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Original Research

Clinico-biochemical evaluation of relationship between periodontitis and C-reactive protein: A case control study

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ABSTRACT:
Aim: The aim of this study is to ascertain C-reactive protein levels in patients with periodontitis and to correlate it with clinical parameters. **Methods**: The case control study consisted of 100 test group patients diagnosed with periodontitis and 100 control group patients with no periodontitis using clinical parameters. A detailed case history was recorded. Clinical parameters like plaque index, gingival index and probing pocket depth and biochemical parameters like C - reactive protein were assessed. The values obtained were compared by statistical analysis using student's T- test and Pearsons' correlation. **Results**: Plaque index, gingival index, probing pocket depth and C-reactive protein levels were significantly higher in test group as compared to control group ($P \leq 0.001$). Significant positive correlation was observed between the clinical parameters and biochemical parameters. **Conclusion**: Periodontal status was poorer in patients of test group as compared to control group. The c-reactive protein levels were notably higher in patients with test group as compared to control group. A significantly positive correlation was seen between test and control group.
Keywords: Periodontal disease, C - reactive protein, periodontitis, inflammation, acute phase proteins.

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INTRODUCTION:
Periodontal disease is a multifactorial infectious process resulting from a complex interplay between chronic bacterial infection and the inflammatory host response, leading to destruction of tooth-supporting tissues which is irreversible and finally causes loss of tooth[1]. Active periodontal inflammation contributes to a prothrombotic state by recurrent bacteremia, platelet activation, and elevated clotting factors, which increase the risk of infection of systemic organs like cerebrovascular systemand cardiovascular system. [2]The bacterial bye products along with inflammatory cells, trigger a cell-mediated inflammatory response and produces lipopolysaccharides and proinflammatory cytokines which includes tumour necrosis factor, interleukin 1 and 8 . Release of LPS into the periphery activates both inflammatory cells, and endothelial cells and cytokines are carried to the liver where they induce the production of acute-phase proteins such as C-reactive protein (CRP)[3].

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. 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. CRP has also been considered a significant risk factor for many systemic diseases, such as cardiovascular disease and type 2 diabetes[4]. Many studies have evaluated the fact that periodontitis may be associated with changes in the

levels of inflammatory markers but only few studies have assessed the relationship between periodontitis and levels of CRP. Scientific evidence on this relationship is still controversial and reduction in CRP levels is not always observed after periodontal therapy[5]. Therefore, we have performed this case control study to assess the relationship between periodontitis and c- reactive proteinlevels correlating the clinical parameters.

MATERIALS AND METHODS:
Test group included 100 patients who were diagnosed with periodontitis from their case history and clinical examination and control group included 100 age matched patients selected from Department of Periodontology and Implantology, Jaipur Dental College and were systemically healthy.

INCLUSION CRITERIA
- Both male and female patients were considered.
- Age : 35-70 years

Exclusion criteria
- Patients who are completely edentulous
- Female patients who are pregnant or lactating
- Patients who have undergone any periodontal therapy in previous 12 months
- Patients who were unable to give informed consent
- Patients with any other known systemic disease.
- Patients on any known medication

CASE HISTORY:
Informed written consent was obtained from all patients or their blood relations/spouse. A detailed medical and dental history was recorded for every patient which included diet, family history, habits like smoking, alcohol intake, and tobacco. Patients in the control group were age matched with test group. Patients were also assessed for systemic conditions like diabetes, hypertension to rule out other risk factors for periodontal disease. Out of 587 patients examined, about 216 patients gave no history of any systemic disease. 16 patients were unable to give consent for the study so they were excluded. Rests of the patients were recruited for study in the test group and control group.

Periodontal examination:
The patients were subjected to a complete periodontal examination by the same clinician. Patients were examined in supine position with the help of a regular torch for illumination, a mouth mirror, a periodontal probe (UNC-15). Clinical parameters like Gingival Index: (Loe and Silness, 1963)[6], Plaque index: (Silness and Loe 1964)[6]and Probing pocket depth (using UNC 15 periodontal probe)[7] were assessed. Two milliliters of blood sample was withdrawn from anticubital fossa to assess C-Reactive protein[8]. The data obtained was subjected to statistical analysis.

STATISTICAL ANALYSIS:
Results of the following study were subjected to statistical analysis by applying Students' T Test and Pearson's correlation.

RESULTS:
The comparison between the clinical and the biochemical parameters was done between control group and the test group.

Control group:
The mean (mean ± SD) plaque index, gingival index and probing pocket depth was calculated to be 0.81±0.13, 0.91± 0.10 and 3.86±0.70 respectively. The mean (mean ± SD) serum C - reactive protein levelwas calculated to be 0.94± 0.24(Table 1).

