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Serum ACP And CRP Response To Periodontal Therapy

Keywords
Acid phosphatase, C-reactive protein, chronic periodontitis, scaling and root planing, biomarkers, periodontal therapy

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Abstract

Background: Chronic periodontitis is characterized by hyperplastic tissue damage and inflammation. The inflammatory cells C-reactive protein (CRP) is a systemic acute phase proteins and acid phosphatase (ACP) is a local osteoclastic enzyme. Their relative response of non-invasive treatment for periodontal disease is under researched.

Objective: To evaluate serum levels of ACP and CRP in long-term periodontal disease patients compared to healthy controls, assess their changes after root planning and scaling (SRP), and examine their correlation. **Methods:** In this prospective study, 86 chronic periodontitis patients (probing depth ≥5mm at ≥30% sites) and 86 periodontally healthy controls were enrolled. Serum ACP (p-nitrophenyl phosphate method) and CRP (latex-enhanced turbidimetric immunoassay) were measured at baseline for all participants. Periodontitis patients underwent full-mouth SRP, with biomarker re-assessment at 1 week and 1-month post-therapy. **Results:** Baseline ACP (14.23±3.36 vs. 2.61±1.01 U/L, $p<0.001$) and CRP (16.34±3.76 vs. 2.03±0.95 mg/L, $p<0.001$) were significantly higher in periodontitis patients versus controls. Following SRP, both markers showed progressive reduction (Repeated Measures ANOVA, $p<0.001$): ACP decreased to 10.75±2.73 U/L at 1 week and 7.14±1.72 U/L at 1 month; CRP decreased to 10.50±2.63 mg/L and 5.87±1.45 mg/L, respectively. No important correlation existed between baseline ACP and CRP levels ($r=0.192$, $p=0.077$). **Conclusion:** non-invasive treatment for periodontal disease effectively reduces both local tissue-destructive (ACP) and systemic inflammatory (CRP) biomarkers. Their independent behavior suggests they represent distinct pathological pathways in periodontitis, supporting comprehensive biomarker assessment for monitoring disease activity and therapeutic response.

INTRODUCTION

Chronic periodontitis is a widespread inflammatory disorder of the tooth-supporting apparatus, which is the gradual demolition of periodontal tissues such as the alveolar bone [1]. In addition to its oral form, periodontitis has been identified as a cause of systemic inflammation, and this has implications on different systemic diseases [2]. Circuitry is involved in the pathogenesis of the interaction between pathogenic biofilm and host immune-inflammatory responses [3]. This systemic type of inflammation that is commonly quantitated by sensitive biomarkers such as high-sensitivity CRP (hs-CRP) is a central agent in the pathogenesis of diseases such as atherosclerosis, and this type of biomarker is a cardiovascular risk predictor tool [4]. This interaction liberates a number of mediators and enzymes which are possible biomarkers of disease activity. One of them, C-reactive protein (CRP), which is produced by hepatocytes as an acute-phase protein, has been widely investigated as a systemic inflammatory surrogate protein produced in periodontitis [5,6]. Notably, high levels of CRP (especially the high-sensitivity version, hs-CRP) in the body are also identified as a predictor of future cardiovascular morbidity in other chronic inflammatory conditions, including type 2 diabetes, which highlights its clinical significance [7] Its levels are also associated with the severity of the disease and drop after treatment for periodontal, which connects oral inflammation to the body state [8]. Unlike systemic markers, local tissue infiltrating enzymes would give an insight on periodontal breakdown on site of disease. ACP is a lysosomal enzyme that is highly present in osteoclasts, neutrophils, and macrophages, which is significant in the breakdown of bones and tissues [9,10]. Periodontitis has been associated with high levels of ACP in the gingiv crevularia fluid and serum which indicates a higher

activity of osteoclastic and involvement of cells that are found during inflammation [11,12]. Nevertheless, its reaction to non-surgical treatment and its correlation with the indicators of systemic inflammation is not sufficiently defined. Although, different levels of CRP (systemic inflammation) and ACP (local tissue destruction) are increased in periodontitis, the comparative dynamics of these processes during the treatment process and their mutual relationship are not well known. The autonomous or mutual behaviour of these markers may give information about specific pathological pathways that are functional in periodontal disease [13,14].The study aimed to provide a comparison between serum level of acid phosphatase (ACP) and C-reactive protein (CRP) in comparison to healthy controls, compare levels after scaling and root planing (SRP) at one week and one month, and determine the correlation between the two at baseline. We assumed that both the markers would be high in the periodontitis, will reduce after SRP and will correlate positively.

