



## Is “PRF”-The Add-On Precedence To Procure Better Bone To Implant Contact? A Randomized Control Trail

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### Abstract

**Introduction / Background:** The prime focus of this study was to assess the additive capabilities of platelet rich fibrin membrane in achieving better osseo-integration. Both the primary and secondary stabilities at particular time intervals were taken into account.

**Materials and Methods:** 30 edentulous sites among 15 Patients of both the genders, with age ranging from 25 to 60 years were enrolled in this study. The duration was about 4 months and the Patients were randomly divided into two groups with 15 sites in each group. Patients enrolled in Test group were subjected to implant placement along with the PRF placed in the osteotomy site. Patients in control group were subjected to only implant placement. The implant stability scores were measured using resonance frequency analysis (RFA) at baseline and after 4 months, before abutment placement in both the groups.

**Results:** Statistical significant difference was observed in both Inter and Intra-group comparisons as the secondary stability scores were higher than the primary stability scores. The secondary stability scores showed a mean difference of  $11.67 \pm 3.31$  and  $6.0 \pm 1.20$  for the test and control groups respectively and this was statistically significant as the scores in test group were higher when compared to the control group.

**Conclusion:** The abundance existence of growth factors in the PRF has the potential to enhance the wound healing process which provides good secondary stability, thus better osseointegration.

**Keywords:** Dental Implants, Growth Factors, Osseointegration, Platelet Rich Fibrin (PRF), Primary Stability And Secondary Stability

### Introduction

Rehabilitation is the most important aspect which has been hunting the whole dental community since decades. With the newer advancements in medical field the life expectancy of humans have been drastically increased, this however has forced them to be edentulous for a longer span of period ie, either partially or completely. The need of the hour is to

rehabilitate the lost teeth so that the lost aesthetic and masticatory function is restored. In recent times dental implants have come under the lime-light and have proved to be a preeminent alternate<sup>[1]</sup> to fixed and partial dentures in means of providing better aesthetics, speech and mastication. It also improved the standard of living, by boosting up the individual's self-confidence.

The crucial key for the long-term success of an implant solely depends on its osseointegration or bone to implant contact (BIC). In 1985 Branemark defined “osseointegration” as “A direct structural and functional connection between ordered, living bone and the surface of a load carrying implant”.<sup>[2]</sup> The main criteria for the implant success is bestowed on its ability to be surrounded by the host bone. The stability of an implant can broadly be divided into primary and secondary.<sup>[3]</sup> After placement of implant in the prepared osteotomy site the initial mechanical engagement with cortical bone occurs. This mechanical interlocking between the implant surface and bone prevents the connective tissue layer formation thus, ensuring a proper seal between the implant surface and bone. This primary interlocking mechanism is known to be the primary stability whereas the secondary stability is achieved after the biological healing phase. The secondary stability is governed by the osteoblastic activity favouring bone regeneration and remodelling around the implant surface.<sup>[4]</sup>

Stability of an implant can be measured by various methods, of which resonance frequency analysis (RFA) can be considered to be safe, non-invasive and reliable. The implant stability can be enhanced by modifying the implant surfaces or by altering the design and topography of the implants which leads to change in the surface chemistry, and contributes in enhancing the bone to implant contact (BIC). One recent approach to enhance the BIC, is the addition of plasma concentrates to the implant surface which helps in enhancing the osteoblastic differentiation and functional integration of implants.<sup>[5]</sup> The plasma concentrates are believed to deliver concentrated molecules rich in growth factors, which play a vital role in healing and bone regeneration. Accelerated bone remodelling and regeneration<sup>[6]</sup> enhances the stability and also helps in the maintenance of dental implants.

