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EFFECT OF AUTOLOGOUS PLATELET RICH FIBRIN ON OSSEOUS REGENERATION IN SURGICALLY TREATED IMPACTED MANDIBULAR 3RD MOLARS: A COMPARATIVE STUDY

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Abstract

Objective: *To determine the efficacy of PRF in promoting osteosynthesis in extraction sockets and reducing post-op pain following surgical removal of mandibular 3rd molars.*

Background: *The extraction sockets heal by secondary intention. To speed up this healing process and to reduce postoperative complications, different strategies are employed after wisdom tooth removal.*

Methodology: *A comparative study was conducted in OMFS department of PIMS from February till November 2025 after having received ethical approval. A sample size of 60 was calculated using the WHO sample size calculator. Either gender of age 18 years and above who needed mandibular third molar extraction was included in the study. The selected patients were split into two groups, namely test group (A) and control group (B). Patients of the test group (group A) received PRF while patients of the control group (group B) were treated without PRF application after surgical extraction of mandibular 3rd molars. These patients were assessed for osseous regeneration and pain status at multiple time points. The osseous regeneration was assessed through grayscale histogram on OPG using ImageJ software at immediate post-operative period, 3rd and 5th post-operative months. The pain status was evaluated at 48hrs, 72hrs and 1 week post-operatively using the Visual Analog Scale (VAS). Data was analyzed through SPSS V27.0. Quantitative variables were calculated through mean and standard deviation while qualitative variables were calculated through frequency and percentages.*

Results: *To assess the effect of PRF on bone healing/osseous regeneration, immediate post-operative greyscale values on OPG were recorded and compared with values at 3rd and 5th post-operative months between test group (group A) and control group (group B). No statistically significant difference was noted between the two groups in this study in terms of osseous regeneration, indicating that healing parameters improved in both groups overtime regardless of PRF*

application. Similarly, pre-operative and post-operative pain levels were compared between test group (group A) and control group (group B) during 1st post-operative week. A statistically significant pain reduction was observed in test group (group A) who received PRF following wisdom tooth removal, particularly at 72hrs and onwards till the 7th post-operative day. P-value of less than 0.05 was considered significant.

Conclusion: *After surgical removal of impacted mandibular 3rd molars, application of autologous PRF lessens early post-operative discomfort. However, the radiographic effect of autologous PRF on bone healing was not found to be statistically significant between the two groups in this study. These results are in line with recent research that demonstrates better post-operative pain recovery but inconsistent effects on bone repair.*

Introduction:

Wound healing is recognized as a highly structured and coordinated flow of cellular, biochemical and physiological responses. This integrates numerous cell types, growth factors, hormones, cytokines, and other proteins that work together for regeneration and restoration of normal tissue function.[1-2] Healing of extraction sockets occur by secondary intention, which involves a sequence of events to promote socket healing and reduce complications after surgical extraction of the lower third molars .[3-4] One such biologic approach is the application of Platelet-Rich Fibrin (PRF). Platelet rich fibrin helps the healing process by delivering beneficial growth factors directly to the surgical area.[5] PRF has risen as a promising and useful addition in oral and maxillofacial bone reconstructive surgical procedure mainly because of the platelets which promote wound healing by initiating coagulation cascade and releasing cytokines and growth factors such as platelet-derived growth factor (PDGF), transforming growth factor (TGF-β1, β2), and vascular endothelial growth factor (VEGF).[8-9] These mentioned factors enhance cellular recruitment and their differentiation, collagen production, angiogenesis and processes essential for early wound healing.[9-10] Whitman et al. was the first to introduce the concept of PRF to the community back in 1997 as an autologous alternative to fibrin glue, with the expectation that platelet activation and growth-factor release would improve wound healing. Its popularity increased significantly after the landmark study by Marx et al. in 1998, which demonstrated that the combination of PRF with autogenous bone in mandibular continuity defects led to quicker radiographic healing and the formation of more densely structured bone.[11-12] Based on the growing evidence supporting the benefits of PRF, this study was designed to analyze the efficacy of platelet-rich fibrin in promoting osteosynthesis and reducing pain after surgical removal of impacted mandibular third molars.

