

## Evaluation of Effects of PRF in Diabetic Patients- A Randomized Controlled Trial

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**Abstract: Introduction:** Dental extraction is a routine procedure, with immediate post-extraction healing crucial for preventing complications. However, conditions like diabetes can impair this process due to microcirculatory deficiencies. Platelet-rich fibrin (PRF) is gaining attention for its regenerative properties. This study aims to assess PRF's impact on extraction socket healing in diabetic patients. **Materials and Methods:** A randomized controlled trial was conducted on 20 diabetic patients requiring multiple extractions. PRF was placed in one socket (experimental) while the control remained untreated. Parameters including tissue color, bleeding, granulation tissue, and pain were evaluated at 1st, 7th, and 21st days post-extraction. **Results:** Patients exhibited varied glycemic control (110-200 mg/dl). Initial healing was satisfactory, with no major complications. By the 3rd week, 50% achieved complete socket closure. PRF-treated sockets showed significant improvement in tissue color, bleeding, and granulation tissue compared to controls. Suture margin dehiscence and suppuration were notably reduced in PRF-treated sockets. Pain levels were comparable between groups. **Discussion:** Previous studies yielded conflicting results on diabetic wound healing. However, PRF's potential in promoting tissue repair has been recognized. PRF, with its ease of preparation and application, offers advantages over other platelet concentrates. This study contributes to existing knowledge by assessing both soft and hard tissue healing over an extended follow-up period. **Conclusion:** PRF application in extraction sockets of diabetic patients significantly improves soft tissue healing compared to untreated sockets. Pain levels remained similar between groups. These findings advocate for the routine use of PRF in diabetic patients undergoing tooth extraction, offering potential benefits for overall healing outcomes.

**Key Words-**Platelet-rich fibrin (PRF) ,Diabetic patients ,Dental extraction, Wound healing, Soft tissue regeneration, Blood glucose control, Oral surgery, Randomized controlled trial, Microcirculatory deficiencies, Postoperative complications

## **Introduction**

Dental extraction is one of the most commonly performed oral surgical procedures on an outpatient basis. Immediately after teeth are extracted, blood flowing from the alveolar bone and gingiva begin to clot [1]. The clot functions by preventing debris, food and other irritants from entering the extraction site.

Tissue damage provokes the inflammatory reaction, hence causes vasodilation. Leucocytes and fibroblasts invade from the surrounding connective tissues until the clot is replaced by granulation tissue. Leucocytes gradually digest the clot, while epithelium begins to proliferate over the surface with in one week [2].

Many medical conditions/habits may alter this process of healing. Diabetes is a common metabolic disorder characterized by inability to regulate blood glucose due to insulin defiance or resistance [3]. Poor glycemic control predisposes a range of complications that have been categorized as microvascular, macro-vascular and neuropathic. Microcirculatory deficiencies particularly have significant bearing on wound healing post surgically.(4)

It has been stated that wound healing is impaired due to several reasons. First, collagen structure is weakened due to the accumulation of glycemic end products. Second, blood circulation that is necessary for healing is impaired due to microangiopathy. Third, impaired neutrophil function increases the risk of postoperative wound infection.(5) This states the necessity to employ techniques that can expedite and foster the healing process.

One technique, currently gaining importance both in medicine and dentistry, involves the use of platelet concentrates. In particular, the placement of platelet-rich fibrin (PRF) in the healing site delivers platelet-derived growth factors, which has been shown to reduce bleeding,[3] and stimulate soft tissue and bone regeneration in extraction sockets.[4]

The aim of this study was to evaluate the effect of PRF in extraction socket of type 2 diabetic patients.The objective was to compare the extraction socket of teeth as against no intra socket medicament for tissue colour, bleeding on palpation, presence or absence of granulation tissue, suture margin dehiscence, and presence or absence of suppuration.

## **Materials and Methods**

The source of the study were patients who reported to the department of oral and maxillofacial surgery for extraction of two or more teeth in more than one quadrant.Method of collection of data was as follows

- General information including name, age, gender and address will be recorded.
- Patient's medical and dental history will be assessed.
- Clinical and radiographic examination of the tooth to be extracted.