Test group:
The mean (mean ± SD) plaque index, gingival index and probing pocket depth was calculated to be 1.20±0.15, 1.40±0.09 and 6.52±1.09 respectively. The mean (mean ± SD) serum C - reactive protein levelwas calculated to be 6.90±1.41(Table 1).

On correlation of plaque index, gingival index, probing pocket depth and c-reactive protein level of test and control group it was found to be more for test group which was statistically significant ($p \leq 0.001$)(Table 2). In this study it was also observed that males, regular alcohol drinkers, smokers and non vegetarians were more affected by periodontal disease. The difference was statistically significant. ($p \leq 0.001$) (Table 3).

Table 1: Statistical analysis of clinical and biochemical parameters using Students' T- Test

PLAQUE INDEX(PI)							
Variable	**Disease**	**N**	**Mean**	**Std Dev**	**Std Err**	**Minimum**	**Maximum**
PI	Control	100	0.81	0.1374	0.0194	0.6	1
PI	Test	100	1.206	0.1557	0.022	1	1.5
PI	Diff (1-2)		-0.396	0.1468	0.0294		
Variable			**Method**	**Variances**	**DF**	**t Value**	**Pr > |t|**
PI			Pooled	Equal	98	-13.48	**<.0001**
PI			Satterthwaite	Unequal	96.5	-13.48	<.0001
GINGIVAL INDEX(GI)							
Variable	**Disease**	**N**	**Mean**	**Std Dev**	**Std Err**	**Minimum**	**Maximum**
GI	Control	100	0.916	0.1037	0.0147	0.7	1.2
GI	Test	100	1.408	0.0966	0.0137	1.2	1.6

GI	Diff (1-2)		-0.492	0.1002	0.02		
Variable			**Method**	**Variances**	**DF**	**t Value**	**Pr > |t|**
GI			Pooled	Equal	98	-24.55	**<.0001**
GI			Satterthwaite	Unequal	97.5	-24.55	<.0001
PROBING POCKET DEPTH(PPD)							
Variable	**Disease**	**N**	**Mean**	**Std Dev**	**Std Err**	**Minimum**	**Maximum**
PPD	Control	100	3.86	0.7001	0.099	3	5
PPD	Test	100	6.52	1.0925	0.1545	5	8
PPD	Diff (1-2)		-2.66	0.9175	0.1835		
Variable			**Method**	**Variances**	**DF**	**t Value**	**Pr > |t|**
PPD			Pooled	Equal	98	-14.50	**<.0001**
PPD			Satterthwaite	Unequal	83.4	-14.50	<.0001
C-REACTIVE PROTEIN(CRP)							
Variable	**Disease**	**N**	**Mean**	**Std Dev**	**Std Err**	**Minimum**	**Maximum**
CRP	Control	100	0.944	0.24	0.0339	0.5	1.5
CRP	Test	100	6.904	1.4155	0.2002	4	9.7
CRP	Diff (1-2)		-5.96	1.0152	0.203		
Variable			**Method**	**Variances**	**DF**	**t Value**	**Pr > |t|**
CRP			Pooled	Equal	98	-29.35	**<.0001**
CRP			Satterthwaite	Unequal	51.8	-29.35	<.0001

Table 2: Correlation of clinical and biochemical parameters using Pearsons' correlation

Correlations					
		plaque index	**gingival index**	**pocket probing depth**	**CRP levels**
plaque index	Pearson Correlation	1	.844(**)	.851(**)	.873(**)
	Sig. (2-tailed)		.000	.000	.000
gingival index	Pearson Correlation	.844(**)	1	.836(**)	.905(**)
	Sig. (2-tailed)	.000		.000	.000
pocket probing depth	Pearson Correlation	.851(**)	.836(**)	1	.910(**)
	Sig. (2-tailed)	.000	.000	.000	
CRP levels	Pearson Correlation	.796(**)	.873(**)	.905(**)	1
	Sig. (2-tailed)	.000	.000	.000	
** Correlation is significant at the 0.01 level (2-tailed).					