Methodology:

A comparative study was conducted in the Oral and Maxillofacial Surgery Department of Pakistan Institute of Medical Sciences, Islamabad from February to November 2025 following ethical approval from Ethical Review Board of Shaheed Zulfiqar Ali Bhutto Medical University, Islamabad. The non-probability consecutive sampling technique was used, and sample size was determined by WHO sample size calculator by using 95% confidence at the population osteosynthesis mean and Standard deviation of 5.40±1.07 in test group (group A)[13] and mean and Standard deviation of 3.37±1.273 in control group (group B)[13] with power of test 80%. The sample size consisted of 60 patients in total with 30 patients per group. Patients aged 18 years and above of either gender who required lower third molar extraction were included, while those unwilling to participate or presenting with acute pericoronitis, fascial space infection, or systemic comorbidities such as uncontrolled diabetes mellitus were excluded. After obtaining informed consent, eligible patients were randomly allocated into test group A as PRF group and control group

B as non-PRF group. As indicated in figure I. the PRF group received platelet rich fibrin into the extraction socket, while the control group was allowed to heal without PRF. All surgical procedures were performed by a single surgical team under standardized conditions using local anesthesia (2% lignocaine hydrochloride with 1:100,000 epinephrine). A modified Ward's incision was used to elevate a full mucoperiosteal flap, followed by tooth removal with or without sectioning and the buccal bone was removed with a slow speed handpiece under copious saline irrigation. For patients in the test group (group A), 10 mL of venous blood was drawn from antecubital vein into plain vials without anticoagulants before surgery. PRF was prepared using Choukron et al. protocol by centrifugation of freshly withdrawn blood at 3000rpm for 10 minutes. The prepared PRF gel was adapted into the extraction socket using sterile tissue forceps before wound closure with simple interrupted 3-0 vicryl sutures, whereas the control group (group B) underwent identical closure without PRF placement. All patients received standardized postoperative medications and uniform verbal and written postoperative instructions with advice to avoid any non-prescribed medications. Bone healing was evaluated radiographically by digital orthopantomograms and measured by grayscale histogram using ImageJ software at immediate post-op period, 3rd and 5th post-operative month. Pain assessment was performed using a 10-point Visual Analogue Scale (VAS) preoperatively, at 48hours, 72hours and 7th post-operative day.

