Evaluation of Osteocalcin Level in Gingival Crevicular Fluid in Periodontal Intrabony Defects Treated with Autologous Platelet Rich Fibrin: Non-Randomized Experimental Study

Sahana Srinivas[1], Shruthi Sethuraman[1], Nisha Krishnavilasom Jayakumari[1]

[1]Department of Periodontics, Vydehi Institute of Dental Sciences and Research Centre, Bangalore, Karnataka, India.

Corresponding Author:
Shruthi Sethuraman
Department of Periodontics
Vydehi Institute of Dental Sciences and Research Centre
82, Nallurahalli Main Rd, near BMTC 18th Depot, Vijayanagar,
Nallurhalli, Whitefield, Bengaluru, Karnataka 560066
India
Phone: +919886824276
E-mail: docshruthi1984@gmail.com

ABSTRACT

Objectives: The aim of this non-randomized experimental study is to evaluate and correlate the gingival crevicular fluid osteocalcin levels with clinical and radiographic parameters in patients with intrabony defects treated with autologous platelet-rich fibrin.

Material and Methods: Thirty intrabony defects in 14 patients were treated with autologous platelet-rich fibrin with open flap debridement. Clinical and radiographic parameters were recorded at baseline and 9 months postsurgery. Gingival crevicular fluid (GCF) was collected prior to the surgery, 3 months, 6 months and 9 months postsurgery and was analysed for levels of osteocalcin using ELISA.

Results: All the clinical and radiographic parameters like plaque index (2.41 to 1.38) and gingival index (2.37 to 1.4) scores, probing pocket dept (6.43 to 3.78 mm), clinical attachment level (7.25 to 4.61 mm), relative attachment level (10.35 to 7.42 mm) and vertical depth (7.46 to 4.9), alveolar crest height (6.2 to 5.9), area of the defect (17.8 to 14.5) respectively showed improvement which was statistically significant ($P < 0.001$) except for the defect width (8.86 to 8.77) with $P = 0.39$. A moderate negative correlation was established between the GCF osteoclcin levels and the clinical and radiographic parameters at baseline and 9 months except for the % of defect fill which showed moderate positive correlation at 9 months ($r = 0.55$, $P = 0.002$).

Conclusions: The gingival crevicular fluid osteocalcin can serve as a potential bone turnover biomarker in periodontal regeneration. In addition platelet-rich fibrin has made it possible to define natural bone regeneration as well as improve the clinical and radiological parameters.

Keywords: biomarkers; gingival crevicular fluid; osteocalcin; platelet-rich fibrin; regeneration.

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INTRODUCTION

Periodontitis is characterized by the formation of deep periodontal pockets, loss of periodontal ligament and cementum attachment, and resorption of the alveolar bone, which can ultimately lead to tooth loss [1]. The primary goals of periodontal therapy are to eliminate the inflammatory process, prevent the progression of periodontal disease, and regenerate lost periodontal tissues [2].

Periodontal intrabony defects pose a significant challenge in periodontal therapy due to their complex nature and potential for progressive attachment loss and alveolar bone resorption [3]. Conventional treatment modalities aim to reduce inflammation and promote periodontal tissue regeneration; however, achieving optimal outcomes remains elusive in many cases.

Recently, the use of bone grafts has become one of the most common surgical techniques for augmenting bone defects. However, the limitations associated with autogenous bone and xenografts have spurred the development of biomimetic agents with the potential for rapid regeneration [4]. Among these agents, autologous platelet-rich fibrin (PRF) has shown promise for better outcomes in periodontal treatment. Autologous PRF has emerged as a promising adjunctive therapy in periodontal regeneration, leveraging the regenerative properties of platelet-derived growth factors and cytokines [5]. Previous researches have demonstrated its effectiveness in promoting soft and hard tissue healing in various clinical scenarios [6-9].