Platelet rich fibrin (PRF), a second generation autologous indigenous armour capable of providing different growth factors such as TGF- $\beta$ , IGF, PDGF and VEGF which efficiently induces soft and hard tissue healing.<sup>[7]</sup> PRF consists of highly structured polymerized fibrin matrix which is embedded with platelets, cytokines, circulating stem cells and leukocytes. These platelets and cytokines release various growth factors which promote healing at a

faster rate. PRF acts as a biodegradable scaffold which induces epithelial cell migration, and enhances the micro-vascularization at the site of interest.<sup>[8]</sup>

The present study focuses on the role of PRF in enhancing the stability around the implant.

## Materials And Methods

A randomised, prospective bilateral clinical study was done to evaluate the role of PRF in the enhancement of implant stability. Patients who reported to the Department of Periodontics and Implantology, in Dr's. Sudha and nageswararao Siddhartha Institute of Dental Sciences, Chinnaoutpalli, were enrolled in this study. A total of 15 patients with 30 edentulous sites in either maxilla or mandible molar area of both the genders participated in this study. The duration was about 4 months and a random division of patients were done into two groups using Coin toss method which consisted of 15 sites in each group. All the 15 patients read and signed an informed consent form before starting the treatment and the Institutional Ethical Committee approval was obtained prior to the start of the study.

**Test group:** Patients were subjected to implant placement and PRF was placed in the osteotomy site. (n=15).

**Control group:** Patients were subjected to only implant placement (n=15).

MIS seven implants were used in both the groups and Resonance Frequency Analysis (RFA) was used to measure the implant stability.

Inclusions criteria were : 1) an age range of 25-60 years, 2) bilaterally edentulous sites in either maxillary or mandibular posterior region, 3) Presence of adequate bone height and width.(1.5 - 2 mm of bone all around the implants after implant placement, 4) Healing period of bone crest of more than 4 months prior to implant placement. Exclusion criteria involved: 1) Patients with uncontrolled systemic disease, 2) Patients who have smoking habit, 3) Pregnant and lactating females, 4) Patients with gingival hyperplasia, 5) Patients who needed bone augmentation procedures, 6) Patients with blood dyscrasias and 7) Patients with poor oral hygiene and untreated periodontal disease All the patients were enrolled based on the above criteria.

A detailed case history and investigations were taken and evaluated. Diagnostic casts, OPG and CBCT scan were done to access the quality and quantity of the bone at the implant site before the start of the surgical procedure. Once implant treatment was found to be feasible, the procedure, advantages, maintenance and post-operative care were clearly described to each of them. 30 implants in total were placed in the molar region in the upper and lower jaws. Primary stability was evaluated at baseline ie immediately after implant placement and secondary stability was evaluated and compared before abutment placement ie, at the end of 4 months in both the groups.

### Prf Preparation:

A freshly fabricated prf was prepared prior to the placement of implant. Prf was prepared as per Choukroun's criteria<sup>[9]</sup>. Prf is categorized as platelet concentrate belonging to the second generation, since no anticoagulants or jellifying agents are used in its preparation. This is the striking advantageous feature which naturally activates the platelets present in the fibrin polymerization matrix. After following the centrifugation protocol, 3 distinct zones are observed

- (1) a acellular plasma layer occupies the top-most position,
- (2) Prf clot in the middle zone and
- (3) At the base a dark thick zone of rbc.

Concentrated amounts of platelets and leukocytes are embedded in the fibrin network laid by the prf clot. Following the Choukroun's et al criteria for prf preparation, a 22 gauge syringe was inserted in the ante-cubital vein and 10 ml of venous blood was drawn from all the participants. At 3000 rpm the obtained sample was immediately centrifuged for about 12 minutes. The fibrin clot that has occupied the middle portion of the test tube is procured and placed in the osteotomy site.

### Surgical Procedure:

Antisepsis was performed extra-orally with 5% povidine iodine solution and intra-orally with 0.2% chlorhexidine mouth rinse before starting the procedure. Local infiltration with 2% lidocaine hydrochloride solution with 1:80,000 adrenaline was used for anaesthesia. A full thickness muco-periosteal flap is reflected and the required osteotomy site is

prepared through sequential drilling. The length and diameter are prepared to the pre-planned measurements in the cbct in both the groups. The final diameter of the osteotomy site should be less than that of the intended size of the implant to be placed.

