ORIGINAL RESEARCH

C- reactive protein levels in patients with periodontal disease: A case control study

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ABSTRACT
Background: To compare c- reactive protein levels in patients with periodontal disease. **Materials & methods:** A total of 30 systemically healthy subjects were divided into two groups: Group I, non-periodontitis subjects and group II, chronic generalized periodontitis patients. The results were analysed using SPSS software. The p – value less than 0.05 was considered significant. **Results:** A total of 30 subjects were included. CRP values of the two groups were significantly different from each other, with CRP levels in the group II greater than those in the group I subjects. **Conclusion:** Increase in serum CRP levels in subjects with generalized periodontitis.
Keywords: Periodontitis, CRP, Inflammation.

INTRODUCTION

Periodontitis is a progressive inflammatory disease of bacterial etiology characterized by gum bleeding, increased probing depth, and attachment loss. The aggression caused by bacterial biofilm stimulates an immune and destructive response to periodontal tissues, leading to collagen destruction, apical migration of junctional epithelium and loss of alveolar bone. [1] Periodontitis is an inflammatory disease of the supporting tissues of the teeth which is caused by specific microorganisms and characterized by extensive destruction of periodontal ligament and alveolar bone with pocket formation, gingival recession or both. Gingivitis is a gum inflammatory disease and clinically the presence of identifiable attachment loss in periodontitis makes it be distinguishable from gingivitis. [2]

CRP is a pentameric plasma protein with homologs in vertebrates and many invertebrates that participate in the systemic response to inflammation. It is a pattern recognition molecule, that is extremely sensitive and non-specific acute-phase marker for inflammation, produced in response to many forms of injury other than binding to specific molecular configurations that are typically exposed during cell death or found on the surfaces of pathogens. [3] It is regulated by cytokines like interleukin-6 (IL- 6), interleukin-1β (IL-1β) and tumour necrosis factor-α (TNF-α). [4,5] C-reactive protein (CRP) is an acute phase protein considered a non-specific and highly sensitive inflammatory marker, produced by liver cells in response to various forms of injury to the body.[6]Systemic infection, trauma and hypoxia are associated with an increased production of CRP. Moreover, inflammatory cytokines, such as interleukin 6, interleukin 1 and tumor necrosis factor α can trigger the production of CRP by hepatocytes.[7] Factors, such as smoking, obesity, diabetes and pregnancy have been associated with high serum levels of CRP.[6] The translocation of bacteria and bacterial products of oral cavity can induce a systemic inflammatory process, characterized by high levels of pro-inflammatory cytokines, including increased levels of CRP.[8] CRP has also been considered a significant risk factor for many systemic diseases, such as cardiovascular disease and type 2 diabetes.[7,9] In this scenario, the hypothesis that individuals with periodontitis present modified levels of CRP has been raised. Hence, this study was conducted to compare c- reactive protein levels in patients with periodontal disease.

MATERIALS & METHODS

A total of 30 systemically healthy subjects were divided into two groups: Group I, non-periodontitis subjects and group II, chronic generalized periodontitis patients. 15 patients in each group were included. Gingival index was calculated. Samples were centrifuged in the centrifuge machine at 3000 rpm for 10 min to separate the serum from blood. All participants were subjected to quantitative CRP analysis using enzyme-linked immunosorbent assay. The results were analysed using SPSS software. The p – value less than 0.05 was considered significant.

RESULT

A total of 30 subjects were included. The two groups showed plaque index with score in group I as 0.60 and in group II was 2.32. The mean CRP (mg/L) levels for both groups were 0.97 and 2.38, respectively. CRP values of the two groups were significantly different from each other, with CRP levels in the group II greater than those in the group I subjects.

Table 1: clinical parameters and serum CRP levels

Groups	PI	GI	CAL(mm)	CRP (mg/dL)
Group I	0.60	0.56	0.70	0.97
Group II	2.32	2.18	4.09	2.38

GI: Gingival index, PI: plaque index, CAL: clinical attachment loss

DISCUSSION

CRP, a marker for acute inflammation, is produced by the liver as a result of various types of injuries, including infectious illnesses. Inflammatory mediators arising from periodontitis may stimulate hepatocytes to produce CRP. Among these mediators, interleukin-1, interleukin-6 and tumor necrosis factor alpha are particularly involved in this process. [6] In this sense, periodontal infection may lead to systemic inflammation with a significant increase in CRP levels. Hence, this study was conducted to compare c-reactive protein levels in patients with periodontal disease.