Common diagnostic methods for assessing periodontal regeneration include clinical probing pocket depth (PPD), loss of clinical attachment level (CAL), and radiological measurements [10]. Histologic evaluation and surgical re-entry remain the gold standard for re-evaluating periodontal regeneration [11]. However, ethical issues and the need to avoid unnecessary surgical re-entry limit their use [12]. Consequently, the success of regenerative therapies has traditionally been evaluated using clinical and radiographic parameters, which may not provide definitive assessments [13,14].

Therefore, there is a need for non-invasive, highly sensitive diagnostic methods for detecting periodontal regeneration in clinical practice. A well-validated biomarker with high sensitivity, specificity, and reproducibility, which has either a causal or mechanistic association with the therapeutic intervention, can serve as a surrogate endpoint to predict clinical outcomes [15]. When evaluated objectively, bone biomarkers can indicate normal bone healing processes, pathogenic processes, and responses to therapeutic interventions [16].

Osteocalcin, a small matrix protein synthesized by mature osteoblasts, odontoblasts, and chondrocytes, functions in bone mineralization and calcium ion homeostasis [17]. Elevated serum osteocalcin levels are associated with bone regeneration [18]. Hence, its levels in the gingival crevicular fluid (GCF) can reflect the activity of bone metabolism at periodontal sites [19].

Most biomarker studies in periodontology aim to distinguish between patients with periodontitis and periodontally healthy individuals (at the population level) or to detect disease activity in periodontal pockets (at the site level). Longitudinal studies are required for applying "periodontal regeneration" as periodontal endpoints, which explains the scarcity of such studies [15].

Therefore, this non-randomized experimental study aimed to evaluate and correlate gingival crevicular fluid osteocalcin levels with clinical and radiographic parameters in patients with intrabony defects treated with autologous platelet-rich fibrin.

MATERIAL AND METHODS

Study design

This study was conducted at Department of Periodontics, Vydehi Institute of Dental Sciences and Research Centre (Bengaluru, Karnataka, India) from August 2022 to February 2024.

Fifteen subjects with 34 sites of vertical defects were selected. The participants, aged between 35 to 50 years were included in the study. All procedures were performed according to the Helsinki declaration of 1975 (revised in 2013). Ethical approval was obtained from the Vydehi Institute of Dental Sciences Institutional Ethics Committee (Ethical approval letter: VIDS-IEC/PG/APP/2022/28).

The study was registered under the Clinical Trials Registry - India (CTRI) with registration number: CTRI/2023/02/049488. The protocol can be accessed at WHO International Clinical Trials Registry Platform: https://trialsearch.who.int/Trial2.aspx?TrialID=CTRI/2023/02/049488

Sample size calculation

Sample size was calculated using the formula:

$$n = \frac{(Z_{1-\alpha/2} + Z_{1-\beta})^2}{(d/\sigma)}$$

$Z_{1-\alpha/2}$ = 1.96 at 95% CI

$Z_{1-\beta}$ = power (80%)

d/σ = effect size (0.5)

$$n = \frac{(1.96 + 0.84)^2}{(0.5)^2}$$

n = 30

Considering the effect size to be measured (Cohen's d [dz]) at 53% at two-tailed hypothesis based on the results of previous literature from Hakobyan et al. [10], power of the study at 80% and the alpha error at 5%, the total sample size needed is 30. The total number of sites with intra bony pockets were 30 sites. Anticipating 10% dropout during the follow-up period, the sample size were increased to 34 samples.

Study participants

Inclusion criteria were as follows:

- Patients within the age group of 35 to 50 years.
- Patients with stage III grade B periodontitis according to 2017 world workshop on periodontal and peri-implant diseases and conditions [20].
- Presence of minimum of 16 natural teeth.
- Molars with the presence of two wall or three wall intrabony defect ≥ 3 mm as detected on cone-beam computed tomography (CBCT).

Exclusion criteria were as follows:

- Medically compromised patients.
- Patients on any medications known to affect the outcomes of periodontal therapy.
- Insufficient platelet count.
- Pregnant or lactating women.
- Smokers or subjects using any form of tobacco.
- Furcation involvement more than 3 mm and grade III mobile teeth.