- Blood investigations.
- Patients aged between 18-70 years, diagnosed with diabetes mellitus who required extraction of two or more teeth in more than one quadrant were being included in the study. Selected patients were non-smokers. Patients with the following criteria were excluded from the study
- Diseases of oral mucosa.
- Patients irradiated to the jaws in the past.
- Pregnant patients.
- Patient with poor oral hygiene
- Patients with psychiatric illness.
- Systemic diseases: Liver diseases, Heart problems, bleeding disorders and steroid therapy will be excluded from study.

## **Procedure**

This study was approved by the Institutional Review Board. Signed informed consent was obtained from all patients. The patient's demographic details such as age, gender, relevant medical history, and teeth indicated for extraction were recorded. The blood glucose level for each patient was checked immediately before the procedure. After administration of local anesthesia (2% lignocaine with adrenaline), extraction was done by a closed method. Extraction for both the experimental and control teeth was carried out at the same time. The control socket was compressed and sutured without packing.

## **Preparation of platelet-rich fibrin**

PRF was prepared by Choukroun's method.[6] Following extraction, 6 ml of blood was withdrawn from the patient's antecubital vein and collected in a sterile test tube. The test tube was centrifuged at 3000 rpm for 12 min. After centrifugation, the blood separated into three distinct layers – a bottom layer comprising red blood cells, middle layer containing PRF, and a top layer containing platelet-poor plasma. Both red blood cells and platelet-poor plasma were discarded. PRF was then collected and isolated. For each patient, one extraction socket (experimental side) was packed with PRF and sealed with a figure of 8 sutures. The socket in the control side was sutured and left to heal naturally.

### Follow Up Intervals

The following clinical parameters were assessed postoperatively on 1<sup>st</sup> 7<sup>th</sup> and 21<sup>st</sup> day of the study; Tissue colour, bleeding on palpation, presence or absence of granulation tissue, suture margin dehiscence, presence or absence of suppuration

### Soft Tissue Parameters

Modified version of Landry's index was used to assess the soft tissues.[7] This index measured tissue color (measured as a percentage of red vs. pink tissue), bleeding on palpation, presence or absence of granulation tissue, suture margin dehiscence, and presence or absence of suppuration

### Pain Assessment

This was measured using the visual analog scale for pain, on a scale from 0 (no pain) to 10 (worst possible pain). All parameters were recorded in the data extraction form and analyzed. Statistical analysis was done using the SPSS software (V26, IBM Corporation, Armonk, USA). The tests that were carried out included independent t-test, paired t-test, repeated analysis of variance, and Chi-square test.

### Results

A total of 20 patients were included in this study. The demographic data collected from the patients are projected in Table 1.1 These patients had varied levels of glycemic control, ranging from 110 to 200 mg/dl.

Table-1

Distribution of Diagnosis among study subjects			
Variable	Category	n	%
Diagnosis	Dental Caries with root caries	6	30%
	Deep Dental Caries with mobility	3	15%
	Grossly Destroyed Tooth(non restorable)	4	20%
	Root Stump	3	15%
	Chronic Irreversible Pulpitis associated with endo-perio lesion.	4	20%

Table1.1

Age & gender distribution among study subjects				
Variable	Category	n	%	
Age	45-50 yrs.	4	20%	
	51-55 yrs.	7	35%	
	56-60 yrs.	6	30%	
	> 60 yrs.	3	15%	
		Mean		SD
		Mean	54.95	5.16
		Range	45 - 63	
Gender	Males	9	45%	
	Females	11	55%	

The most common cause for extraction of teeth was unrestorable dental caries, followed by chronic periodontitis. The reasons for extraction are summarized in Table 2.