In the present study, a total of 30 subjects were included. The two groups showed plaque index with score in group I as 0.60 and in group II was 2.32. A study by Esteves- Lima RP et al, individuals with altered C-reactive protein levels showed a higher prevalence of periodontitis than individuals with normal C-reactive protein levels (p=0.008). In the final logistic regression model, individuals with periodontitis were more likely to present altered C-reactive protein than individuals without periodontitis (OR=3.27, CI=1.42-7.52, p=0.005). The alteration of the C-reactive protein levels among individuals with a higher prevalence of periodontitis corroborates clinical evidence that periodontal infection has a systemic impact. [10]

In the present study, the mean CRP (mg/L) levels for both groups were 0.97 and 2.38, respectively. CRP values of the two groups were significantly different from each other, with CRP levels in the group II greater than those in the group I subjects. Another study by Shojaee M et al, subjects were divided into three groups of healthy (n = 30), gingivitis (n = 30), and chronic periodontitis (n = 30), based on Gingival Index (GI) and Clinical Attachment Loss (CAL) indices. 2ml saliva samples were collected from these people and clinical indicators including GI, CAL, Periodontal Pocket Depth (PPD), and Bleeding Index (BI) were assessed. The mean salivary CRP levels were 5332.62±5051.63pg/ml in periodontitis patients, 3545.41±3061.38pg/ml in gingivitis group and 3108.51±3574.47pg/ml in healthy subjects. The statistic analysis showed a significant difference in salivary CRP concentrations between the periodontitis patients and healthy subjects (P=0.045). The results indicate that there is a significant association between periodontitis and salivary CRP concentrations. [11] CRP was first reported by Tillett and Francis in 1930 and was named so because it was discovered as a substance in the serum of patients with acute inflammation that reacted with the C-(capsular) polysaccharide of Pnuemococcus. [12] It was initially thought that CRP might be a pathogenic secretion as it was elevated in people with a variety of illnesses including cancer however, discovery of hepatic synthesis demonstrated that it is a native protein. [13,14] It is normally present in ng/ml quantities but may increase dramatically to hundred of μg/ml within 72hrs following tissue injury. CRP is a trace protein in overtly normal, healthy individuals, the median value being 0.8 mg/l, with an interquartile range of 0.3 to 1.7 mg/l. [15] CRP plays a key role in the host's defense against infection. [16] Kamil et al. in 2011 [17] investigated the effects of treatment of advanced periodontitis on serum CRP levels and the results showed that the serum CRP level decreased significantly after the non-surgical treatment, and the decrease in CRP had a significant relationship with decrease in PI, BI, GI in a direct and linear way .After statistical analysis, it was observed that the periodontitis patients had the highest CRP levels followed in order by gingivitis patients and healthy subjects. These results suggest that periodontal problems can affect the salivary CRP level and enhance it. Afrah et al. in 2013 examined the salivary CRP levels in diabetic and non-diabetic patients with periodontitis. They showed that salivary CRP levels in the control group was lower than the other two groups and there was no significant diff-erences between the diabetic and non diabetic patients with periodontitis. The results of this study indicate that diabetes as a metabolic disease, had no effect on salivary CRP levels but the periodontitis due to its inflammatory nature, increases salivary CRP. [18] Since CRP is an acute-phase reactant produced by the liver in response to diverse inflammatory stimuli, recent studies have shown that their levels are elevated in periodontal disease. However, not all studies have reported an

association between destructive periodontal disease and CRP. These reports may possibly reflect differences in destructive periodontal disease severity or disease progression in different study populations. CRP value <10mg/L were considered normal, while acute bacterial infections have been reported in 80% to 85% of patients with CRP values >100mg/L. [19] Historically, CRP values >10 mg/l were regarded as diagnostic for a bacterial infection, while values <10 mg/l were neglected. This may be because CRP assays in the past were not very accurate and sensitive as in present and thus were less efficient in detecting the levels of CRP <10mg/l. So, these days' high-sensitivity assays for CRP have come into widespread use, allowing laboratories to determine CRP levels in serum as low as 0.15 mg/l. Hage&Szalai reported that CRP can bind phosphoethanolamine and phosphocholine of disrupted bacterial and host cell membranes as well as chromatin, small nuclear ribonucleoproteins, laminin and fibronectin in the presence of calcium. CRP, when bound to these ligands can activate the complement cascade. CRP receptors also exist on macrophages, monocytes and neutrophils and thus bound CRP can target bacterial and damaged host cells for phagocytosis and help direct and amplify the subsequent local inflammatory response to infection, trauma and necrosis. In acute inflammation serum CRP levels exceed 100 mg/L, and the level decreases in chronic inflammation. [20]Further, in periodontitis patients elevated serum CRP is associated with high levels of infection with periodontal pathogens [21,22] Dye et al., [23] reported a high serum titre to Porphyromonasgingivalis and the presence of periodontal disease which are independently related to high CRP levels. In contrast, the titre of A. actinomycetecomitans was not related to the high CRP levels. Similar results for P. gingivalis were also observed by Pitiphat et al.[24]

CONCLUSION

Increase in serum CRP levels in subjects with generalized periodontitis.