Clinical and radiographic examinations

Demographic details, including age, sex, and medical history, were recorded in a standard proforma after obtaining written consent. Patients received oral hygiene instructions and underwent scaling and root planing to control supra- and sub-gingival plaque. Clinical parameters such as gingival index (GI), plaque index (PI), PPD, CAL, and relative attachment level (RAL) were recorded [13,14]. CBCT was used to obtain three-dimensional visualizations of the vertical defects at baseline and 9 months postsurgery (Figure 1). Radiographic parameters such as vertical depth (VD), width, alveolar crest height (ACH), area of the defect (AD), and percentage of defect fill were recorded.

Collection of GCF

GCF samples were collected from the sites after phase 1 therapy before surgery. After removing supra-gingival plaque, 1 µl of GCF was collected using a calibrated volumetric micro capillary pipette (Sigma-Aldrich, Chemical Company, St. Louis, Missouri, USA). The GCF was immediately transferred to an Eppendorf micro centrifuge tube containing 199 µl of phosphate-buffered saline to create a 200 µl sample volume. Samples were stored at -70°C until assay time. The GCF samples were analysed using the ELISA technique (Human N-MID-OT (N-MID Osteocalcin) ELISA Kit, EC Biolabs; Faridabad, Haryana, India).

Surgical therapy

Routine tests were conducted before the surgery,

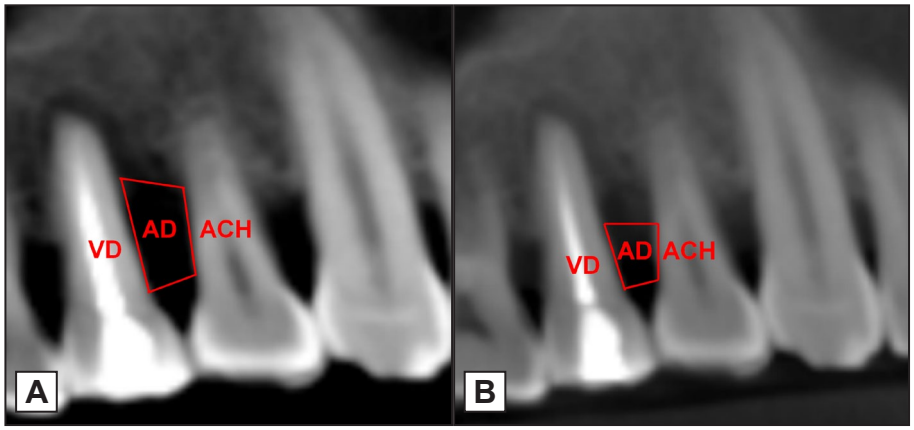

Figure 1. Cone-beam computed tomography measurements of vertical defect site with vertical depth (VD), alveolar crest height (ACH) and area of the defect (AD). A = at baseline; B = at 9 months.

which was performed under local anaesthesia with 2% lignocaine hydrochloride containing adrenaline at a concentration of 1 : 200,000 (Warren Lignox Lignocaine 2% A - Indoco Remedies Ltd.; Verna, Goa, India). The defect was debrided, and PRF was prepared from the patient's blood. Pre-suturing was done, and the defect was filled with PRF.

Preparation of PRF

PRF was prepared according to the protocol developed by Choukroun et al. [5] Intravenous blood was collected in 10-ml sterile tubes without anticoagulant and immediately centrifuged (Neya 4 Swing Out Rotar SN8-5 Benchtop centrifuge - Remi Elektrotechnik Ltd; Mumbai, India) at 3,000 revolutions (approximately 400 g) per minute for 10 minutes. This process results in a structured fibrin clot in the middle of the tube, between the red corpuscles at the bottom and acellular plasma (platelet-poor plasma [PPP]) at the top. The platelet-rich plasma (PRP) and PPP were carefully removed. The PRF clot was then gently separated from the underlying red blood cell layer using sterile tweezers and scissors, preserving a thin layer of red blood cells.