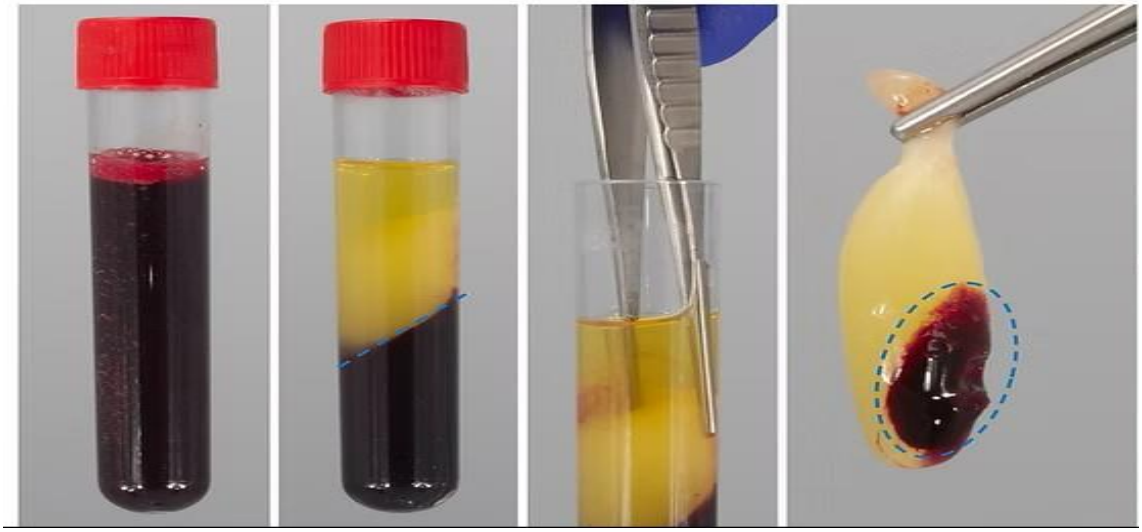

Figure I: PRF- Preparation Protocol; whole blood collected in a plain vacutainer tube prior to centrifugation, (b) post-centrifugation separation showing three distinct layers; acellular plasma (top), PRF fibrin clot (middle), red blood cell base (bottom), (c) PRF clot being retrieved from the tube using sterile tweezers, (d) final prepared PRF plug ready for placement into the extraction socket

Figure II: Intraoral and intraoperative photographs depicting the surgical sequence; (a) pre-operative view of partially impacted and grossly carious mandibular left 3rd molar, (b) occlusal view of the surgical site after tooth removal, (c) extracted mandibular 3rd molar tooth, (d) freshly prepared platelet-rich fibrin plug, (e) placement of PRF plug into the extraction socket, (f) primary wound closure by resorbable sutures

Data Analysis:
SPSS software version 27.0 was utilized for data analysis. Normality of data was determined and reported in results sections. Descriptive statistics were used for demographic variables, and mean ± standard deviation were calculated for quantitative variables, including grayscale values. For a Statistically significant consideration, the p-value was determined to be <0.05.

Results:
A total of 60 individuals were divided into two groups, each group consisting of 30 patients. Their distinction was based on the use of PRF after extraction in test group (group A) and no PRF

application in control group (group B). To determine the normality of variables, Shapiro-Wilk test was applied. For variables that followed a normal distribution, the Independent Samples t-test was applied, whereas the Mann–Whitney U test was used for variables that were not normally distributed. Demographic variables such as age, gender, address, socioeconomic status, education level, impaction type and side of mandible between the test group (A) (n = 30) and control group (B) (n = 30) were recorded. P-values were calculated using the chi-square test and data are displayed as frequency (%). Of all the demographic variables and different impaction types studied between the two groups, the socioeconomic status and impaction type were found to be statistically significant P – value < 0.05.

Table I: Comparison of Demographic Characteristics and Impaction Types Between PRF and Without PRF Groups Using Chi-Square Test

Variables		Groups		P-Value
		Group A (%)	Group B (%)	
Gender	Male	11(36.7%)	17(56.7%)	0.196
	Female	19(63.3%)	13(43.3%)	
	Total	30(100.0%)	30(100.0%)	
Address	Urban	21(70.0%	18(60.0%	0.588
	Rural	9(30.0%)	12(40.0%)	
	Total	30(100.0%)	30(100.0%)	
Socioeconomic Status	Upper Class	9(30.0%)	7(23.3%)	0.041
	Middle Class	20(66.7%)	15(50.0%)	
	Lower Class	1(3.3%)	8(26.7%)	
	Total	30(100.0%)	30(100.0%)	
Education	Uneducated	3(10.0%)	1(3.3%)	0.605
	Educated	27(90.0%)	29(96.7%)	
Impaction Type	Mesioangular	16(53.3%)	17(56.7%)	0.023
	Distoangular	7(23.3%)	7(23.3%)	
	Vertical	0(0.0%)	5(16.7%)	
	Horizontal	7(23.3%)	1(3.3%)	
Impaction Side	Left Mandible	13(43.3%)	14(46.7%)	1.000
	Right Mandible	17(56.7%)	16(53.3%)	
	Total	30(100.0%)	30(100.0%)	

Greyscale value represents bone density in extraction sockets on digital radiographs. Higher values at immediate post-op represent fresh blood clot density. Progressive decrease at 3rd and 5th post-operative month indicates socket remodeling as shown in Figures II(a) and II (b). All comparisons by independent sample t-test indicate no statistically significant difference between the two groups at any time point p > 0.05) shown in table no II.