In test group the freshly prepared prf membrane was inserted in the osteotomy site before the implant placement. Implant of preplanned diameter and length is placed and the flap was approximated by simple interrupted suture using 3-0 bbs. In the control group only implants were placed in the osteotomy site and suturing was done in a similar manner. A minimum of 3 mm of inter-implant distance were maintained. Implants were placed by two stage technique and were covered with healing caps. Post surgical instructions and medications that is ibuprofen 400 mg qid daily for 2 days and mox cv 625 mg bid daily for 7 days were prescribed. Suture removal was done after a week's duration. Patients were instructed to use chlorhexidine mouthwash 0.2% daily twice until complete oral hygiene habits were resumed.

The implant stability was evaluated using resonance frequency analysis (RFA). An "osstell device" was used to which a transducer (smart peg) was connected. RFA quantifies the motion of the implant by making the implant to vibrate over a range of frequencies. This quantification is termed as an implant stability quotient (ISQ). During the measurement, smart peg was attached to the implant and the sleeve of the hand piece was placed about 0.5 mm from the implant. Mean implant stability quotients (ISQ) were calculated by taking the buccolingual and mesio-distal site values. ISQ values were noted down both after the surgical procedure as well as after 4<sup>th</sup> month in both the groups. The scale ranged from 0 to 100. Implant stability was considered to be higher if the ISQ values was nearer to 100.

### Statistical Analysis:

Patient's demographic data were assessed using descriptive statistics. The stability values within the study groups (test and control groups) were analysed using paired t-test at baseline and at 4<sup>th</sup> months interval (Intra-group comparison). An unpaired t-test was used for the inter-group comparison of the stability scores for the same interval period.

## Results

Table 1 depicts the demographic data. The test group enrolled 15 individuals out of which 5 were males and 10 were females. This distribution of males and females were similar in both the group, since standardization of the arch was done to overcome bias and the implants were placed bilaterally. The percentage of males in both the groups was 33.33% and females were 66.67% with no statistical significant results (Table 1; Graph 1). Table 5 depicts the inter-group stability scores between the study groups as per the mentioned time intervals. The primary stability scores at baseline were  $76.73 \pm 4.33$  and  $74.47 \pm 2.56$  for the test and control groups respectively. Mean stability scores were similar in both the groups with no significant difference. However the stability scores for the test and control group after 4 months were  $88.47 \pm 2.59$  and  $80.47 \pm 2.07$  respectively (Table 2; Graph:2). A significant

statistical difference was seen as the test group showed higher mean stability scores when compared to control group at 4 months-time interval. A mean difference of  $11.67 \pm 3.31$  and  $6.0 \pm 1.20$  for the test and control groups were observed respectively and this was statistically significant as the scores in test group were higher than the control group. Table 6 shows the intra-group comparison of the study groups with respect to the stability scores at baseline and 4 months. The stability scores for the test group at baseline and 4 months were  $76.73 \pm 4.33$  and  $88.40 \pm 2.59$  respectively. Statistical significant difference was observed as the secondary stability scores were higher than the Primary stability scores. Similarly the stability scores for the Control group at baseline and 4 months were  $74.47 \pm 2.56$  and  $80.47 \pm 2.07$  respectively (Table 3; Graph: 3), which also showed statistical significance (P value< 0.05).