Statistical analysis

Statistical Package for Social Sciences (SPSS) for Windows, version 22.0 (IBM Corp., Armonk, New York, USA) was used to perform statistical analyses. Continuous values were summarized as mean and standard deviation (M [SD]), and categorical variations were presented as frequency and percentages. The paired t-test was used to compare the means of PI, GI, CAL, and PPD. Pearson's correlation test was performed to check the correlation between GCF osteocalcin levels in intrabony defects at baseline, 3, 6, and 9 months. Repeated measure ANOVA was used to check significant mean differences of PI, GI, CAL, PPD, RAL, GCF osteocalcin levels, and radiographic parameters at different time intervals. The level of significance will be set at $P < 0.05$.

RESULTS

Fifteen subjects with 34 sites of vertical defects were initially assessed for the eligibility (Figure 2). However, only 14 subjects with 30 sites of vertical

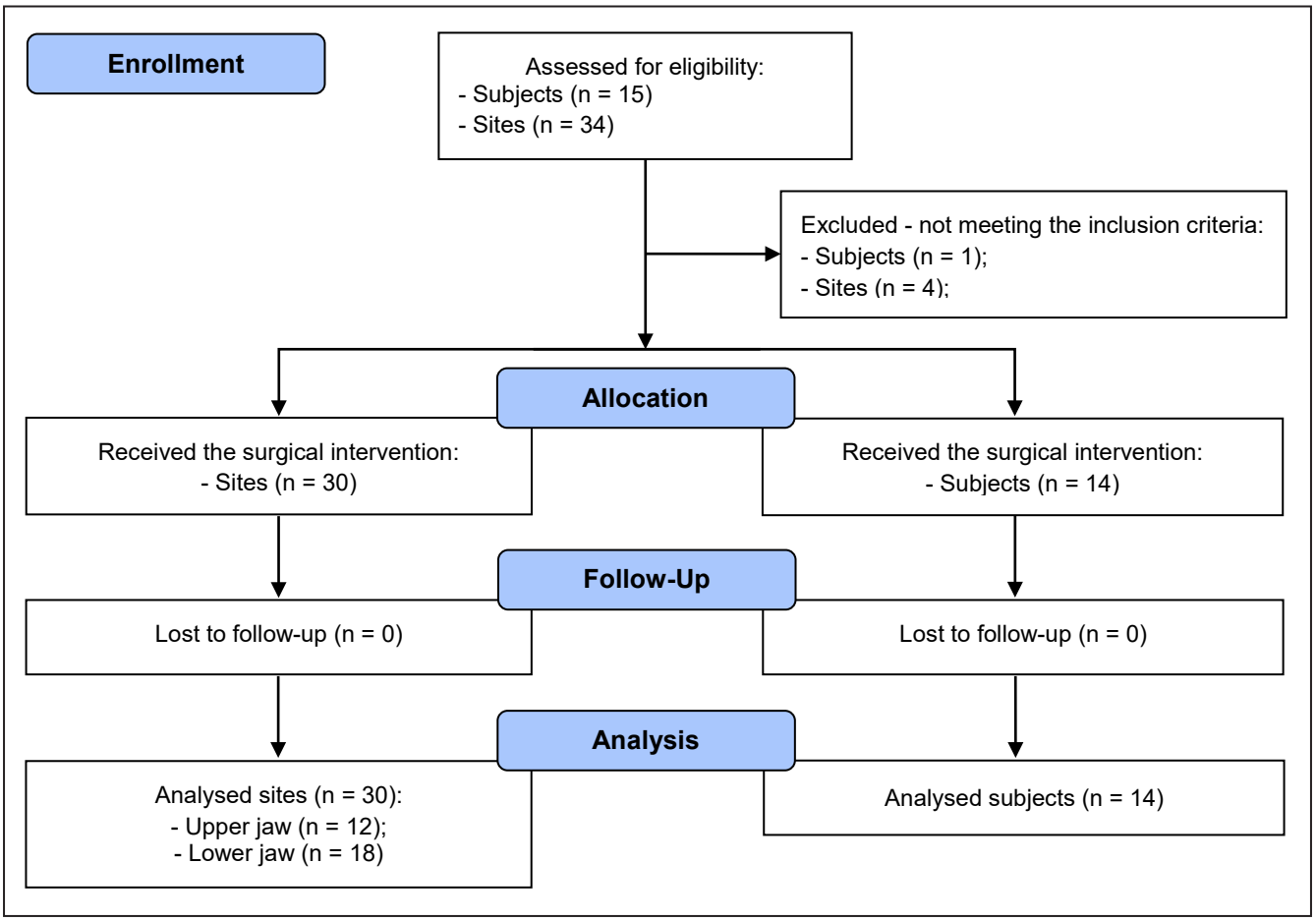

Figure 2. Flowchart for patient selection.

Table 1. Comparison of mean plaque index and gingival index scores between baseline and 9 months among study subjects

Parameter	Time	N	Mean	SD	Mean difference	P-value
Plaque index	Baseline	14	2.41	0.31	1.03	< 0.001[a]
	9 months	14	1.38	0.15		
Gingival index	Baseline	14	2.37	0.41	0.98	< 0.001[a]
	9 months	14	1.4	0.35		

[a]Statistically significant at P < 0.001 (Student's paired t-test).
N = number of subjects; SD = standard deviation.

defects completed the study, as one patient with 4 vertical defects did not meet the inclusion criteria and was excluded. Of the 30 sites, 12 were located in the upper jaw and 18 in the lower jaw.

Clinical and radiographic parameters

Table 1 shows the mean values and statistical analysis of the PI and GI scores between baseline and 9 months postsurgery. The significant decrease in both PI (from 2.41 to 1.38) and GI (from 2.37 to 1.4) indicates a substantial improvement in oral hygiene and gingival health following the treatment with autologous PRF. The mean differences