Table II: Independent sample t-test shows the Comparison of Radiographic Outcomes Between test group A (with PRF) and control group B (without PRF) at immediate post-operative, 3rd and 5th post-operative months

Grayscale Value	Grroup A Mean & SD	Group B Mean & SD	P-Value
Immediate post-operative period	1632.55 ± 36.54	1716.96 ± 41.09	0.764
3rd post-operative month	1145.11 ± 38.50	1422.61 ± 42.16	0.390
5th post-operative month	638.68 ± 185.45	1072.46 ± 312.30	0.112

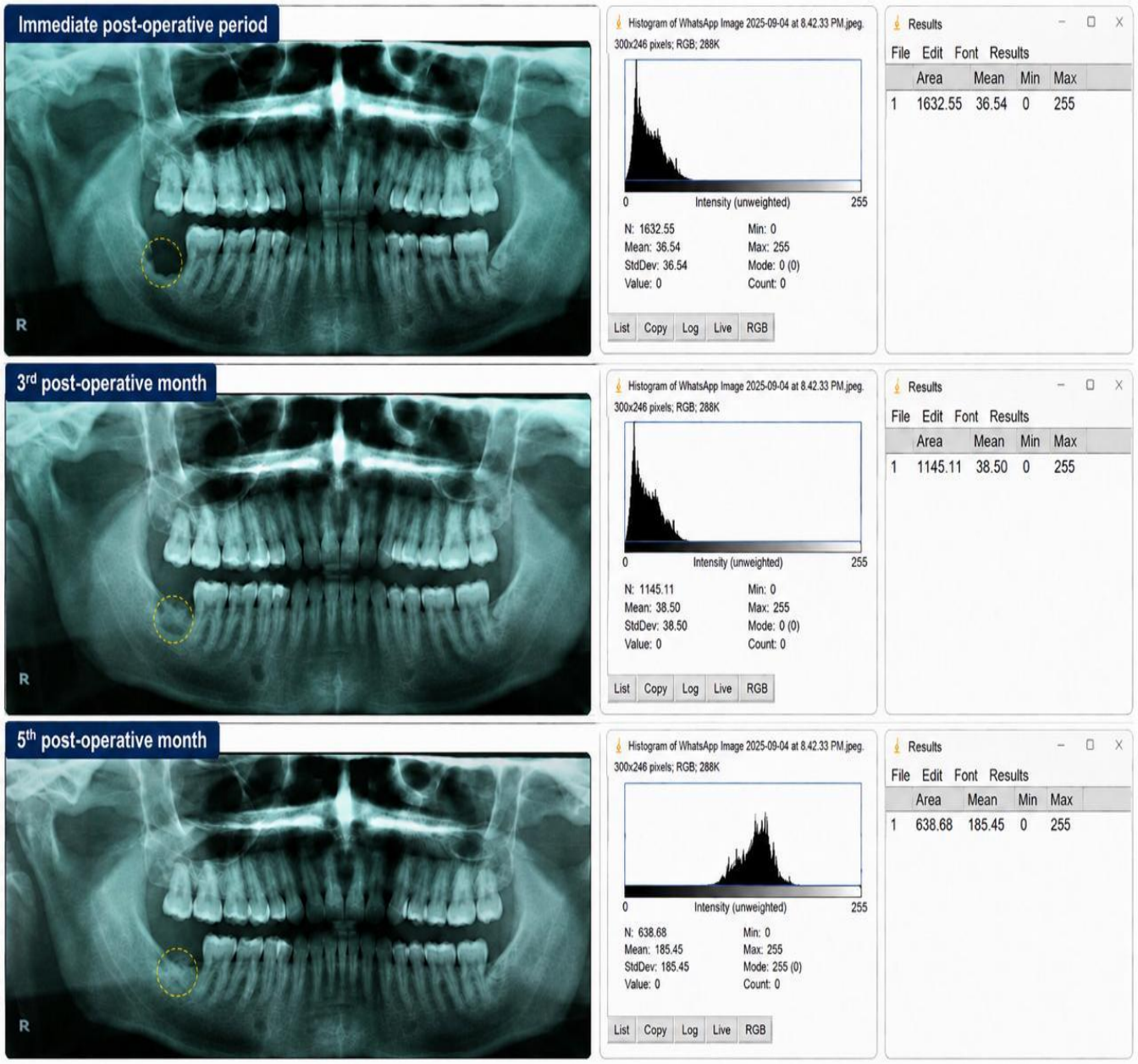

Figure III (a) Serial Panoramic Radiographs of The Test Group A (With PRF) Show Extraction Socket of Mandibular Right 3rd Molar (yellow circle) at Immediate Post-Operative, 3rd and 5th Post-Operative Month, With Corresponding ImageJ Greyscale Histogram Analysis Demonstrating Progressive Socket Remodeling Over Time