### Table/s

**“Table 1: Distribution of male and females in two study groups (Test and Control)”**

Gender	Test	%	Control	%	Total
Male	5	33.33	5	33.33	10
Female	10	66.67	10	66.67	20
Total	15	100.00	15	100.00	30

**“Table 2: Comparison of two study groups (Test and Control) with stability scores at baseline and 4 months-time points by unpaired t test.”**

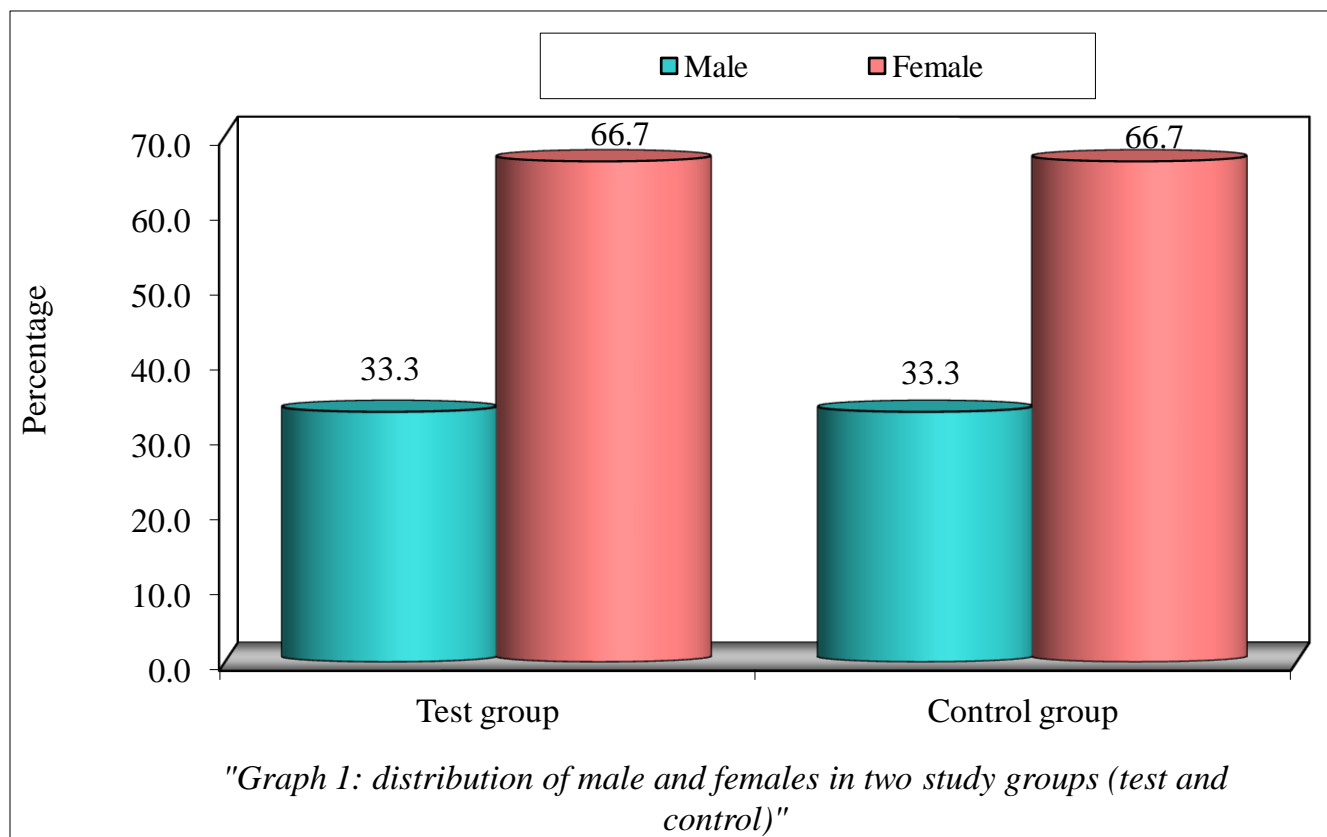
Time	Groups	Mean	SD	SE	Mean Diff.	t-value	p-value
Baseline	Test	76.73	4.33	1.12		1.7442	0.0921
	Control	74.47	2.56	0.66	2.2667		
4 months	Test	88.40	2.59	0.67		9.2843	0.0001*
	Control	80.47	2.07	0.53	7.9333		
Changes	Test	11.67	3.31	0.85		6.2373	0.0001*
	Control	6.00	1.20	0.31	5.6667		