were statistically significant (P < 0.001), suggesting that the intervention effectively reduced plaque accumulation and gingival inflammation. Table 2 presents the mean values and statistical analysis of the probing depth, CAL loss, RAL, VD, width, ACH, and AD at baseline and 9 months. The reduction in the mean PPD values at 9 months postsurgery was significant (from 6.43 to 3.78 mm, P < 0.001). Both CAL (from 7.25 to 4.61 mm) and RAL (from 10.35 to 7.42 mm) showed a reduction in the mean values at 9 months postsurgery this reduction in CAL and RAL was statistically significant at P < 0.001.

Significant reductions were observed in VD (from 7.46 to 4.9), ACH (from 6.2 to 5.9), and AD (from 17.8 to 14.5), indicating successful bone regeneration and defect fill. The mean differences were statistically significant (P < 0.001). However, the change in width (from 8.86 to 8.77) was not statistically significant (P = 0.39), suggesting that the width of the defect did not change significantly over the study period.

Biomarker assay

Table 3 shows the mean levels of GCF osteocalcin at baseline, 3 months, 6 months, and 9 months postsurgery. There was a significant increase in osteocalcin levels over time, with mean values rising from 2.358 ng/ml at baseline to 5.291 ng/ml at 9 months (P < 0.001). This suggests a progressive increase in bone turnover and regeneration following the intervention.

Table 2. Comparison of mean PPD, CAL, RAL, VD, width, ACH and area of the defect between baseline and 9 months among study subjects

Parameter	Time	N	Mean	SD	Mean difference	P-value
PPD	Baseline	30	6.43	0.79	2.64	< 0.001[a]
	9 months	30	3.78	0.77		
CAL	Baseline	30	7.25	0.73	2.64	< 0.001[a]
	9 months	30	4.61	0.88		
RAL	Baseline	30	10.35	0.78	2.93	< 0.001[a]
	9 months	30	7.42	0.85		
VD	Baseline	30	7.46	0.81	2.56	< 0.001[a]
	9 months	30	4.9	0.85		
Width	Baseline	30	8.86	1.29	0.09	0.39
	9 months	30	8.77	1.15		
ACH	Baseline	30	6.2	0.68	0.3	< 0.001[a]
	9 months	30	5.9	0.7		
AD	Baseline	30	17.8	1.0	3.3	< 0.001[a]
	9 months	30	14.5	1.01		