Table 3: Comparison of the variables assessed

Variables	**Cases**	**Controls**	**Chi Square Value**	**p Value**
Age	92.59±3.97	92.53±4.47	0.567	0.4061[a]
Gender				
Females	25	36	7.2936	0.0197[*b]
Males	75	64		
Smoking[1]				
Never	8	62	10.794	0.00453[*b]
Ex-Smoker	22	12		
Current	70	26		
Alcohol[1]				
Never	29	52	14.653	0.000658[*b]
Occasional	13	15		
Regular	58	33		
Family History				
Positive	72	33	14.5859	0.0001[*b]
Negative	28	67		
Diet3				
Vegetarian	27	62	9.0036	0.0027[*b]
Non-Vegetarian	73	38		
* Statistically Significant				
[a] Student's t-Test				
[b] Chi Squared Test				

DISCUSSION:

Periodontal diseases constitute one of the most common infections in the world. Its initiation and progression is influenced by a wide variety of determinants and factors, including subject characteristics, social and behavioral factors, systemic factors, genetic factors, tooth level factors, microbial composition of dental plaque and other emerging factors.[9] Periodontitis are associated with elevated markers of inflammation which are also an important risk factor for systemic diseases.

CRP is a component of the innate immune system with an ability to recognize the foreign pathogens, phospholipids of damaged cells and also binds to the phosphocholine. It activates the complement system by bounding to one of its ligands, and it can also bind to phagocytic cells. CRP plays an important role in inflammatory processes and host responses to infection whichincludes the complement pathway, apoptosis, phagocytosis, nitric oxide [NO] release, and theproduction of cytokines, like interleukin-6 and tumour necrosis factor-α [10]. Long-standing periodontal disease and raised CRP levels enhances the risk of cardiovascular disease, cerebrovascular accidents and preterm low birth weight infants. Periodontitis with all its clinical symptoms and consequences can also pose a potential risk of systemic exposure to inflammatory stress with increased values of the markers of inflammation [leukocytes and neutrophils, CRP, and fibrinogen], and thus create a close connection with the systemic status of the patients . Literature states there is a strong association between periodontitis and cardiovascular disease with CRP and IL-6 as risk factors. A number of studies have reported elevated serum CRP levels in periodontitis subjects[11].

In the present study, we assessed the relationship between C-reactive protein levels and periodontal disease. Periodontal examination of patients in test group revealed that the mean values of clinical parameters like plaque index, gingival index and probing pocket depth were significantly higher than that of control group patients ($p \leq 0.001$). The results of this study are in accordance with the study conducted by Bolla V et al.; 2017[12] which assessed the associations of different periodontal parameters with CRP levels and found out that patients with chronic periodontitis had higher CRP levels than the control population. Torrungruang K et al.; 2019[13] also conducted a study to assess the relationship between periodontal disease and CRP levels in which the values of mean plaque index, gingival index probing pocket depth of subjects with chronic periodontitis were significantly higher when those compared to control group.Gomes-Filho IS et al.; 2011[4] also explained the association of periodontal disease with elevated CRP levels and concluded that patients with CRP levels > 3mg/dl had higher loss of attachment than controls. Periodontal disease is a chronic inflammatory disease with periods of acute exacerbations and quiescence. Oral microorganisms including periodontal pathogens enter the blood stream during transient bacteremia and play an important role in the development and progression of systemic diseases.[1] Deshpande et al.; 1998[14] reported that organisms such as Aggregatibacter actinomycetem comitans, Porphyromonas gingivalis and Tanerella forsythia interact with neutrophil and monocyte T cell axis to elicit an acute and chronic inflammatory response. These results provide indirect evidence for a causal role of periodontitis in pathogenesis of atherosclerosis.

In the test group the mean C- reactive protein level was significantly higher than control group ($p \leq 0.001$). This was in accordance with study done by J. David Curb 2003[15]who assessed the relation between C-reactive protein levels and stroke and found out that C-reactive protein quartile increased over time to a 3.8-fold excess in patients with stroke. Balwant Rai 2009[16]inhis study alsofound that c-reactive protein was raised significantly in periodontitis patients as compared to controls.Elevated levels of C-reactive protein are related to higher risk of myocardial infarction, stroke, periodontal disease and peripheral vascular disease. Inflammation contributes to the progression of cardiovascular and cerebrovascular disease because inflammatory cells cause local weakening of atherosclerotic plaques, leading to rupture and thrombus formation. Moreover, C-reactive protein induces monocyte to express tissue factor, the initiator of the extrinsic pathway of coagulation, which further stimulates vascular thrombosis[17].

On correlating biochemical parameters with the clinical parameters in the test and control group, a significant positive correlation was found. Hence in the present study it was seen that the patients in test group had poorer periodontal status and elevated CRP tests level as compared to control group. The foundation of the association between periodontal disease and other systemic inflammatory conditions is chronic inflammation, and individuals with periodontitis have greater risk of presenting endothelial dysfunction and cerebrovascular diseases. Therefore, the pathogeny of destructive periodontal disease and atherosclerotic disease can be related through common inflammatory cascade which has a direct effect on elevated biochemical parameters[2].