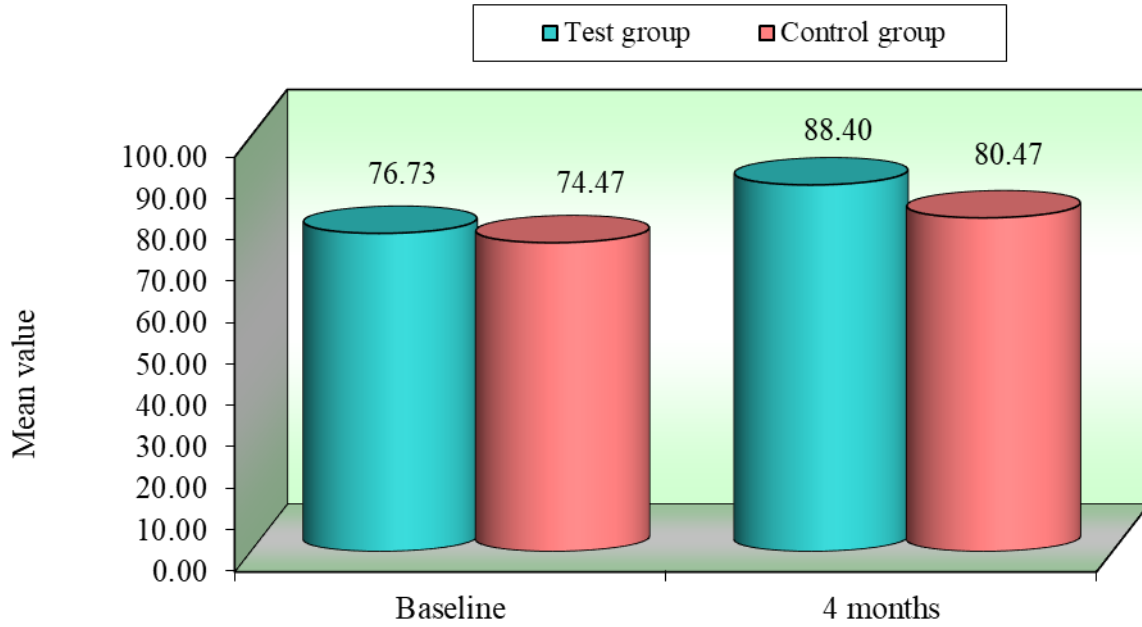
\* p<0.05

**“Table 3: Comparison of baseline and 4 months-time points with stability scores in Test and Control group by paired t test”**