[a]Statistically significant at P < 0.001 (Student's paired t-test).
PPD = probing pocket depth; CAL = clinical attachment loss; RAL = relative attachment level; N = number of sites; SD = standard deviation, VD = vertical depth; ACH = alveolar crest height; AD = area of the defect.

Table 3. Comparison of mean gingival crevicular fluid osteocalcin levels (ng/ml) between different time intervals among study subjects

Time	N	Mean	SD	Min	Max	P-value
Baseline	30	2.358	0.458	1.17	3.4	< 0.001[a]
3 months	30	4.055	0.478	3.38	5.03	
6 months	30	4.766	0.359	4.13	5.78	
9 months	30	5.291	0.268	4.72	6.23	

[a]Statistically significant at P < 0.001 (repeated measures of ANOVA test).
N = number of sites; SD = standard deviation.

GCF osteocalcin levels and clinical parameters

Table 4 shows the Pearson correlation coefficients (r) between GCF osteocalcin levels and various clinical parameters at baseline and 9 months. At baseline, there were moderate negative correlations between GCF osteocalcin levels and PPD, CAL, RAL, and VD. At 9 months, the correlations remained negative and significant for PPD, CAL, RAL, and VD, except for width, which showed no significant correlation. Notably, there was a moderate positive correlation between osteocalcin levels and the percentage of

Table 4. Relationship between gingival crevicular fluid osteocalcin levels and clinical parameters at baseline and 9 months

Time	Values	PPD	CAL	RAL	VD	Width	ACH	AD	Defect fill
Baseline	r	-0.45	-0.46	-0.48	-0.4	-0.21	-0.26	-0.05	-
	P-value	0.01[a]	0.01[a]	0.008[a]	0.03[a]	0.27	0.15	0.79	-
9 months	r	-0.41	-0.46	-0.45	-0.43	0.03	-0.48	-0.16	0.55
	P-value	0.03[a]	0.01[a]	0.01[a]	0.02[a]	0.89	0.006[a]	0.38	0.002[a]

[a]Statistically significant at P < 0.001 (Pearson's correlation test).
r = correlation coefficient; PPD = probing pocket depth; CAL = clinical attachment loss; RAL = relative attachment level; VD = vertical depth; ACH = alveolar crest height; AD = area of the defect.

defect fill (r = 0.55, P = 0.002) at 9 months, indicating that higher osteocalcin levels were associated with better defect fill outcomes.

Table 5 presents the results of multiple linear regression analysis to predict GCF osteocalcin levels using clinical parameters. At baseline, RAL was a significant predictor of osteocalcin levels (β = -0.282, P = 0.008), with an r^2 value of 0.23, indicating that 23% of the variability in osteocalcin levels could be explained by RAL. At 9 months, the percentage of defect fill was a significant predictor (β = 0.016, P = 0.002), with an r^2 value of 0.27, indicating that 27% of the variability in osteocalcin levels could be explained by the defect fill percentage.

Table 5. Stepwise multiple linear regression analysis to predict gingival crevicular fluid osteocalcin levels at baseline period using clinical parameters

Time	Independent variable	Unstd. coefficients		t-statistic	P-value	r^2
		β	SE			
Baseline	Constant	5.28	1.017	5.189	< 0.001[a]	0.23
	RAL	-0.282	0.098	-2.88	0.008[a]	
9 months	Constant	4.746	0.163	29.178	< 0.001[a]	0.27
	Defect fill	0.016	0.005	3.465	0.002[a]	

[a]Statistically significant at P < 0.001 (stepwise multiple linear regression analysis).
β = beta coefficient; SE = standard error; r^2 = coefficient of determination.