Table-2

Distribution of Teeth Extracted among Test & Control sites			
Variable	Category	n	%
Test Sites	Upper Anteriors	11	55%
	Rt. Upper Posteriors	1	5%
	Lt. Upper Posteriors	2	10%
	Lower Anteriors	1	5%
	Lt. Lower Posteriors	3	15%
	Rt. Lower Posteriors	2	10%
Control Sites	Upper Anteriors	4	20%
	Rt. Upper Posteriors	0	0%
	Lt. Upper Posteriors	0	0%
	Lower Anteriors	10	50%
	Lt. Lower Posteriors		
		4	20%
	Rt. Lower Posteriors	2	10%

Table-3

Distribution of Teeth Extracted among Test & Control sites			
Variable	Category	n	%
Test Sites	Upper Anteriors	11	55%
	Rt. Upper Posteriors	1	5%
	Lt. Upper Posteriors	2	10%
	Lower Anteriors	1	5%
	Lt. Lower Posteriors	3	15%
	Rt. Lower Posteriors	2	10%
Control Sites	Upper Anteriors	4	20%
	Rt. Upper Posteriors	0	0%
	Lt. Upper Posteriors	0	0%
	Lower Anteriors	10	50%
	Lt. Lower Posteriors	4	20%
	Rt. Lower Posteriors	2	10%

Table-4

Comparison of Healing Index parameters between Test & Control sites among study subjects using Chi Square Test						
Parameters	Category	Test		Control		p-value
		n	%	n	%	
Color of Gingiva	Completely Pink	17	85%	12	60%	0.04*
	Reddish Pink	3	15%	8	40%	
Bleeding on Palpation	Absent	18	90%	12	60%	0.03*
	Present	2	10%	8	40%	
Presence of Granulation	Absent	19	95%	12	60%	0.008*
	Present	1	5%	8	40%	
Suppuration	Absent	17	85%	16	80%	0.68
	Present	3	15%	4	20%	
Suture Dehiscence	Absent	17	85%	13	65%	0.14
	Present	3	15%	7	35%	

### **Soft tissue analysis**

All patients experienced reasonably satisfactory initial healing. None of the patients experienced major problems, such as alveolar osteitis. Approximately 50% of patients had complete socket closure at the 6-week checkup.

The results for each individual parameter are as follows in table-3 and table 4:

### **Tissue color**

Patients were recalled after 24 hours for the first follow-up, and approximately 42% of the study sockets had developed a reddish pink tint, compared to just 34% of the control sockets. At one week, 98% of the study sockets and 96% of the control sockets had reached a reddish pink tint, with just 2% of the research sockets having already transitioned to pink. At three weeks, 85% of the study sockets and 60% of the control sockets were fully pink. Statistical results showed that these results were significant ( $p=0.04$ )

### **Response to palpation**

After 24 hours, 25% of the study sockets and 8% of the control sockets were bleeding-free. At one week, there was no bleeding in 88% of the study sockets and 83% of the control sockets. After three weeks, there was no bleeding in 90% of the study socket and 60% in control socket. Statistical results showed that these results were significant ( $p=0.03$ )

### **Granulation tissue**

Granulation tissue was found in 48% of the study sockets and 57% of the control sockets by the end of the first week. Granulation tissue was found in only 2% of the control group after third week, it was present in 5% of study group and 40% of control group. Statistical results showed that these results were significant ( $p=0.008$ )

### **Suture margin dehiscence**

At the conclusion of the first week, 5% of the control sockets had suture margin dehiscence, but it was absolutely absent in the study sockets. In the third week, it was noted that suture dehiscence was present in 15% of study site and 35% of control site. Statistical results showed that these results were significant ( $p=0.14$ )

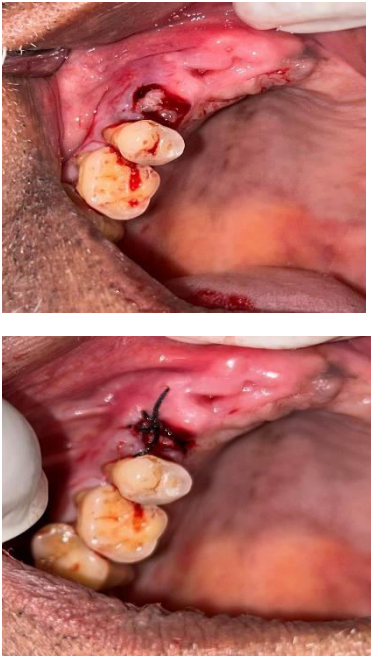
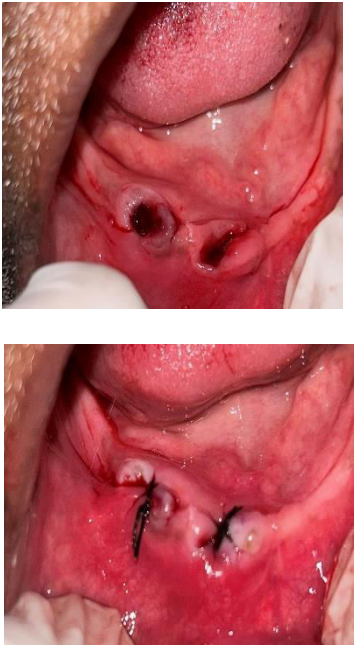
**Suppuration**