REFERENCES

1. Albandar JM. Global risk factors and risk indicators for periodontal diseases. Periodontol 2000. 2002;29:177–206.
2. Laxman VK, Annaji S. Tobacco use and its effects on the periodontium and periodontal therapy. J Contemp Dent Pract. 2008;9:97–107.
3. Black S, Kushner I, Samols D. C-reactive Protein. J Biol Chem. 2004;279:48487–90.
4. Ebersole JL, Cappelli D. Acute-phase reactants in infections and inflammatory diseases. Periodontol. 2000;23:19–49.
5. Bennett JC, Plum F. The acute phase response. Cecil textbook of Medicine Edition 20th. Saunders. Philadelphia. 1996;2:1535–37.
6. Gomes-Filho IS, Coelho JMF, Cruz SS, Passos JS, Freitas COT, Farias NSA. Chronic periodontitis and C-reactive protein levels. J Periodontol. 2011;82:969–978.
7. Bansal T, Dhruvakumar D, Pandey A. Comparative evaluation of C-reactive protein in peripheral blood of patients with healthy gingiva, gingivitis and chronic periodontitis: A clinical and particle-ennanced turbidimetric immuno-analysis. J Indian Soc Periodontol. 2014;18:739–743.
8. Tawfig A. Effects of non-surgical periodontal therapy on serum lipids and C-reactive protein among hyperlipidemic patients with chronic periodontitis. J Int Soc Prevent Communit Dent. 2015;5:49–56.
9. Demmer RT, Trinquart L, Zuk A, Fu BC, Blomkvist J, Michalowicz BS. The influence of anti-infective periodontal treatment on C-reactive protein: a systematic review and meta-analysis of randomized controlled trials. PLoS One. 2013;8:e77441.
10. Esteves-Lima RP, Reis CS, Santirocchi-Júnior F, Abreu LG, Costa FO. Association between periodontitis and serum c-reactive protein levels. J Clin Exp Dent. 2020 Sep 1;12(9):e838-e843.
11. Shojaee M, FereydooniGolpasha M, Maliji G, Bijani A, Aghajanpour Mir SM, Mousavi Kani SN. C - reactive protein levels in patients with periodontal disease and normal subjects. Int J Mol Cell Med. 2013 Summer;2(3):151-5.
12. Tillett WS, Francis T. Serological reactions in pneumonia with a nonprotein somatic fraction of pneumococcus. J Exp Med. 1930;52(4):561–71
13. Pepys MB, Hirschfield GM. C-reactive protein: a critical update. J Clin Invest. 2003;111(12):1805–12
14. Pradhan AD, Manson JE, Rifai N, Buring JE, Ridker PM. C-reactive protein, interleukin 6, and risk of developing type 2 diabetes mellitus. JAMA. 2001;286(3):327–34.
15. Weatherall DJ, Ledingham JGG, Warrell DA. The acute phase response and C-reactive protein. Oxford textbook of Medicine. Edition 3rd. New York: Oxford university press; 1996. pp. 1527–33.
16. Marnell L, Mold C, Du Clos TW. C-reactive protein: ligands, receptors and role in inflammation. Clin Immunol. 2005;117:104–11.
17. Kamil W, Al Habashneh R, Khader Y, et al. Effects of nonsurgical periodontal therapy on C-reactive protein and serum lipids in Jordanian adults with advanced periodontitis. J Periodontal Res. 2011;46:616–21.
18. Afrah AA, Al-Jubouri R. Evaluation of salivary levels of Proteinaceous biomarkers Matrix Metalloproteinase (MMP-8) and C-Reactive Protein (CRP) in type 2 diabetic patients with periodontitis. J Bagh College Dentistry. 2013;25:63–9.
19. 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;74:1007–16.
20. Hage FG, Szalai AJ. C-Reactive Protein Gene Polymorphisms, C-Reactive Protein Blood Levels, and Cardiovascular Disease Risk. J Am Coll Cardiol. 2007;50(12):1115–22.
21. Gabay C, Kushner I. Acute-phase proteins and other systemic responses to inflammation. N Engl J Med. 1999;340:448–54.
22. Reeves G. C-reactive protein. Aust Prescr. 2007;30:74–76
23. Dye BA, Choudhary K, Shea S, Papapanou PN. Serum antibodies to periodontal pathogens and markers of systemic inflammation. J Clin Periodontol. 2005;32:1189–99.

24. Pitiphat W, Savetsilp W, Wara-Aswapati N. C-reactive protein associated with periodontitis in a Thai population. J Clin Periodontol. 2008;35:120–25.