DISCUSSION

The primary objective of this study was to evaluate and correlate GCF osteocalcin levels with clinical and radiographic parameters in patients with intrabony defects treated with autologous PRF. The results indicate a significant improvement in clinical and radiographic parameters, which underscores the efficacy of PRF in periodontal regeneration.

The significant clinical improvements observed, including reductions in probing depth and gains in CAL, corroborate previous studies demonstrating the benefits of PRF in periodontal therapy. Choukroun et al. [5] highlighted that PRF enhances wound healing and promotes soft tissue regeneration due to its high concentration of growth factors. Our study supports these findings, as the clinical parameters showed substantial improvement post-treatment with PRF.

A significant aspect of our study was the utilization of CBCT to evaluate radiological parameters. Previous research has predominantly relied on conventional radiographic techniques such as intraoral periapical radiography (IOPAR), radiovisiography (RVG), and radiographic grids, which offer only two-dimensional assessments of bone defects [21,22]. With CBCT, however, we could appraise bone defects in a three-dimensional perspective, incorporating measures like defect width, ACH, and AD, unlike earlier studies that primarily focused on defect height alone. The rationale behind employing CBCT in our investigation was to achieve more accurate radiographic assessments, given its demonstrated high sensitivity and diagnostic precision, as demonstrated by Bagis et al. [23] in 2015.

Currently, a variety of bone graft materials and growth factors are recommended for periodontal regeneration. Among these PRF, introduced by Choukroun et al. [5], stands out as a second-generation platelet concentrate widely recognized for its ability to accelerate the healing of both soft and hard tissues. The PRF clot forms a robust natural fibrin matrix, concentrating nearly all platelets and growth factors from the harvested blood. This matrix exhibits a complex architecture, offering mechanical properties unmatched by other platelet concentrates. Therefore, PRF was chosen as the regenerative material for this study. Our findings are consistent with those of Thorat et al. [24] and Sharma et al. [25], who investigated the clinical effects of autologous PRF in treating intra-bony defects and three-wall intrabony defects in patients with chronic periodontitis, respectively.

Histological assessment and surgical re-entry continue to be the benchmark for evaluating the efficacy of any regenerative therapy, yet they pose numerous challenges. Surgical re-entry can induce discomfort for the patient and potentially disrupt tissue healing; thereby increasing the risk of postoperative complications [11]. Histological evaluation necessitates obtaining tissue samples from the regeneration site, which may not always be practical due to the small size of the defect or patient hesitance and it also needs extraction of the teeth.

To address these challenges, clinical and radiographic parameters were employed as practical methods. However, they may not serve as definitive indicators of regeneration. The utilization of biomarkers in periodontal regeneration presents several advantages over traditional clinical or radiographic examinations. Biomarkers have the capability to detect biochemical changes in periodontal tissues before they manifest clinically or are visible on radiographs [26]. Therefore, in this study, osteocalcin levels in GCF, a bone turnover biomarker, were evaluated and correlated with clinical and radiographic parameters. Osteocalcin is currently recognized as a valid marker of bone turnover, reflecting both bone resorption and formation when coupled, and specifically indicating bone formation when formation and resorption are uncoupled [27].

As far as we are aware, there have been no studies documenting GCF osteocalcin levels in intrabony defects following periodontal regenerative therapy with PRF. Hence, direct comparison with other studies is not feasible.

In our study, the average osteocalcin levels post-periodontal surgery demonstrated an increase from baseline to 3 months, 6 months, and 9 months following therapy. These findings indicated that as osteocalcin levels increased nine months postsurgery, there was a reduction in PI, GI, PPD, and an increase in CAL, RAL, defect depth, and defect fill. This rise in GCF osteocalcin levels can be attributed to its role as a protein primarily synthesized by osteoblasts during bone formation [28]. Osteocalcin has been recognized to participate in angiogenesis, thereby promoting the formation of new blood vessels. As angiogenesis is integral to bone regeneration, there may be a correlated increase in osteocalcin levels in GCF. Additionally, the inflammatory mediators released during this phase may stimulate osteoblast activity, contributing to the release of osteocalcin into the GCF. Thus, these observations reflect the dynamic processes of bone formation, remodeling, and tissue repair [29].