MATERIALS AND METHODS

Study Design and Ethical Considerations

This prospective clinical trial was held at the department of biochemistry in conjunction with the department of periodontics at the NIMS dental college and hospital. The study protocol was approved by the Institutional Ethics Committee (IEC/P596-/2024) and the Institutional Ethics Committee (IEC/P596-/2024) accepted the study protocol, and it was conducted in accordance with the Declaration of Helsinki. Each subject signed the informed consent.

Study Participants

The enrolled number of participants was 172, including 86 patients with a persistent periodontal disease diagnosis and 86 periodontally healthy controls of the age category 20-60 years. The sample size has been computed to identify a difference in CRP levels of 30 percent and power of 80% at 0.05 alpha level. Periodontitis patients were requested to take part in the study able to meet the following criteria: systemic health, adults, clinical diagnosis of persistent periodontal disease ≥5 mm probing depth (PD) and clinical attachment loss (CAL) ≥3 mm at ≥30% of sites, and bone loss on radiographs. Participants for the healthy control group were included if they exhibited PD ≤3 mm, had no bleeding when probed (BOP) at more than 10% of sites, lacked radiographic proof of bone loss, and had no history of periodontal disease. Those who were pregnant or nursing were not allowed to participate in the study; had systemic conditions known to affect inflammatory status, such as rheumatoid arthritis, diabetes mellitus, heart disease, or problems with the liver or kidneys; had a history of smoking or tobacco use in any form; had used antibiotics or anti-inflammatory drugs within the preceding three months; had undergone any treatment for periodontal within the previous 12 months; or were receiving immunosuppressive therapy or chemotherapy.

Clinical Examination and Calibration

One qualified examiner conducted a full-mouth periodontal examination (intra-examiner reliability κ=0.92) using a Williams periodontal probe (Hu-Friedy, Chicago, IL, USA). PD, clinical attachment level (CAL), bleeding with probing , and plaque index (PI) were recorded at six sites per tooth. Calibration was achieved by duplicate examinations of 10 patients not included in the study, performed 24 hours apart.

Biochemical Analysis

Peripheral venous blood (5 mL) was collected from the antecubital vein under aseptic conditions between 8:00 and 10:00 AM to minimize diurnal variation. For periodontitis patients, samples were obtained at three time points: baseline (before SRP), 1-week post-SRP, and 1-month post-SRP, while control participants provided a single baseline sample. Samples of blood were sedimentation for 15 minutes at 3500 rpm following a half-hour clotting period at room temperature. To avoid deterioration, the separated serum was divided into aliquots and kept at -80°C until analysis. Acid Phosphatase (ACP) was measured using the p-nitrophenyl phosphate (PNPP) method (GPL Diagnostics, India) on a semi-automated analyzer (ERBA CHEM-7, Transasia Bio-Medicals Ltd., India), with results expressed in U/L. The latex enhanced turbidimetric immunoassay was utilized to measure CRP (ERBA Diagnostics, Germany, Lot No. S022480) on the same analyzer, and the sensitivity of the test was 0.1 mg/L with results being given in mg/L. All tests were done in duplicate by a blinded technician and the intra-assay coefficient of variation of the two parameters was less than 5%.

Periodontal Intervention

Full-mouth SRP in two quadrants Using local anesthesia each session (2% lignocaine with 1:100,000 adrenaline) was done on patients in the periodontitis group, and they were done in one week. An experienced periodontist conducted treatment with the application of ultrasonic scaler (EMS Piezon, Switzerland) and Gracey curettes (Hu-Friedy, USA). The teeth-brushing education was enhanced, and the patients were prescribed two portions of mouthwash 0.2% chlorhexidine per day during two weeks.

