

Comparative Assessment of Serum C-reactive Protein as a Diagnostic Marker in Healthy Individuals, and Patients with Gingivitis and Periodontitis: A Biochemical Study

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Abstract

Introduction: C-reactive protein (CRP) is an acute phase protein and sensitive systemic marker which rises in response to inflammation. Studies indicate that CRP levels are raised in periodontal diseases. **Aim:** To determine the association of CRP with periodontal disease. **Objective:** To measure serum level of CRP in healthy individuals and subjects with gingivitis, healthy individuals and subjects with periodontitis, and in subjects with gingivitis and periodontitis. **Method and Material:** The present study was under taken to determine the serum CRP levels in normal healthy individuals which ranges from 3mg/l to 5 mg/l, in patients having gingivitis and patients having periodontitis without any inflammatory or immunological conditions or diseases. A total of 45 Systemically healthy subjects were selected for the study, subjects were divided into groups A, B and C, with group A having healthy controls, group B with gingivitis, and group C having periodontitis patients. The serum samples were collected and analyzed using slide agglutination technique and immunoturbidity method in the laboratory. **Result:** The result showed significantly raised level of serum CRP in individuals with periodontitis. It was concluded that periodontitis acts as a factor to add to the inflammatory burden of the individual and may result in increased risk of atherosclerosis based on serum CRP concentrations. **Conclusion:** The results of the present study shows that periodontitis is suggestively associated with increased systemic CRP levels.

Keywords: C-reactive, Gingivitis, Inflammatory marker, Periodontal disease.

INTRODUCTION

Periodontal disease is an infection of the periodontal tissues that produces a local and systemic host response as a consequence of local or systemic bacterial burden. Further to this, it is a source of bacteremia. The present-day understanding of the pathogenesis of periodontal disease suggests that the bacteria that cause periodontal disease are recognized to produce a number of factors capable of destroying the tissues of the infected host, which stimulates the host inflammatory progression and releases cytokines and enzymes capable of destroying host tissues.^[1,2] This gives emphasis to the important role that systemic factors, diseases, and conditions may play protagonist in the causation and progression of periodontal disease.^[3] Periodontal disease may be associated with a number of inflammatory diseases including diabetes mellitus, rheumatoid arthritis and cardiovascular ailments.^[3] There are a numerous biomarkers such as interleukin (IL)-6, tumor necrosis factor α ,

and pro-inflammatory cytokines along with C-reactive protein (CRP) suggested to be mediating the inflammatory process. Plasma levels of CRP and IL-6 are suggestively higher in patients with periodontitis, compared to healthy individuals that can be reduced by suitable periodontal management therefore decreasing the risk for systemic infection.^[1,3] Saliva, serum, and gingival crevicular fluid have been evaluated as diagnostic marker vehicles for periodontal disease activity.^[1] Saliva, however, has downsides as its constituents are derived from

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various sources involving salivary glands, serum, crevicular fluid, bacteria cells, epithelial cells, and foreign substances in the oral cavity.^[4] GCF due to its multifarious gingival atmosphere, investigative values cannot be consistent in determining one specific enzyme or biomarker and will be meaningless without knowing the cause of the bacterial insult.^[4] CRP is an acute phase protein found in blood, the intensities of which rise as a reaction to inflammation. Its biological role is to bind to phosphocholine expressed on the surface of dead or dying cells to activate the complement system cascade.^[1,4] It is produced by the liver in response to factors released by adipocytes. It is a member of the pentraxin family of calcium dependent ligand-binding plasma proteins. It is not related to C-peptide or protein C. Plasma CRP is formed only by hepatocytes, mostly under transcriptional mechanism by the cytokine IL-6.^[1,2,5]

Assessing and monitoring CRP values can prove beneficial in determining disease progression or the efficacy of treatments. Blood, can be collected in a serum-separating tube, analyzed in a medical laboratory. Various systematic methods for CRP determination, such as ELISA, immunoturbidimetry, rapid immunodiffusion, and visual agglutination are easily accessible.^[1,6,7]

Aims and objectives

The aim of the study is to determine the association of CRP with periodontal disease.

The objective is to compare:

1. Serum level of CRP in healthy individuals and subjects with gingivitis
2. Serum level of CRP in healthy individuals and subjects with periodontitis
3. Serum level of CRP in subjects with gingivitis and periodontitis.