The findings of our study align with those of Hakobyan et al. [10], who observed an increase in serum osteocalcin levels from baseline to 3 months after periodontal therapy, correlating with clinical parameters. Additionally, in another investigation comparing the release of bone markers during the osseointegration of immediately loaded and non-loaded implants, higher levels of osteocalcin were noted between 60 to 120 days compared to the seventh day [30]. Immunohistochemical analysis conducted to evaluate the efficacy of a corticocancellous block allograft revealed the presence of biomarkers commonly associated with active bone formation, including alkaline phosphatase, osteocalcin, and bone morphogenetic protein-2 [31].

A study done by Nakashima et al. [32] aimed to investigate the presence of osteocalcin in GCF and to evaluate the associations between osteocalcin, prostaglandin E2 and Alkaline phosphatase levels in GCF with periodontal conditions. The findings indicate that a substantial proportion of osteocalcin found in GCF is locally produced by periodontal tissues. Our study similarly observed the presence of osteocalcin in GCF, and we noted an elevation in its levels, which corresponded with clinical and radiographic parameters [32].

A study was conducted by Taiseer et al. [33] in 2018, where they evaluated the effect of PRF system (PRF mixed with bone graft) in the regeneration of intra-bony defects by assessing osteocalcin in GCF. A randomized double blind, split-mouth study was undergone on 12 patients with twenty four intrabony defects the selected defects were randomly divided into Group I (Test group): including eight defects that received PRF mixed with grafting material. Group II (Collagen group): including eight defects that received collagen membrane and PRF mixed with grafting material and Group III (Control group): including eight defects that received open flap debridement only. The clinical parameters were measured and recorded at base line and six months postoperatively. The results showed better improvement in radiographic parameters which was observed in defects treated with PRF mixed with grafting material (group I). Regarding mean osteocalcin concentration, defects treated with collagen membrane and PRF mixed with grafting material (group II) reported maximum reduction at the end of the study. However the radiographic parameters were analysed after 9 months in our study as periodontal regenerative therapy outcomes are best assessed in 9 to 15 months after surgery and with the use of the CBCT we could appraise bone defects in a three-dimensional perspective which provided accurate radiographic assessments. In contrast to the study by

Taiseer et al. [33], our study showed statistically significant increase in osteocalcin levels after 9 months [28,29].

Our investigation into osteocalcin as a bone marker indicates that assessing the clinical state of the bone metabolism can be achieved through the examination of highly specific biochemical properties related to bone metabolism. Deciding on the appropriate course of action may be facilitated by comprehending the correlation between clinical status and levels of bone metabolism markers.

While our study provides valuable insights into the role of osteocalcin and PRF in periodontal regeneration, there are limitations to consider. The sample size was relatively small, and the study was non-randomized, which may affect the generalizability of the findings. Future studies should aim to include larger, randomized controlled trials to validate these results.

Additionally, while osteocalcin levels provide a snapshot of bone turnover, combining this biomarker with other indicators such as bone-specific alkaline phosphatase or C-terminal telopeptide of type I collagen could offer a more comprehensive assessment of bone regeneration dynamics.

CONCLUSIONS

Considering the limitations of this study, it can be concluded that estimating gingival crevicular fluid osteocalcin levels may offer an effective alternative to clinical and radiographic evaluation, as well as histologic and surgical re-entry. This non-invasive procedure can be conducted chairside and provides real-time monitoring due to its simplicity. Consequently, these advantages position gingival crevicular fluid osteocalcin as a potentially valuable tool for assessing bone regeneration in intrabony defects. These results underscore the potential of platelet-rich fibrin in enhancing periodontal therapy outcomes and provide a foundation for further exploration into biomarker-based assessments in periodontal regeneration.

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