Statistical Analysis

Data analysis was performed using SPSS version 25.0 (IBM Corp., Armonk, NY). Normal distribution was assessed using Shapiro-Wilk test. The mean ± standard deviation (SD) is used to display continuous variables. The independent samples t-test was used to evaluate intergroup comparisons (periodontitis vs. control). Longitudinal changes in biomarkers post-SRP were evaluated using Repeated Measures ANOVA with post-hoc Bonferroni correction for pairwise comparisons. Pearson's correlation coefficient was used to evaluate the

relationship between ACP and CRP. In order to account for multiple comparisons, statistical significance was fixed at $p<0.01$. Sample size calculation was verified post-hoc with observed effect sizes.

RESULTS

Participant Characteristics

The study enrolled 172 participants equally distributed between periodontitis (n=86) and control (n=86) groups. Table 1 displays clinical and demographic characteristics. Groups were matched for age and gender distribution ($p>0.05$). As expected, periodontitis patients exhibited significantly worse periodontal parameters compared to controls ($p<0.001$ for all clinical measures).

Table 1. Demographic and Clinical Characteristics of Study Participants

Parameter	Persistent periodontal disease (n=86)	Healthy Controls (n=86)	p-value
Age (years)	42.3 ± 8.7	40.8 ± 9.2	0.265
Gender (M/F)	44/42	41/45	0.649
Probing Depth (mm)	5.8 ± 1.2	2.1 ± 0.4	<0.001
Clinical Attachment Loss (mm)	4.2 ± 1.1	0.3 ± 0.2	<0.001
Bleeding on Probing (%)	68.4 ± 12.3	4.2 ± 2.1	<0.001
Plaque Index	2.4 ± 0.6	0.8 ± 0.3	<0.001

Baseline Biomarker Levels

Patients with periodontitis had considerably higher baseline serum concentrations of these indicators than healthy controls (Table 2). ACP levels were approximately 5.5-fold higher ($p<0.001$), while CRP showed an 8-fold rise ($p<0.001$) in the periodontitis group.

Table 2. Baseline Serum Levels of Acid Phosphatase and C-Reactive Protein

Biomarker	Persistent periodontal disease	Healthy Controls	p-value
Acid Phosphatase (U/L)	14.23 ± 3.36	2.61 ± 1.01	<0.001
C-Reactive Protein (mg/L)	16.34 ± 3.76	2.03 ± 0.95	<0.001
Data presented as Mean ± SD; p-value from independent samples t-test			

Bar diagram 1: Longitudinal Changes Following Periodontal Therapy

Both biomarkers showed significant progressive reduction following SRP (Table 3, Bar Diagram 1). Significant temporal effects were found for both using repeated measures ANOVA, ACP ($F=285.4$, $p<0.001$) and CRP ($F=312.7$, $p<0.001$).