Periodontal disease and elevated inflammatory makers like CRP become common risk factors for systemic diseases like diabetes, hypertension, hyperlipidemia,. In our study, the test group included patients who gave no history of any other systemic disease. But still some

underlying unknown systemic factor may also be involved or sometimes multiple risk factors can play a role in causing periodontitis and elevated CRP levels.
In the course of our study the other risk factors responsible for causing periodontal disease were also assessed which include age, gender, family history of systemic diseases, diet, smoking, and alcohol. All these factors increase the risk of periodontal disease which in turn are responsible for elevating the CRP levels.

Age:
In the present study the mean age was (mean± SD) 42.10± 4.70 Periodontitis was an independent risk factor in young patient and men. Research identified that age is associated with periodontal disease, and clinical AL was significantly higher among individuals aged 60-69 years compared with group of adults 40-50 years[18]. This may be due to difference in health awareness among people and decreasing role of periodontitis as an independent risk factor for systemic disease in increasing age.

Gender:
In the present study it was seen that males (66%) were more affected by periodontitis as compared to females (34%). This finding in our study correlates with the study conducted by Effie Ioannidou(2017) who found out that periodontitis has a documented higher prevalence in men (~57%) compared to women (~39%) signifying a possible sex/gender bias in disease pathogenesis[19].

Family history:
It was observed from the results of the present study that people having a family history of were more likely to be affected with periodontal disease than those with no family history. Possibly, a family history of periodontal disease may be an early marker of shared genetic, epigenetic and environmental influences associated with periodontal disease risk, and allow for early intervention to minimise adverse environmental factors (Dara M Shearer et al 2011)[20].

Diet:
It was observed from the results of the present study that non vegetarians were more affected with periodontal disease as compared to vegetarians. Yvonne Bachmann in 2012[21]concluded that vegetarians had significantly lower probing pocket depths, bleeding on probing, and periodontal screening index scores, better oral hygiene index scores and fewer mobile teeth. A recent study done by IStaufenbiel2013[22] also revealed that vegetarians had better periodontal conditions.

Smoking:
In the present study on statistical analysis of the results obtained it was seen that smokers were more affected with periodontal than nonsmokers. The present study goes in hand with the study done byPreber et al.; 1980[23] who found that people with smoking habits were more prone to develop periodontal disease.Cigarette smoking could cause a lowering of the oxidation-reduction potential, and this could cause an increase in anaerobic plaque bacteria which can lead to formation of atheromas and also can lead to periodontal attachment loss[2].

Alcohol consumption:
In the present study on statistical analysis of the results obtained it was seen that regular alcohol drinkers were more affected with periodontitis as compared to those who do not drink alcohol regularly. Alcohol affects the host response; impairs neutrophil, macrophage, and T-cell functions; and increases the frequency of infections. Ethanol, a constituent of alcohol beverages stimulates bone resorption, suppresses bone turnover, and may have a direct toxic effect on periodontal tissues[2].

SUMMARY AND CONCLUSION:
The results of the statistical analysis concluded that:
1. Statistical analysis showed a significant difference between test and control group with higher values of clinical parameters (i.e. Plaque index, Gingival index and Probing Pocket Depth) recorded in test group. Hence, we can conclude that periodontal status was poorer in patients of test group as compared to control group.
2. Statistical analysis showed a significant difference between test and control group with higher values of C reactive protein level recorded in test group. Hence, we can conclude that that the CRP levels were notably higher in patients with test group as compared to control group.
3. When the biochemical parameters were correlated with clinical parameters a significantly positive correlation was seen between test and control group.
In addition to this it was also seen that males, non-vegetarians, smokers, regular alcohol drinkers and patients with positive family history were found to be more affected with periodontitis. Periodontal disease and systemic diseases have complex etiologies and risk factors and also share pathogenic mechanisms. In this study, individuals with periodontitis presented higher levels of CRP in comparison with individuals without periodontitis. This positive association reinforces the theory that periodontitis has a significant influence on the levels of inflammatory biomarkers, suggesting that periodontal infection can lead to a systemic impact, favoring the development and aggravation of other pathologies. However, additional studies, in particular intervention and longitudinal studies, with special attention to confounding factors, are needed to further assess the association between periodontitis and serum levels of CRP.