Suppuration was found in only 1% of the study sockets by the conclusion of the first week. After third week , suppuration was present in 15% of study site and 20% of control site. Statistical results showed that these results were significant (p=0.68)







**Pain assessment**

The average visual analog scale value at the end of the first week was 1.45 in the study group and 1.40 in the control group. The value was virtually equal on both sides until dropping to zero after the third week. These findings were not significant.

The healing differences between a typical study and control socket are depicted in table-5

TABLE-5		
	STUDY SOCKET	CONTROL SOCKET
<b>IMMEDIATE</b>		



<p>1<sup>ST</sup> DAY</p>		
<p>7<sup>TH</sup> DAY</p>		
<p>21<sup>ST</sup> DAY</p>		

## **Discussion**

This was a prospective randomized control experiment that compared the wound healing of extraction sockets in diabetes individuals treated with and without PRF. It was expected that using PRF might promote wound healing in this specific demographic. Few studies have looked at how diabetics repair their extraction sockets. In a study on diabetic rabbits, Younis et al.[11] found that untreated rabbits had longer healing periods than insulin-treated rabbits, owing to a delay in cell proliferation and osteoblast differentiation.

The same findings, however, have not been replicated in humans. Huang et al.[12] conducted a prospective analysis of extraction socket healing in 224 diabetics and 232 nondiabetics and found no difference in healing rates between the two groups. Aronovich et al.[5] prospectively studied 115 diabetes patients who needed dental extractions and looked for a link between the rate of postextraction epithelialization and glycemic control status. They concluded that there was no statistically significant relationship between postextraction epithelialization and preoperative blood glucose levels.

However, more well-designed investigations are needed to validate this approach. Regardless of the findings of the preceding research, any further aid in wound healing would be advantageous to the diabetic patient. Hard tissue healing: with and without platelet-rich fibrin Platelet concentrates have been utilized in surgery for many years. The goal of employing autologous preparations was to concentrate platelets and growth factors and transfer them to a surgical site, promoting local healing. Platelet concentrate has been shown to promote hard and soft tissue healing, as well as reduce postoperative pain suffering. Choukroun et al. created PRF, a new generation of platelet concentrate, in 2001.[6]

PRF provides various advantages over PRP, including ease of preparation and application, low cost, and the lack of biochemical alteration because no bovine thrombin or anticoagulant is necessary for preparation. PRF has a robust fibrin matrix that allows for continuous, delayed release of growth factors to the wound site.[12] We consequently chose to use PRF in this study.

The utility of PRF in patients whose wound healing is impaired has not been fully investigated. Mozzati et al.[13] studied the efficiency of plasma-rich growth factors in

promoting socket healing after tooth extraction in 34 Type I diabetes patients. This was again a split mouth trial, with each subject acting as the control. According to the authors, the PRGF-treated side healed better and faster, whereas pain levels were practically equal on both sides.

The authors also presented a questionnaire, which revealed that patients were completely satisfied and supported PRGF treatment. However, this study did not assess hard tissue repair. Furthermore, the follow-up time was short (21 days). The current study tried to improve the design of the study by Mozzati et al.[13] by expanding the sample size and follow-up time. The present study also looked at how hard tissue heals. Overall, the findings of this investigation support the findings of Mozzati et al.[13] Wound healing, both hard and soft tissue, was much better in PRF-filled extraction sockets than in control sockets, while pain levels remained comparable.