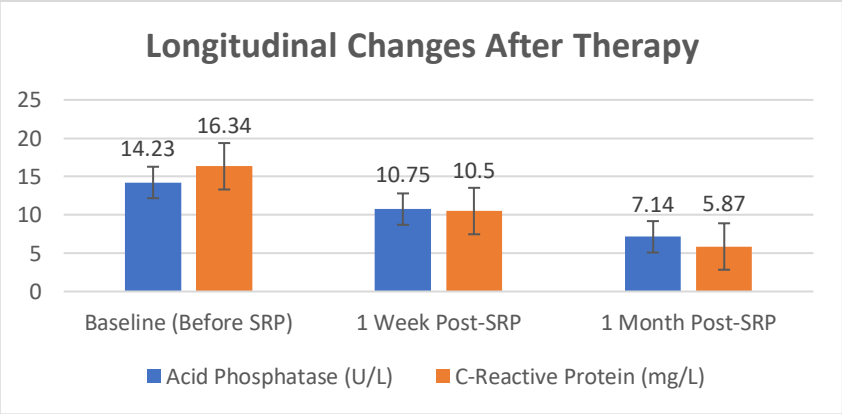
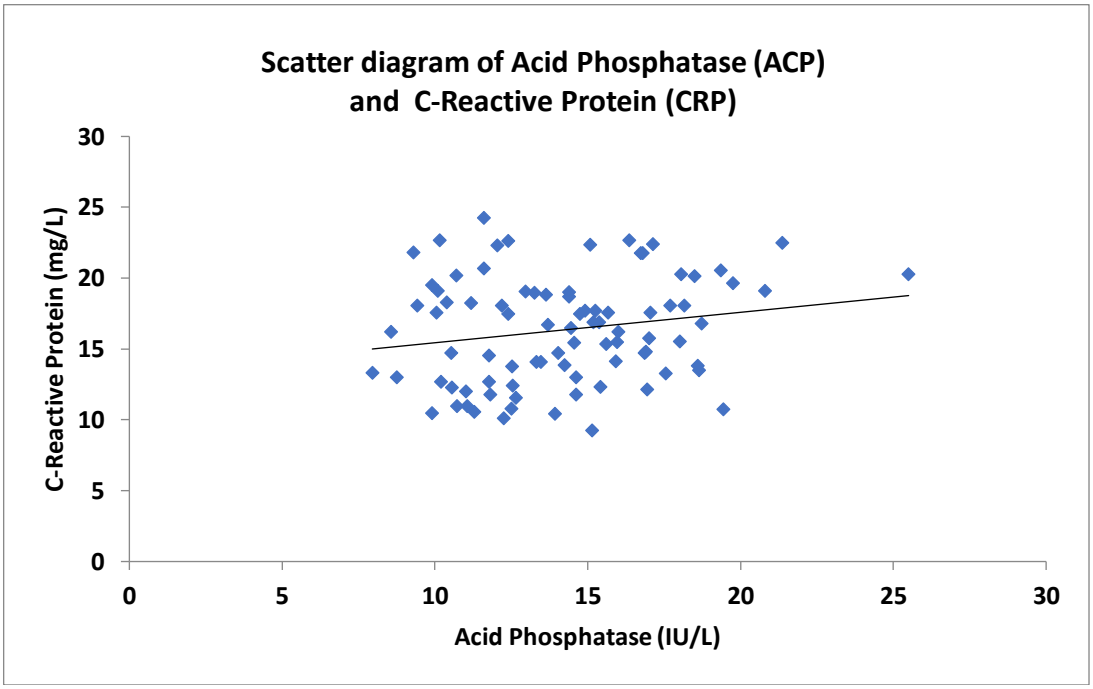


Table 3. Changes in Serum Biomarkers Following Scaling and Root Planing

Time Point	Acid Phosphatase (U/L)	C-Reactive Protein (mg/L)
Baseline (Before SRP)	14.23 ± 3.36	16.34 ± 3.76
1 Week Post-SRP	10.75 ± 2.73*	10.50 ± 2.63*
1 Month Post-SRP	7.14 ± 1.72*†	5.87 ± 1.45*†
p-value (Repeated Measures ANOVA)	<0.001	<0.001
*Data presented as Mean ± SD; *p<0.01 vs. Baseline; †p<0.01 vs. 1 Week (post-hoc Bonferroni test)*		

Scatter plot 1: Correlation of ACP and CRP



Scatter plot 1: showing correlation between baseline serum acid phosphatase and C-reactive protein levels in persistent periodontal disease patients. Dashed line represents linear regression fit (r=0.192, p=0.077).

DISCUSSION

Principal Findings and Interpretation

This prospective study demonstrates that persistent periodontitis is associated with significant elevations in both serum ACP, a marker of local tissue destruction, and CRP, a systemic inflammatory marker (Table 2). Following non-invasive treatment for periodontal disease, both biomarkers showed progressive, significant reduction at 1 week and 1-month post-treatment (Table 3, Bar Diagram 1). Notably, despite similar response patterns to therapy, There was no discernible relationship between baseline ACP and CRP levels (Scatter plot 1), suggesting independent pathological pathways. The significant increase in ACP in periodontitis patients (5.5-fold higher than the controls, Table 2) complies with the known bone resorption effects of ACP. The ACP and especially tartrate-resistant acid phosphatase (TRAP) isoform is expressed in osteoclasts and activated macrophages [15,16]. Its expression in the condition of periodontal inflammation indicates an amplified osteoclastic activity and tissue destruction. Our results are in agreement with other studies which have indicated high levels of ACP in the gingival tissue and serum of gingivitis patients [11,17]. The major decrease after SRP (50% less at 1 month, Table 3) demonstrates that local destructive processes are successfully modulated, presumably by diminishing the activation of osteoclasts and the infiltration of inflammatory cells. This justifies the use of ACP as a biomarker in the assessment of periodontal tissue degradation and treatment outcome.