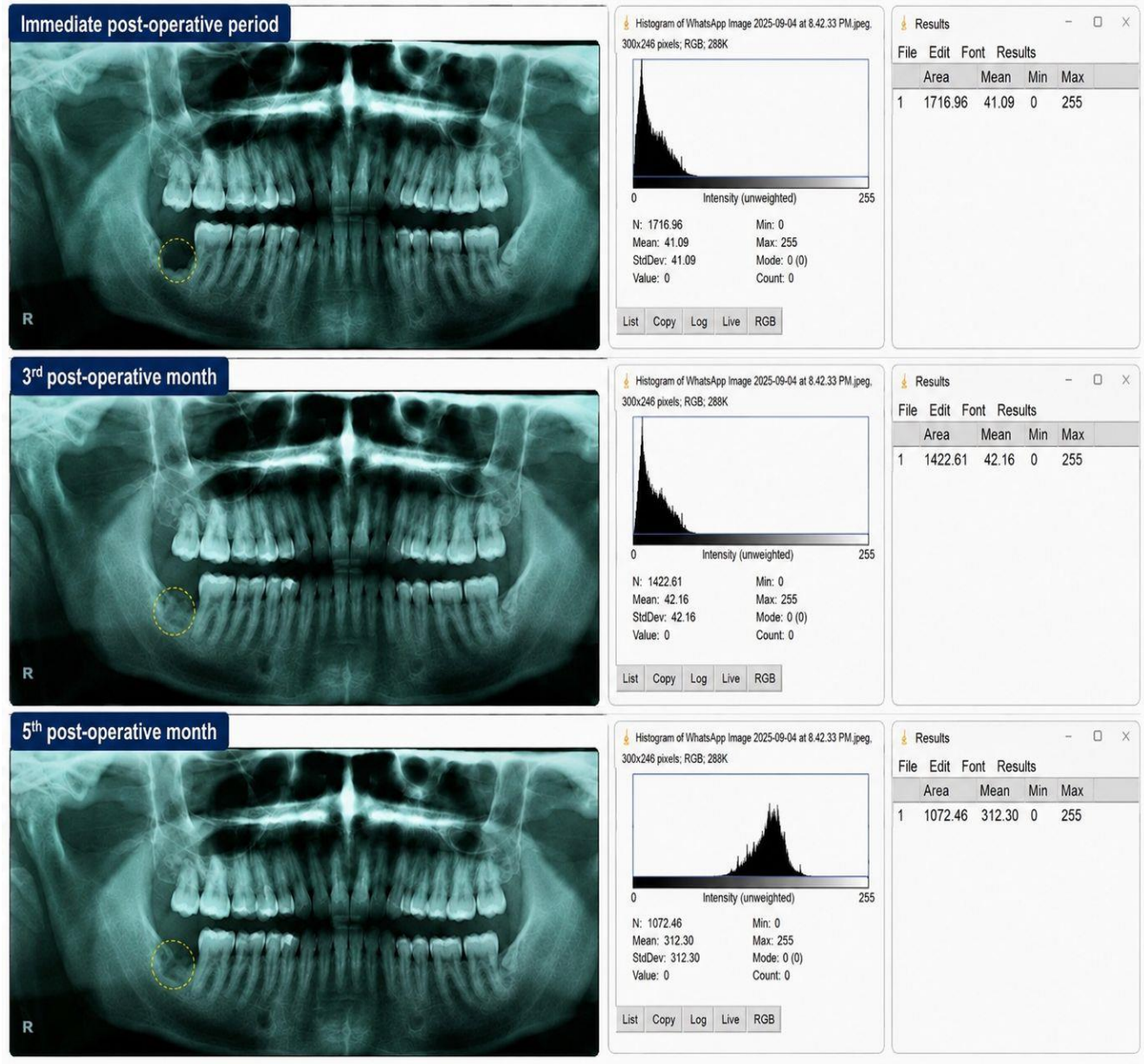

Figure III (b) Serial Panoramic Radiographs of The Control Group B (Without PRF) Show Extraction Socket of Mandibular Right 3rd Molar (yellow circle) at Immediate Post-Operative, 3rd and 5th Post-Operative Month, With Corresponding ImageJ Greyscale Histogram Analysis Demonstrating Progressive Socket Remodeling Over Time

Table No III: Comparison of Pain Levels Between PRF and Non-PRF Groups at Different Time Intervals Using Pearson Chi-Square Test

Pain		Groups		P-Value
		Group A (%)	Group B (%)	
Preoperatively	No Pain	0(0.0%)	0(0.0%)	0.228
	Mild Pain	28(93.3%)	25(83.3%)	
	Moderate Pain	2(6.66%)	5(16.7%)	
	Severe Pain	0(0.0%)	0(0.0%)	
	Worst Possible Pain	0(0.0%)	0(0.0%)	
	Total	30(100.0%)	30(100.0%)	
48hrs post-operatively	No Pain	0(0.0%)	0(0.0%)	0.088
	Mild Pain	3(10.0%)	0(0.0%)	
	Moderate Pain	23(76.6%)	20(66.6%)	
	Severe Pain	4(13.3%)	8(26.7%)	
	Worst Possible Pain	0(0.0%)	2(6.67%)	
	Total	30(100.0%)	30(100.0%)	
72hrs post-operatively	No Pain	20(66.7%)	11(36.7%)	0.022
	Mild Pain	10(33.3%)	15(50.0%)	
	Moderate Pain	0(0.0%)	4(13.3%)	
	Severe Pain	0(0.0%)	0(0.0%)	
	Worst Possible Pain	0(0.0%)	0(0.0%)	
	Total	30(100.0%)	30(100.0%)	
7thday post-operatively	No Pain	26(86.7%)	15(50.0%)	0.007
	Mild Pain	4(13.3%)	12(40.0%)	
	Moderate Pain	0(0.0%)	3(10%)	
	Severe Pain	0(0.0%)	0(0.0%)	
	Worst Possible Pain	0(0.0%)	0(0.0%)	
	Total	30(100.0%)	30(100.0%)	

The pain levels of test group (A) and control group (B) were recorded at various time intervals using the Visual Analog Scale as shown in Figure III. The pain scores of both groups were then compared using the Pearson Chi-square test. Preoperative pain levels did not differ statistically significantly (p = 0.228), suggesting similar baseline features. At 48hrs post-operatively, no statistically significant difference was observed between the two groups (p = 0.088), although group B showed tendency towards higher pain levels. Nonetheless, a statistically significant difference was observed at 72 hours (p = 0.022) and 7 days after surgery (p = 0.007), indicating that the PRF group experienced less discomfort in the early postoperative phase as shown in Table No III.

Table No III: Comparison of Pain Levels Between PRF and Non-PRF Groups at Different Time Intervals Using Pearson Chi-Square Test

The post-operative pain levels of test group (A) and control group (B) were compared using the Mann-Whitney U test. A lower mean rank indicates less pain. All three time points showed statistically significant lower pain levels in group A who received PRF as compared to group B, at 48hrs post-operatively (p = 0.021), at 72hrs post-operatively (p = 0.010) and 7th post-operative day (p = 0.002) as shown in Table No. IV