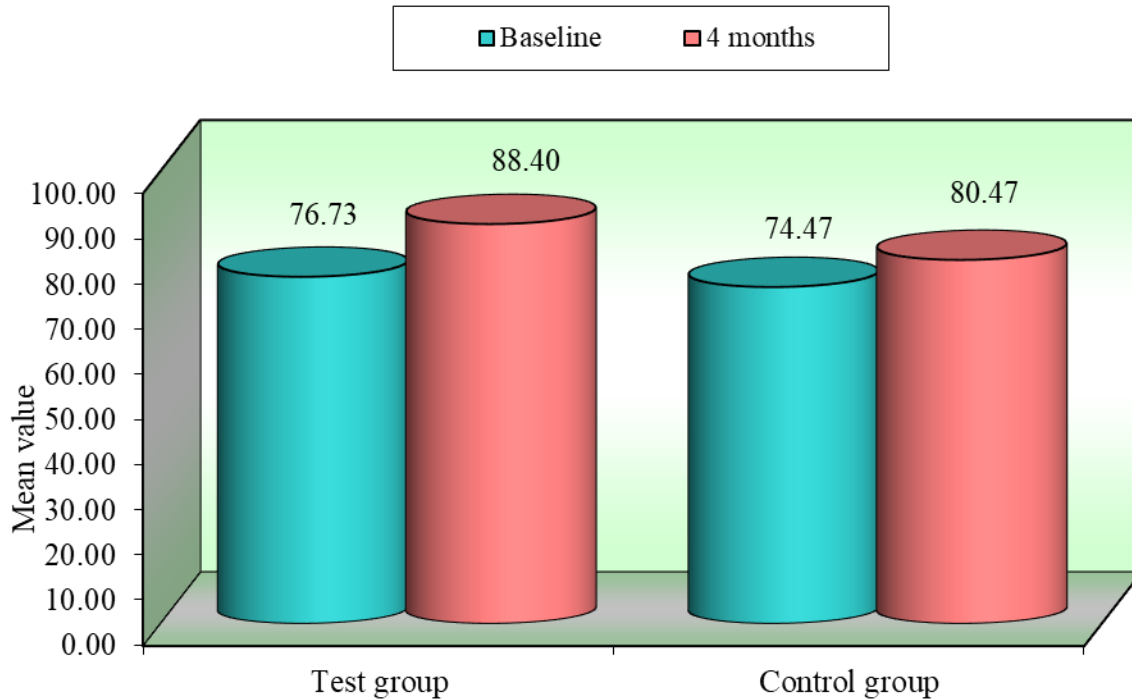
Groups	Time points	Mean	SD	Mean Diff.	SD Diff.	% of change	Paired t	p-value
Test	Baseline	76.73	4.33	-11.67	3.31	-15.20	-13.6533	0.0001*
	4 months	88.40	2.59					
Control	Baseline	74.47	2.56	-6.00	1.20	-8.06	-19.4422	0.0001*
	4 months	80.47	2.07					

\*p<0.05





"Graph 2 : comparison of two study groups (test and control) with stability scores at baseline and 4 months time period by un-paired t test."



"Graph 3: comparison of baseline and 4 months time points with stability scores in test and control group by paired t test."

## Discussion

Earnest and conscientious efforts were made to enhance osseointegration by placing PRF membrane at the osteotomy site, so as to induce and stimulate the regenerative capacity of surrounding tissues at bone-implant interface, which actually governs the success and longevity of the implant. PRF being an autologous source was very easy to obtain and on the other hand it was at ease to deliver all these various growth factors like PDGF, IGF, VEGF, PDAF and TGF- $\beta$  at a particular site. Thus, the main aim of this study was to provide a prolonged action of release of growth factors continuously at the site of placement of the implant. The bacterial load was also effected due to the low  $p^h$  (6.5-6.7) of growth factors.<sup>[10]</sup> This ability of PRF makes it suitable in enhancing bone to implant contact as it improves and accelerates osseous healing. A marked ability of TGF  $\beta$  and PDGF are its chemo-attraction for neutrophils and macrophages. Once epithelialization begins it induces the migration of keratinocytes which is associated in the enhancement of formation of granulation tissue. This in-turn stimulates the fibroblasts, angiogenesis and collagen production thus, promoting a phenotypic shift in wound healing and contraction.<sup>[11]</sup> Bone formation is enhanced in the presence of IGF as osteoblasts and chondrocytes<sup>[12]</sup> are directly stimulated by an increased synthesis of DNA. On the other hand the increased vascularization is induced by FGFS and PDAF as it initiates a direct or indirect action on endothelial cells by which new blood vessels invade the de-vascularized tissue.<sup>[13]</sup>

The stability scores were  $76.73 \pm 4.33$  and  $74.47 \pm 2.56$  for the test and control group respectively at the start of the study. Both the groups showed sufficient amount of ISQ values. "ISQ" is the implant stability quotient which indicates or evaluates the grip of the implant in its prepared osteotomy site and also its relevance with the surrounding soft tissues.<sup>[14]</sup> An ISQ reading of more than 65 is considered to be stable/favourable whereas less than 45 is subjected to its failure.<sup>[15]</sup> Both the test and control groups showed ISQ values greater than 65 at baseline which ensured that the implant was stable in the osteotomy site.