REFERENCES:

1. Kinane DF. Causation and pathogenesis of periodontal disease. Periodontol 2000. 2001; 25:8–20.1.
2. Rose LF, Genco RJ, Cohen DW, Mealey BL, ed. Periodontal medicine, Hamilton: BC Decker; 2000.
3. Jayaprakash D, Aghanashini S, Vijayendra RR, Chatterjee A, Rosh RM, Bharwani A. Effect of periodontal therapy on C-reactive protein levels in gingival crevicular fluid of patients with gingivitis and chronic periodontitis: A clinical and biochemical study. JIndian Soc Periodontol2014;18:456-60.
4. Gomes-Filho IS, Coelho JMF, Cruz SS, Passos JS, Freitas COT, Farias NSA, et al. chronic periodontitis and C-reactive protein levels.J Periodontol. 2011;82:969-978.
5. Quintero AJ, Chaparro A, Quirynen M, Ramirez V, Prieto D, Morales H, et al. Effect of two periodontal treatment modalities in patients with uncontrolled type 2 diabetes mellitus: A randomized clinical trial.J Clin Periodontol. 2018;45:1098-1106.
6. Loe H. The gingival index, the plaque index and the retention index; system. J. Periodontol 1967; 38:610**.**
7. EickholzP;Clinical periodontal diagnosis: probing pocket depth, vertical attachment level and bleeding on probing. Perio 2004; Vol 1, Issue 1: 75–80.
8. RidkerPM .C - reactive protein: A Simple Test to Help Predict Risk of Heart Attack and Stroke. Circulation2003;108:81-85
9. Guyton and Hall. Textbook of Medical Physiology. Saunders; 12th edition 2010
10. Albandar JM. Global risk factors and risk indicators for periodontaldiseases. Periodontol 2000. 2002;29:177-206.
11. Nunn ME. Understanding the etiology of periodontitis: an overview of periodontal risk Factors. Periodontol 2003; 32:11-23.
12. Bolla V, Kumari PS, Munnangi SR, Kumar DS, Durgabai Y, Koppolu P. Evaluation of Serum C-reactive Protein Levels in Subjects with Aggressive and Chronic Periodontitis in Comparison with Healthy Controls: A Clinico-biochemical Study. Int J App Basic Med Res.2017;7:121-124.
13. . Torrungruang K, Katudat D, Mahanonda R, Sritara P, Udomsak A. Periodontitis is associated with elevated serum levels of cardiac biomarkers-soluble ST2 and C-reactive protein. J Clin Periodontol.2019;46:809-818.
14. Deshpande RG, Khan MB, Genco CA; Invasion of aortic and heart endothelial cells by Porphyromonasgingivalis. Infect, immune 1998; 66;5337-43
15. Curb JD, Abbott RD, Rodriguez BL et al C - reactive protein and the future risk of thromboembolic stroke in healthy men. Circulation. 2003; 107:2016-2020.
16. Rai B, Kaur J, Kharb S, Jain R, Anand SC and Singh J; Peripheral blood and C-reactive protein levels in chronic periodontitis, African Journal of Biochemistry Research Vol.3 (4), pp. 150-153, April, 2009.
17. Pepys MB and Hirschfield GM; C-reactive protein: a critical update .J. Clin. Invest.2003 111:1805–1812**.**
18. Rheu GB, Ji S, Ryu JJ, Lee JB, Shin C, Lee JY, et al. Risk assessment for clinical attachment loss of periodontal tissue in Korean adults. J Adv Prosthodont. 2011;3:25–32.
19. Ioannidou E. The Sex and Gender Intersection in Chronic PeriodontitisFront. Public Health 2017; 5:189.
20. Dara M Shearer, W. Murray Thomson, Avshalom Caspi, Terrie E Moffitt, Jonathan M Broadbent, and Richie Poulton. Intergenerational continuity in periodontal health: findings fromthe Dunedin Family History Study.J Clin Periodontol. 2011 April ; 38(4): 301–309.
21. Bachmann Y. Periodontal conditions in vegetarians: A clinical study. European Journal of Clinical Nutrition 2012;66: 541-548.
22. Staufenbiel I, Weinspach K, Forster G, Geurtsen W, Gunay H; Periodontal conditions in vegetarians: a clinical study. European Journal of Clinical Nutrition 2013,67(8) 836-840.
23. Hillbom M, Haapaniemi H,Juvela S,Palomäki H, Numminen H, Kaste M. Recent alcohol consumption, cigarette smoking and cerebral infarct in young adult. Stroke 1995; 26; 40-45.
24. Preber H, Kant T, Bergström J. Cigarette smoking, oral hygiene and periodontal health in Swedish army conscripts. J Clin P 1980; 7; 2.