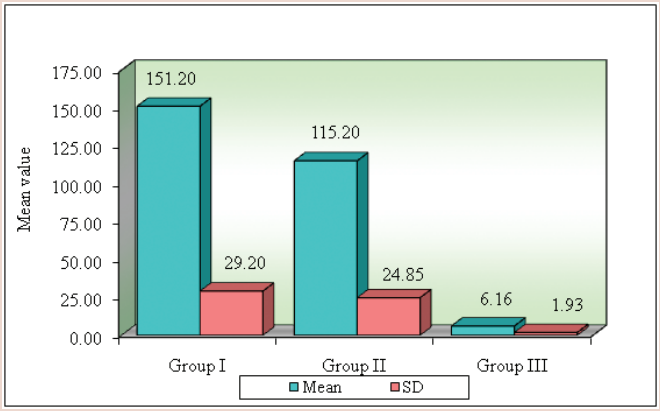

Figure 1: comparison of three groups (I, II, III) with respect to C- Reactive Protein Levels (mg/l).

Table 1: Mean, SD, SE and Coefficient variation in three groups (I, II, III).

Groups	N	Mean	SD	SE	CV
Group I : Chronic periodontitis with CVD	25	151.20	29.20	5.84	19.31
Group II: Chronic periodontitis without CVD	25	115.20	24.85	4.97	21.57
Group III: Control	25	6.16	1.93	0.39	31.32

versus Group III and Group II versus Group III showed a P value of 0.0001*, 0.0001*, and 0.0001*, respectively with a statistical significance between all the three groups. p<0.05 (Table 1, 2 and Figure 1).

DISCUSSION

C-reactive protein [CRP] was the first protein to be discovered which behaves as an acute phase reactant protein produced by the liver in response to pro-inflammatory cytokines.[7] Acute-phase reactant proteins are defined as proteins whose serum concentration is altered by at least 25% in response to inflammation.[8] In 1930 Tilet & Francis were first to identify C-reactive protein in the plasma of patient with pneumonia.[9]C-reactive protein is normally present in mg/ml quantities but may increase dramatically to hundreds of mg/ml within 72 hour following tissue injury. This represents a 100 to 1000 fold increase within hours of tissue damage.[1]

CRP is a trace protein in healthy individuals, the median value of which was determined to be 0.8 mg/L in 483 healthy subjects[7], 90% of whom had CRP levels below 3 mg/L; and 99%, below 10 mg/L.The latter finding has led to the suggestion that values of less than 10 mg/L should be regarded as clinically unimportant.[7] CRP levels can be measured using immunoturbidimetric or immunoelectrophoretic assays or latex slide agglutination method.

In the present study, the patients on clinical examination of periodontal pocket depth ≥ 4 mm[3,] and radiolographical findings, the alveolar bone loss ≥ 5mm from CEJ were included[10]. The CRP levels were measured by latex slide agglutination method with RHELAX-CRP kit. Periodontal infections are strongly associated with increased levels of CRP, and it is widely accepted measure of the level of systemic inflammation.[11]

Table 2: Pair wise comparison of three groups (I, II, III) with respect to C- Reactive Protein Levels (mg/l) by Tukeys multiple posthoc procedures.

Groups	Group I	Group II	Group III
Mean	151.20	115.20	6.16
SD	29.20	24.85	1.93
Group I : Chronic periodontitis with CVD	-		
Group II: Chronic periodontitis without CVD	P=0.0001*	-	
Group III: Control	P=0.0001*	P=0.0001*	-

*p<0.05

In addition the CRP levels were increased in the chronic periodontitis patients with or without CVD when compared to controls, our results were consistent with studies conducted by Freitas COT *et al*[2], Ebersole *et al*[4], Nagarale G *et al*[7], Devi RR *et al*[11], Slade *et al*[12], Noack *et al*[13], Ide *et al*[3], Salzberg *et al*[14] and Armitage *et al*[15], who found a positive correlation between the CRP levels with periodontitis.

Periodontitis and CVD are strongly associated and they potentially share many risk factors like stress, smoking, diet, lack of physical exercise, obesity and atherosclerotic lesions[5]; they share a common pathogenetic process like monocyte hyper responsiveness, formation of atheromas (atherosclerosis) and rise in systemic levels in CRP.[1,10]Moreover the CRP levels were increased in the chronic periodontitis patients with CVD when compared to chronic periodontitis patients without CVD or controls, our results were consistent with studies conducted by Malhotra S[1], Anitha G *et al*[5], Tuter G *et al*[16], Glurich *et al*[17], and Loesche[18] who found a positive correlation between the CRP levels in periodontitis patients with CVD.

In addition it has certain limitations. First, the detection limit of CRP level measurement was 10 mg/L, when compared to other studies conducted by Paraskevas *et al*[19]. Second, smoking also has an adjuvant effect on the CRP levels, where the CRP levels are higher in smokers compared to non-smokers, as reported by Ridker.[20] Third, correlation between CRP levels and severity of periodontitis, as CRP levels increase with the progression of the periodontitis[2,11], which were not recorded in the present study.

The main purpose of the study is to correlate the relationship between periodontal infections and CVD's, the recent data suggests the importance of periodontal infections, which triggers the inflammatory alterations leading to formation of atheromas (atherosclerosis), resulting in risk factor for CVD. The periodontal infections are treatable and preventable. So treating such infections can lower the CRP levels and possibly reduce the risk of CVD.[21]

CONCLUSION

Based on the results of this study. Increased CRP levels in chronic periodontitis patients can be a risk factor for future CVD. Hence, CRP levels can be considered as one of the reference marker for CVD in chronic periodontitis patients.

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