Although this study found that using PRF speeds extraction socket healing in diabetes patients, the technique's downsides must be recognized. A venipuncture must be performed to obtain blood from the patient during PRF preparation. This more intrusive technique is not tolerated by all individuals, particularly those with "needle phobia." This study did not seek to evaluate healing depending on the patient's glycemic condition, as each patient acted as their own control. This could have led to some confusion. To reduce this bias, future research should explore randomly assigning patients to experimental and control sockets.

Figure-1

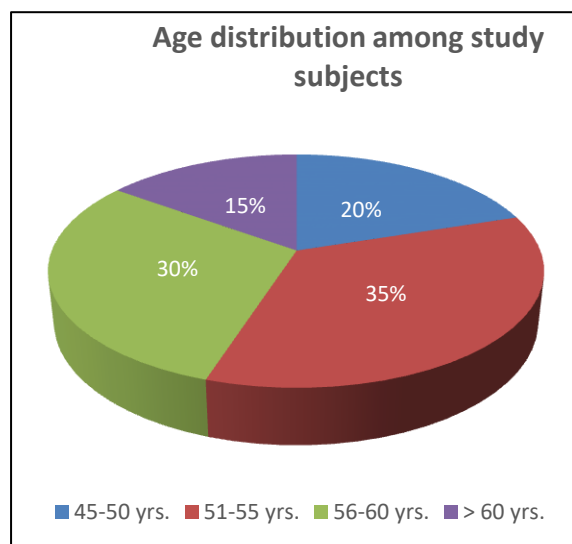


Figure-2

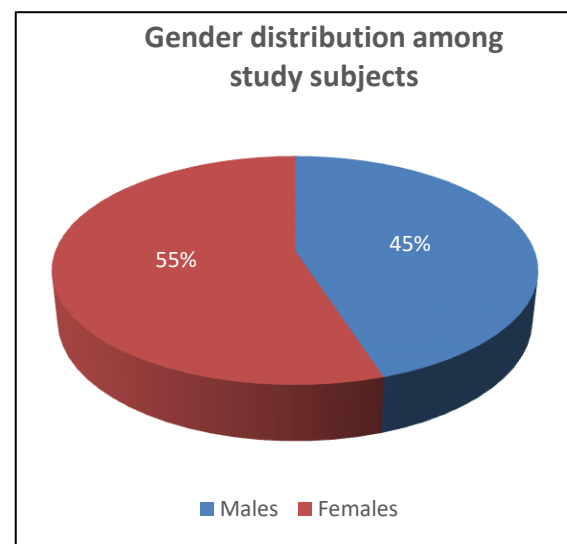


Figure-3

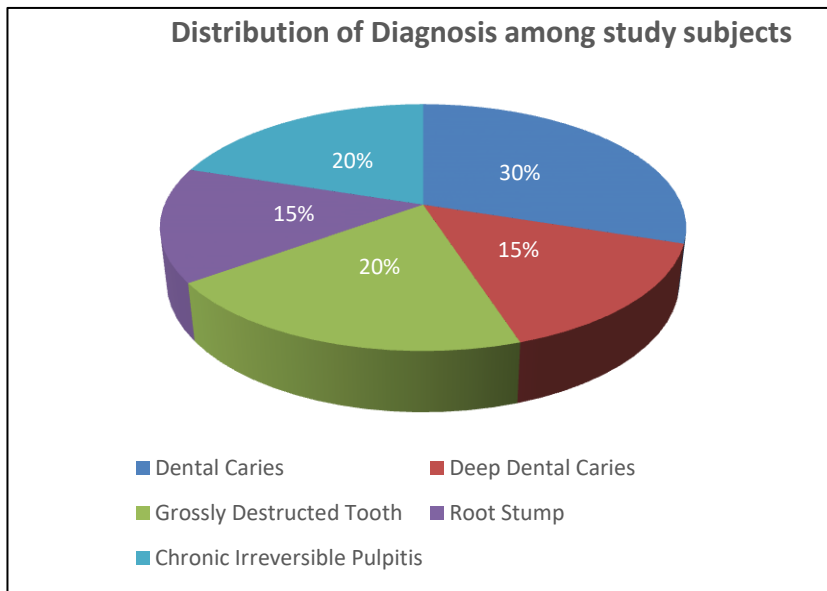


Figure-4

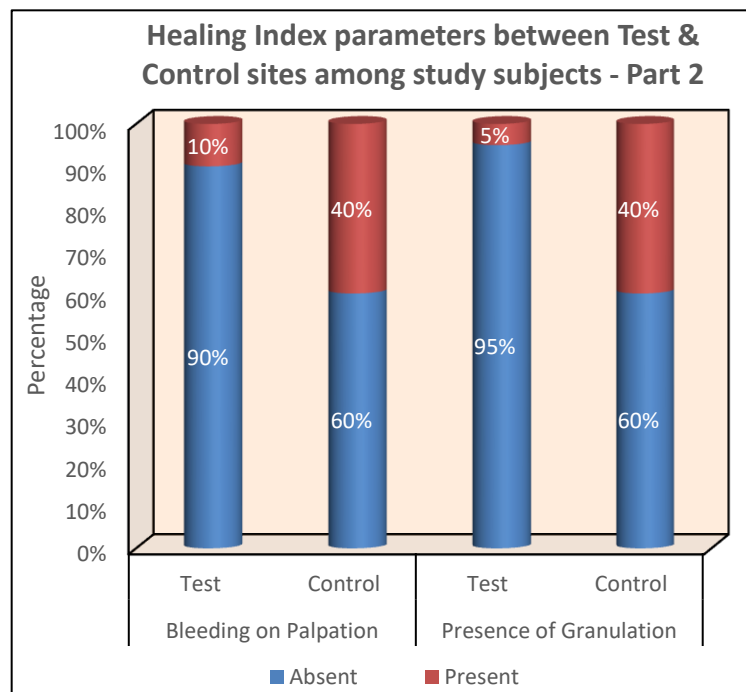


Figure-5

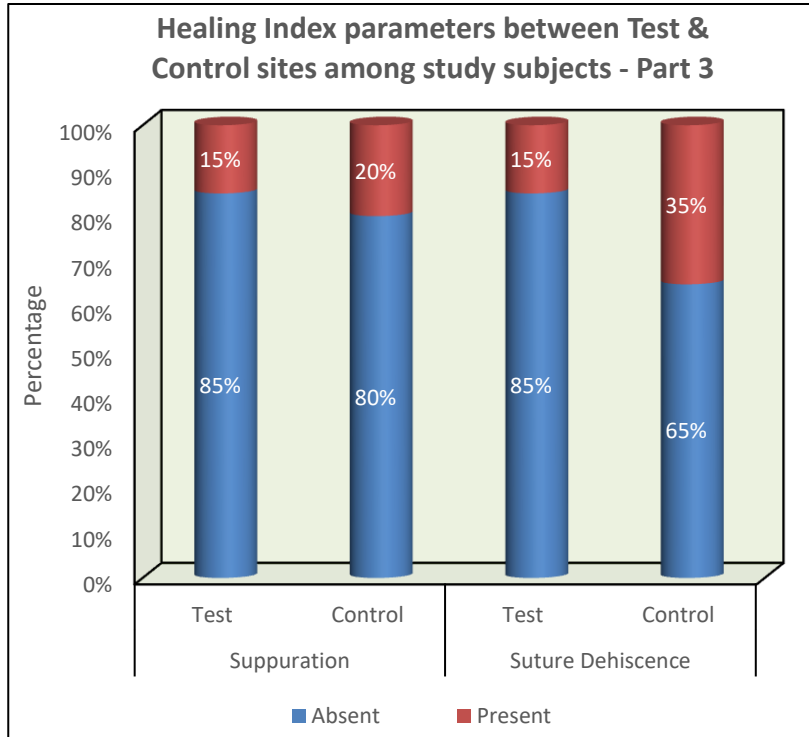


Figure-6

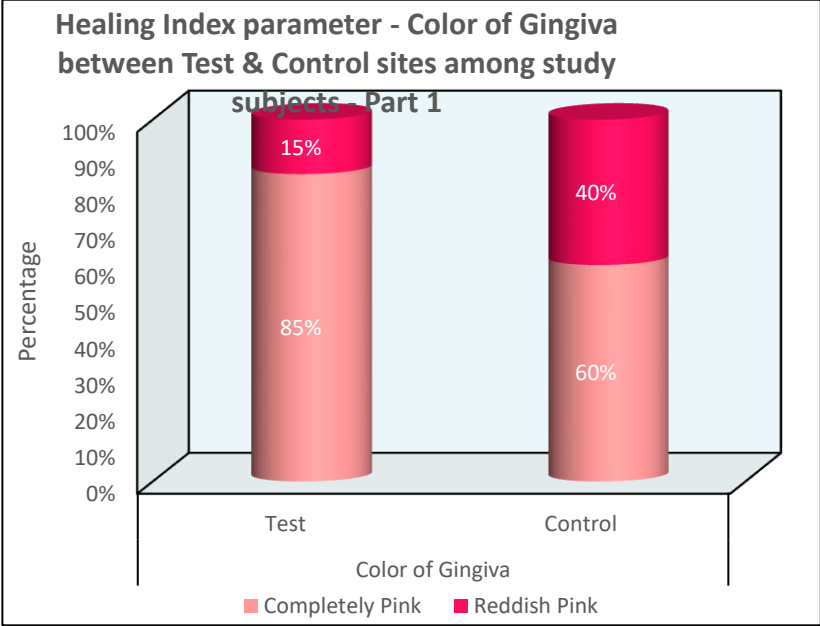
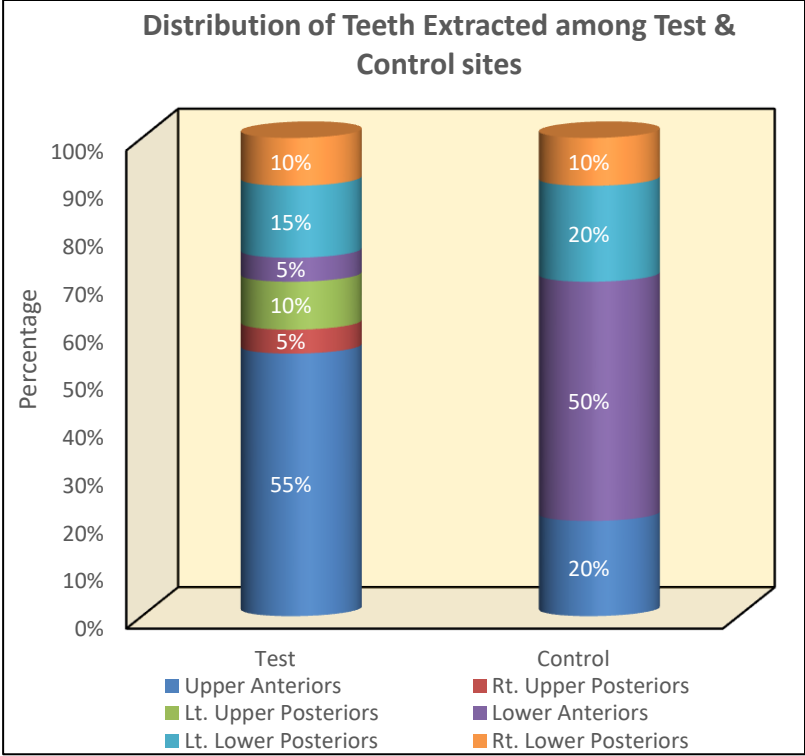


FIGURE-7



## Conclusion

The conclusion drawn from the study indicates that Platelet-Rich Fibrin (PRF) application in dental extraction sockets of diabetic patients yielded improved outcomes soft-tissue healing compared to sockets without PRF, while pain levels remained similar between the two groups. This suggests that PRF contributes positively to the regeneration and repair of bone tissue as well as the healing of gums and surrounding soft tissues following tooth extraction in diabetic individuals.

Despite the observed improvements in healing outcomes, the comparable pain levels suggest that PRF does not significantly impact immediate postoperative pain. Given these findings, the conclusion recommends the routine use of PRF in all diabetic patients undergoing tooth extraction due to its simplicity of application and potential benefits for enhancing overall healing outcomes.

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