MATERIALS AND METHODS

Forty-five systemically healthy subjects referred to the Department of Periodontology and Oral Implantology of Chhattisgarh Dental College and Research Institute, in the age group of 30–50 years were invited to participate in the study. Subjects were divided into three Groups A, B, and C, with Group A having healthy controls, Group B with patients presenting chronic generalized gingivitis, and Group C having Chronic periodontitis patients presenting with moderate to severe generalized periodontitis (probing pocket depths [PPD] ≥ 4 mm affecting at least six teeth of the dentition). Patients with a history of diabetes and/or any other systemic infection, patients under non-steroidal anti-inflammatory drug therapy or on any medication that could affect the manifestation of periodontal disease, such as chronic antibiotic use, phenytoin, cyclosporine, anti-inflammatory drugs, calcium channel blockers or corticosteroids, smokers or users of any tobacco products, patients treated by periodontal therapy in past 6 months, and pregnant females or lactating mothers were excluded from the study. The objective and design of study were explained to patients and an informed consent form was signed by every patient before the initiation of the study. Study

protocol was approved by the Institutional Ethical Committee.

Clinical parameters and measurements

The required medical and dental history were taken on the day of appointment. Clinical parameters for inclusion criteria were sulcus bleeding index (SBI), PPD, clinical attachment level (CAL), and body mass index. Clinical evaluation was based on PPD and CAL at six sites per tooth, Muehleman and Son's full mouth SBI taken on four sites per tooth (mesio-buccal, mid- buccal, disto-buccal, and lingual/palatal) fully erupted permanent dentition. A set of standard periodontal and medical parameters were recorded at all visits for all the participants. Venous blood sample was drawn using a standard 2 ml syringe at the time of visit, the samples were obtained in an Eppendorf serum collecting tube containing clot activating factor and instantly stored in a freezer after serum separation. Serum quantification for CRP determination was accomplished using slide agglutination technique with immunoturbidimetry method in the laboratory.

The analysis was performed at the end of the study and in a blind fashion. The mean and standard deviation (Mean $\pm$ SD) values were calculated for all clinical parameters and CRP levels. The mean data were analyzed for the statistical significance by student's t-test.

RESULTS

The result of the study is demonstrated in the tables and graph: (Tables 1-3 and Graph 1)

Table 1: Demographic data of the patients

Number of patients	Males	Female	Mean age
Group A	11	4	27
Group B	10	5	28.93
Group C	11	4	42.2

Table 2: Mean values for clinical variables

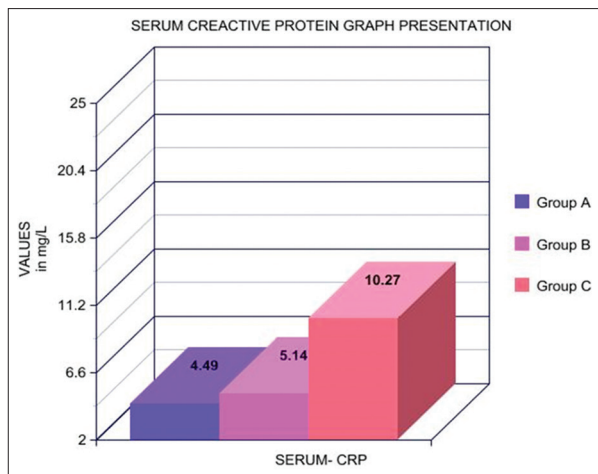
Variables	Group A	Group B	Group C
	Health	Gingivitis	Periodontitis
SBI	0.24	1.98	4.25
PPD	0.89	1.87	5.64
CAL	0.89	2.02	6.40
BMI	20.15	20.01	21.25

SBI: Sulcus bleeding index, PPD: Probing pocket depths, CAL: Clinical attachment level, BMI: Body mass index

Table 3: Proportion of samples with detectable CRP in serum compared between groups

Groups	n	X	SD
Health	15	4.49	2.17
Gingivitis	15	5.14	2.96
Periodontitis	15	10.27	5.30

N: Number of samples, X: Mean, SD: Standard deviation



Graph 1: Antioxidant serum CRP levels in health, gingivitis, and periodontitis

Statistical analysis

The statistical analysis shows that there is a significant difference in the CRP values between gingivitis and periodontitis as well as health and periodontitis, that is, $P < 0.002$, but no significant difference exists between health and gingivitis.

