Research Article

Evaluation of C-Reactive Protein Levels in Patients with Cardiovascular Disease and Periodontitis: A Cross Sectional Study

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Abstract

Background and Aim: Several studies have shown elevated C-Reactive Protein (CRP) levels in patients with chronic periodontitis. In addition to periodontitis, CRP being a marker of systemic inflammation, is also used in studies predicting CVD such as myocardial infarction, stroke, acute coronary syndromes and peripheral arterial disease. Therefore, the aim of this study was to evaluate the levels of CRP in patients with CVD only, CVD and periodontitis and periodontitis only. **Materials & Methods:** The study involved 45 patients aged between 35 years-65 years. Periodontal disease status was determined using parameters like Gingival Index, Plaque Index, Probing Pocket Depth (PPD) and Clinical Attachment Level (CAL). A blood sample was obtained from the patient for evaluating CRP levels. For statistical analysis of assessment between the association of several parameters with patient characteristics, Pearson's correlation coefficient (r) was practiced and its significance was verified with t-test. **Results:** The present study did not show any significant association between CRP levels of the three study groups. **Conclusion:** This study indicated that periodontal disease may add an inflammatory burden of the individual thus increasing the risk of future CVD, the results however were not statistically significant. Randomized controlled clinical trials with large sample size and control of confounding factors are needed to evaluate this relationship between periodontal disease, CRP and CVD.

Keywords: C-reactive protein; Periodontitis; Cardiovascular risk; Infection; Chemical mediators

Introduction

CRP is an acute phase reactant, formed in the liver which is a marker of systemic inflammation in the body. [1] CRP levels are found to be elevated in cardiovascular diseases like ischemia and myocardial infarction. [2] CRP can be a predictor for future cardiovascular disease risk if found to be elevated as suggested by clinical studies after adjustment of shared risk factors like aging, diabetes, smoking, high body mass index and other traditional risk factors. [3-5] However, it remains unclear whether elevated CRP levels suggest an etiologic mechanism for atherogenesis or whether it is merely a marker of systemic inflammation suggesting vascular damage. However, it plays a key role in the host defense mechanism by activating complement system and opsonizing the pathogens for phagocytosis. [6]

Periodontal disease is a chronic infection of the supporting tissues of the teeth characterised by tissue destruction seen as bone loss and attachment loss caused by dental plaque. [7] It is also characterised by elevated CRP levels due to inflammatory changes in periodontal tissues. [8] The chemical mediators released during the interaction between periodontal pathogens and the host defense system such as Interleukin-1 (IL-1), Interleukin-6 (IL-6) and Tumor Necrosis Factor-α (TNF- α) are suggested to be responsible for secretion of CRP from liver cells. 6 Relationship also exists between periodontal disease and CVD. [9,10] The purpose of this study was to investigate the associations among CRP levels, periodontal disease and cardiovascular disease.

Materials and Methods

This observational cross sectional study consisted of 45 patients aged amid 35 years-65 years who came to the outpatient Department of Cardiology which were then examined periodontally and department of Periodontology were included, during the period from December 2013 to November 2014.

The patients were allocated to 3 groups

Group I: Subjects with CVD and healthy periodontium (n=15).

Group II: Subjects with CVD and chronic periodontitis (n=15).

Group III: Subjects with chronic periodontitis and without CVD (n=15).

The cardiovascular diseases included in the study comprise of myocardial infarction, arteriosclerosis, Coronary Heart Disease (CHD) and cardiac arrest. The study comprised of subjects, male and female in the age group of 35-65 years;

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having chronic periodontitis with Probing Pocket Depth (PPD) and Clinical Attachment Loss (CAL) ≥ 4 mm. Group III of the study comprised of systemically healthy subjects. Subjects were excluded if there was past history of known systemic diseases (except cardiovascular disease), antibiotic treatment or medication usage from last six months. Smokers and hypertensive patients were disqualified totally from the study. Expectant and lactating women, subjects taking Calcium channel blockers for management of cardiovascular disease, subjects who have undergone periodontal treatment within 6 months of study and aggressive periodontitis patients were eliminated from the study.

All patients gave written informed consent and the Institutional Ethics Committee permitted the study. The study procedure followed the ethical guidelines of the 2013 Declaration of Helsinki. A case history format was specially designed for recording the past medical and dental history of the patients along with the gingival and periodontal examination and other clinical details.

Periodontal assessment

The periodontal condition was measured with clinical and radiographic parameters. Clinical assessment was based on Gingival Index (GI), Plaque Index (PI), Probing Pocket Depth (PPD) at four sites per tooth and CAL at four sites per tooth with a William's graduated periodontal probe. Alveolar bone level was perceived radiographically by means of a normal Ortho Pantomo Graph (OPG).

Biochemical factor

C-reactive protein assessment: A blood sample was obtained at the time of examination for assessing CRP. Directly after specimen assortment, vials were stowed under appropriate conditions. CRP was quantified by Latex method (Beacon Diagnostics Pvt. Ltd.). This kit contains polystyrene latex particles coated with anti-CRP monoclonal antibody. When serum containing CRP levels ≥ 0.6 mg/dL is mixed with the latex reagent, an evidently noticeable agglutination is detected macroscopically within two minutes. No agglutination is observed if the serum sample contains CRP levels <0.6 mg/dL.