It's a well noted fact that implant stability is directly governed by the osseointegration process.<sup>[16]</sup> After the placement of implant in the bone, Primary stability ensures whether the implant is properly seated or not. Higher the primary stability score

better is the adaptation of the implant mechanically to the host tissues. The primary stability scores were more or less similar and showed no significant difference. However during the healing phase, that is after 4 months the secondary stability scores increased in both the groups. The test group showed a significant increase in the stability scores from baseline ( $76.73 \pm 4.33$ ) to 4 months ( $88.40 \pm 2.59$ ) when compared to the control group (baseline  $74.47 \pm 2.56$  to  $80.47 \pm 2.07$ ). The statistical significance between the groups was attributed to the application of "PRF" in the test group. The steps in the wound healing process is markedly governed by the presence of the growth factors. These bio-active molecules (growth factors) regulate or govern the collagen synthesis production which is essential for the callus formation in the bone, as it resists the soft tissue proliferation. PRF helps in establishing a stable fibrin network which is laid down by several chemical attractants such as thrombocytes, growth factors and cell adhesion proteins which are released into the surrounding cells. Mitogens released from the fibrin clot stimulate the direct osteo-geic cell function.<sup>[17]</sup> A transaction face occurs roughly 2-3 weeks after implantation<sup>[2]</sup> where the primary stability shifts towards a more stable and firm fixation, that is secondary stability. In this phase the implant is at higher risk of failure, if it is subjected to micro-motion movements or heavy occlusal loads.

**Monov et al**<sup>[18]</sup> stated that the implant + PRF group stability values were higher, however no statistical significance was seen. **Kim et al**<sup>[16]</sup> observed that PRP administration in the test group showed enhanced bone to implant contact and the results were statistically significant. **Oncu et al**<sup>[1]</sup> stated that during the initial healing phase the implant stability scores in the PRF+ implant group were higher and placement of PRF in the osteotomy sites in the test group provided faster osseointegration and increased implant stability. **Pirpir et al**<sup>[19]</sup> reported that the stability scores measured at first and fourth week seemed to be higher in PRF+ implant group thus depicting the role of PRF in implant stability. **Abramson et al**<sup>[20]</sup> observed the osseointegration was enhanced due to the presence of PDGF, as it solely responsible for more amount of bone formation around the implant.

The secondary stability scores for the test and control group were  $88.40 \pm 2.59$  and  $80.47 \pm 2.07$ . The test

group showed higher scores and the results were statistically significant. The mean difference between the primary and secondary stability in the test (11.67) and control group (6.00) were also statistically significant. In this study the application of PRF lead to better osseointegration of implants with statistical significant results. The main goal in using PRF in the osteotomy site in the test group was to promote bone healing. PRF showed better soft tissue healing, which indirectly helped the wound to heal faster.

To overcome the bias, the implants placed in this study were of single implant system (MIS-Seven). Surgical osteotomy site preparation for placement of all the implants was done using a speed of 800 rpm using saline coolant resulting in minimal heat generation. A freshly prepared PRF prior to the start of the study was used immediately to gain maximum beneficial effects and the silica present in the glass tube which was used for the centrifugation and manufacturing of PRF acted as a clot activator and directly helped in the polymerization process. The demographic data was also standardized to overcome any further bias. However the follow-up period (4 months) and sample size (30) were accounted to be the limitations of our study.

## Conclusion

Although the gold standard factor which is believed to play a pivotal role in implants longevity is its primary stability, but this is not the sole requisite. Good osseointegration is possible if biologic stability is achieved without a dip in the healing phase. PRF was used to enhance the healing process, which potentially reduces the lag phase, as it induces osteogenesis, thus accelerating the biologic stability. The wound healing phase is highly or mostly governed by the presence of growth factors which in turn helps in achieving good secondary stability which is essential for better osseointegration. Achievement of secondary or long term stability is the current focus or buzzword for the long term success of the implants.

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