DISCUSSION

Periodontal diseases are infections depicting inflammation and damage of the periodontal supporting tissues. Subdued levels of bacteremia, endotoxins originated from Gram-negative microorganisms and supplementary bacterial components, may stipulate a stimulus for systemic inflammatory reactions such as amplified production of CRP due to triggering of the torrent of inflammatory cytokine assembly by monocytes and other cells in the periodontal tissue.^[2,6] CRP and other acute phase molecules possess wide-ranging functions, including pro-inflammatory properties, initiation of complement factors, neutralization of invasive pathogens, and spur of repair and regeneration tissues.^[2,3] Several recent studies have stressed that even somewhat raised level of CRP is predictors of bigger risk of cardiovascular event among apparently healthy individuals. Despite CRP being the most sensitive markers used to assess the inflammatory status, it still is nonspecific acute phase reaction to most form of tissue damage.^[1,4,8] This study was done to determine periodontitis as a possible cause for the rise in the serum CRP levels in the absence of systemic disease or condition. Serum CRP levels in the present study, the healthy individuals were having 4.49 ± 2.17 mg/l, gingivitis having 5.14 ± 2.96 mg/l, and periodontitis having 10.27 ± 5.30 mg/l with a $P < 0.002$. There was a significant raise in the level of CRP in periodontitis. Despite, out of 15 subjects with periodontitis, two subjects were having values < 5 mg/ml, three

were having values < 10 mg/l, with the highest of 21.41 mg/L. A similar kind of study done by Liu *et al.* 2010, Thakare *et al.* in 2010 where they found raised CRP values at baseline with periodontitis with the exception of high sensitivity kit.^[9,10] In contrast to the present study, Nagrale *et al.* in 2010 found negative CRP with periodontitis, and Lopez *et al.* in 2011 found the similar results.^[11,12]

The present study shows values that are much higher than the values obtained in the recent studies. Based on the results of the present study, it shows that periodontitis is associated with increased systemic CRP levels. Further studies are required to determine the effects of antimicrobial periodontal therapy on systemic inflammatory mediators and the increased risk for cardiovascular diseases. Small sample size limited the statistical analysis of the study. Much more research is required with a larger sample size to come to a definite conclusion.

CONCLUSION

The results of the present study shows that periodontitis is suggestively associated with increased systemic CRP levels.

REFERENCES

1. Aurer A, Jorgić-Srdjak K, Plancak D, Stavljenić-Rukavina A, Aurer-Kozelj J. Proinflammatory factors in saliva as possible markers for periodontal disease. *Coll Antropol* 2005;29:435-9.
2. Dennison DK, Van Dyke TE. The acute inflammatory response and the role of phagocytic cells in periodontal health and disease. *Periodontology* 2000 1997;14:54-78.
3. Machado V, Botelho J, Escalda C, Hussain SB, Luthra S, Mascarenhas P, *et al.* Serum C-Reactive protein and periodontitis: A systematic review and meta-analysis. *Front Immunol* 2021;12:706432.
4. Garcia RI, Michellem MM, Krall EA, Relationship between periodontal disease and systemic health. *Periodontology* 2000 2001;25:21-36.
5. Mysak J, Podzimek S, Vasakova J, Mazanek J, Vinsu A, Duskova J. C-reactive protein in patients with aggressive periodontitis. *J Dent Sci* 2017;12:368-74.
6. 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;12:e838-43.
7. Pepys MB, Hirschfield GM. C-reactive protein: A critical update. *J Clin Invest* 2003;111:1805-12.
8. Lau DC, Dhillon B, Yan, H, Szmitko PE, Verma S. Adipokines: Molecular links between obesity and atherosclerosis. *Am J Physiol Heart Circ Physiol* 2005;288:H2031-41.
9. Liu J, Wu Y, Ding Y, Meng S, Ge S, Deng H. Evaluation of serum levels of C-reactive protein and lipid profiles in patients with chronic periodontitis and/or coronary heart disease in an ethnic Han population. *Quintessence Int* 2010;41:239-47.
10. Thakare KS, Deo V, Bhongade ML, Evaluation of the C-reactive protein serum levels in periodontitis patients with or without atherosclerosis. *Indian J Dent Res* 2010;21:326-9.
11. Nagrale SG, Ravindra S, Thakur S, Setty S. Efficacy of chair side diagnostic test kit for estimation of C-reactive protein levels in periodontal disease. *J Indian Soc Periodontol* 2010;14:213-6.
12. López R, Baelum V, Hedegaard CJ, Bendtzen K. Serum levels of C-reactive protein in adolescents with periodontitis. *J Periodontol* 2011;82:543-9.