Results

The present study was undertaken with the aim to estimate the levels of C-reactive protein in these patients. A total of 45 patients were recruited from the Outpatient Department of Cardiology and Periodontology for the present study. The demographic characteristics are shown in Table 1 along with gender distribution [Table 2].

Out of 15 patients, 5(33.33%) patients were positive for CRP and 10(66.67%) were negative in Group I, 9(60%) patients were positive for CRP and 6(40%) were negative in Group II and 9(60%) patients were positive for CRP and 6(40%) were negative. When pairwise comparisons were made, the CRP levels in all the study groups were not statistically significant [Table 3].

Table 1: Summarization of age of study subjects by groups.

	Group 1	Group 2	Group 3	Total
No. of subjects	15	15	15	45
Mean age	42.6	51.133	45.6	46.444
SD	± 6.310	± 8.991	± 7.452	± 8.297

Table 2: Gender distribution of study subjects by groups.

Gender	Group 1	Group 2	Group 3	Total
Male	9	10	6	25
%	60	66.67	40	55.56
Female	6	5	9	20
%	40	33.33	60	44.44
Total	15	15	15	45
%	100	100	100	100

Table 3: Percentage values of CRP.

	Gropu 1	Group 2	Group 3	Total
>0.6 mg/dL	5	9	9	23
%	33.33	60	60	51.1
<0.6 mg/dL	10	6	6	22
%	66.67	40	40	48.89
Total	15	15	15	45
%	100	100	100	100

Values are mean ± standard deviation unless otherwise indicated; SD: Standard Deviation; S: Significant; NS: Not Significant; (P-value=0.241).

Discussion

The fact that chronic inflammation is one of the characteristic features of periodontal disease is of special interest because, in recent years, evidence has been accumulated implicating low-grade inflammatory process in the pathogenesis of atherosclerosis and subsequent ischemic heart disease. Accordingly, chronic infection and inflammation are now being increasingly considered as new risk factors for the development of atherosclerotic cardiovascular disease and the results of recently conducted studies demonstrate that periodontal disease may increase systemic levels of inflammatory mediators and thus potentially contribute to the inflammation-associated atherosclerotic process. [11,12] There are studies in the literature indicating a relationship between periodontal disease and atherosclerosis indicating atheroma development in periodontitis patients. [13]

The present study was designed to estimate the levels of CRP in patients with periodontal disease andCVD. The study involved 45 subjects of the mean age group of 46.4 years ± 8.2 years [Table 1] and there are 55.56% of males in the study and 44.44% of females [Table 2]. With regards to age, the results were not statistically significant among the three groups, for which random selection could be a cause. Though it has been proposed that subclinical atherosclerosis associated tooth loss and periodontal disease are more prevalent in men as matched to women. [14] American Heart Association (AHA) in 2015 on National health and Nutritional survey suggests that theoccurrence of CHD by age and sex, is equivalent in the age group of 20 yearrs-39 years of age and thus the prevalence increases in men in the age group of 40 years-59 years, 60 years-79 years and above 80 years of age.

When the C-reactive protein was evaluated, it was found that 33.3% of patients were positive for CRP in Group I, 60% in Group II and 60% in Group III. When intergroup comparisons were carried out, the results were not statistically significant.

CRP levels in the range 1 mg/L-3 mg/L have been suggested as risk factors for cardiac and cerebrovascular events. [15] The reason for interest in serum levels of CRP in periodontal disease lies in the fact that epidemiological research indicates the relationship between periodontal disease and CVD. It is conceivable that increased levels of CRP in periodontal disease can explain at least in part the association between periodontal disease and CVD.

Cross sectional and prospective studies have established that elevated peripheral blood levels of several systemic inflammatory markers including CRP are associated with increased risk of cardiovascular diseases and severity of atherosclerosis. [16] It has been proposed that CRP could be elevated due to undiagnosed chronic infectious processes; subsequently their proinflammatory properties may increase the existing inflammatory activity in plaque associated lesions in coronary arteries and thus predispose for cardiac events. [17]

The current elevated levels of CRP in patients of Group II and Group III that is in presence of periodontitis confirm previous reports. [18] Also, CRP may act as an intermediate factor that may link periodontal disease to elevated cardiovascular risk. The number of patients positive for CRP in Group I (Patients with cardiovascular disease and healthy periodontium) was comparatively lower as compared to the other groups, but it was not statistically significant. When intergroup comparisons with respect to CRP levels were carried out in the present study, the outcomes were not statistically significant which could be attributed to the fact that the study groups were not absolutely healthy.

Limitation includes that additional biomarkers apart from C-reactive protein should be used in future studies. Better evidence for such a relation between periodontal disease and CRP levels would be provided by the demonstration that successful treatment of periodontal disease is associated with reduction in CRP levels.

Future scope of the study

1. Microbial analysis of the periodontal pathogens and atherosclerotic plaques should be carried out.
2. Role of other cardiovascular risk factors should be considered.
3. Impact of interleukin genotypes on cardiovascular disease and periodontitis should be considered.
4. Interventional studies should be carried out.

Conclusion

Vascular system of human body is prone for atherosclerosis by various risk factors among which periodontitis is an important and independent risk factor. It is one of the major killers throughout the world and Asians are more prone for atherosclerosis compared to western world. So, it is very essential to implement a comprehensive method for identification of initial atherosclerotic events in high-risk patients and also in general population so that more vigorous preventive measures can be taken. CRP levels provide with an important diagnostic tool for preventing serious CVDs thus reducing the morbidity and mortality of these diseases.

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