CRP Response and Periodontal-Systemic Link: In the same manner, the 8-fold increase in the CRP levels in our periodontitis group (Table 2); support the proven connection between periodontal disease and systemic inflammation [18,19]. Inflammatory cytokines especially IL-6, which are produced by periodontal

lesions stimulate CRP production by hepatocytes [20]. The gradual eosinophilism of CRP after SRP (64 percent at 1 month, Table 3, Bar Diagram 1) demonstrates that systemic inflammatory burden may be significantly impacted by local periodontal treatment. The research has significant implications to the periodontal-systemic disease relationship indicating that periodontal therapy can be used to reduce cardiovascular risk linked to chronic inflammation [21,22]. CRP was found to be high in patients with persistent periodontal disease in our research, the same finding I have been able to note in my study when Jagannatha reported the same, that CRP also increases as an indicator of systemic inflammation[23].

Novelty of Non-Correlation and Pathophysiological Implications

The most interesting enlightenment of our study is that ACP and CRP do not show significant correlation ($r=0.192$, $p=0.077$, Scatter plot 1). This implies that although the two markers are upregulated in periodontitis (Table 2) and respond to treatment (Table 3, Bar Diagram 1), they can be different facets of the disease process. ACP mainly indicates local tissue-destructive process that includes osteoclasts and inflammatory cells at the periodontal site, whereas CRP is a marker of systemic inflammatory process that is catalysed by the hepatic synthesis. Their autonomous action means that the evaluation of the two markers might give a better view of periodontal disease activity compared to individually. The conclusion of this finding opposes the hypothesis of simultaneous upsurge of both local and systemic biomarkers and points to the complexity of the periodontal pathophysiology. The main aim of the previous studies was to study either local markers or systemic markers [24,25]. The process of simultaneous evaluation of the two ACP and CRP offers some new information about the interrelation between them. The fact that local tissue destruction (ACP) and systemic inflammation (CRP) are dissociated indicates that the factors that control these mechanisms might be autonomous. An example is that genetic polymorphism in inflammatory mediators may produce a different effect on local responses versus systemic responses [26]. Alternatively, the extent of systemic reaction can be of greater importance with regards to cumulative inflammatory load than local tissue damage at a certain location.

Clinical implications of our discoveries are interesting. The decrease in the two biomarkers after SRP (Table 3, Bar Diagram 1) confirms the nature of non-surgical therapy in regulating the local and systemic components of periodontitis. The use of such biomarkers would be useful in determining the response to the treatment, especially with patients with refractory periodontitis or those with systemic diseases that are mediated by the inflammatory process. The autonomous actions of both ACP and CRP (Scatter plot 1) could indicate that the overall evaluation of the biomarkers could be more appropriate in forecasting disease development and drug response compared to isolated ones.

Several limitations should be acknowledged. First, follow-ups were restricted to one month; further observation will help to understand whether the reductions of biomarkers are maintained (according to the tendencies in Table 3). Second, we assayed total ACP and not the bone-specific isoform, TRAP, but isoform-specific assays should be used in future studies. Third, although we did not consider the presence of major systemic conditions, there is no way to entirely rule out the possibility of subclinical inflammation caused by other factors. Fourth, there was no correlation of clinical parameters with the biomarker levels in our study, and it would have increased the clinical significance of the results. Lastly, the single-center design should be validated in different populations.

Future research should examine the longitudinal association among ACP, CRP, and clinical parameters after a long time. Associative studies on the cellular origins and the regulation mechanisms of these biomarkers in periodontal inflammation would improve the knowledge on their dissociation. Also, interventional researches would be able to check whether varying treatment modalities have a different effect on local versus systemic biomarkers.

CONCLUSION

This study demonstrates the effectiveness of non-invasive treatment for periodontal disease in lowering C-reactive protein, a systemic inflammatory marker, and serum acid phosphatase, an indicator of local tissue degradation, in patients with chronic periodontal disease. A negative correlation between these biomarkers would seem to indicate that these biomarkers are different pathological pathways- local tissue breakdown versus systemic inflammation that are independently controlled by treatment for periodontal. Such results confirm the usefulness of overall assessment of biomarkers in the monitoring of periodontal disease activity and therapeutic effects and demonstrate the complex nature of the effects of treatment for periodontal on both oral and systemic well-being.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest related to this study.

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AUTHOR CONTRIBUTIONS

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