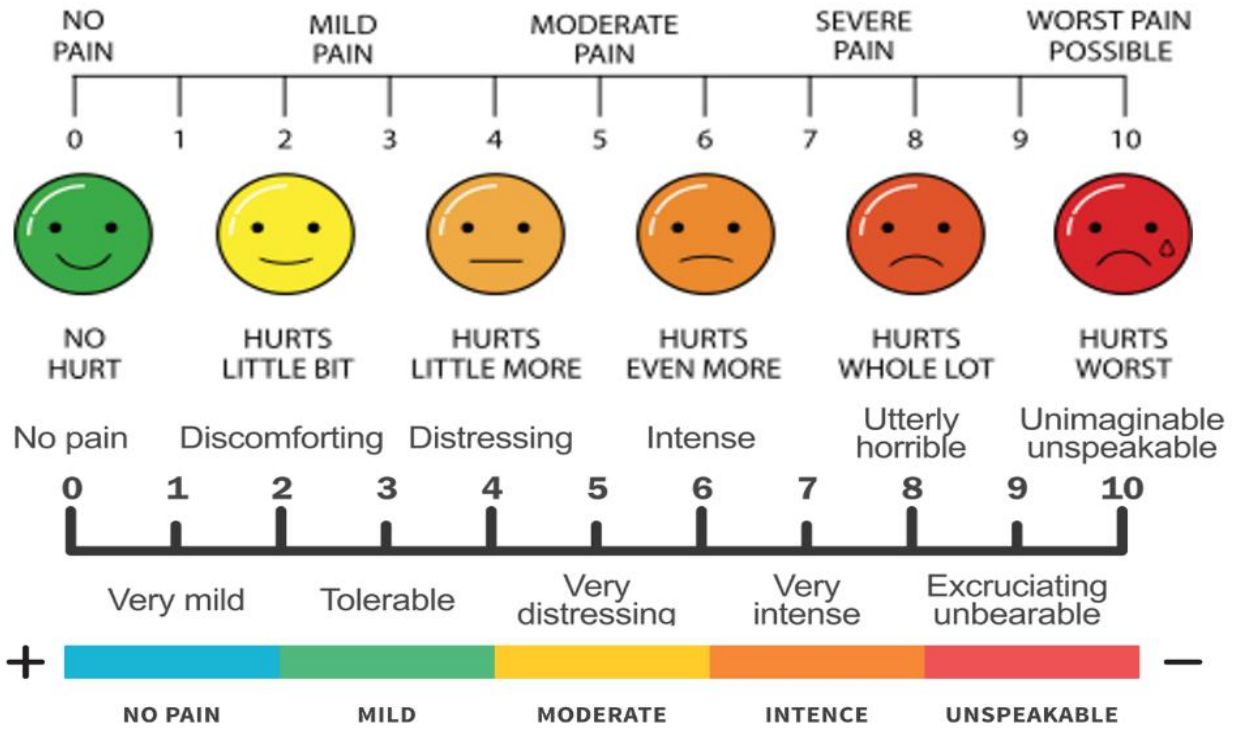

Figure IV. Visual Analog Scale Used for Pain Assessment, Ranging From 0 (no pain) to 10 (worst possible pain), incorporating numerical, descriptive and facial expressions to evaluate pain levels in both Test Group (A) and Control Group (B) at pre-operative, 48hrs, 72hrs and 7th post-operative day intervals.

Table No IV: Postoperative Pain Scores Between PRF and Non-PRF Groups Comparison Using Mann–Whitney U Test

Pain	Groups (n)	Mean Rank	Mann-Whitney U	Z- Value	p-value
48hrs post-operatively	Group A (PRF) (30)	26.37	326.00	-2.321	0.021
	Group B (Non-PRF) (30)	34.63			
72hrs post-operatively	Group A (PRF) (30)	25.33	295.00	-2.579	0.010
	Group B (Non-PRF) (30)	35.67			
7th day post-operatively	Group A (PRF) (30)	24.80	279.00	-3.107	0.002
	Group B (Non-PRF) (30)	36.20			

Discussion:

The study included 60 patients divided into two groups of 30 each, test group (A) who received PRF and control group (B) who did not receive PRF. Demographic characteristics including gender, address, socioeconomic status, education, type and side of impaction were compared between the two groups (Table I). Regarding gender distribution, group A consisted of 11 males (36.7%) and 19 females (63.3%), while group B comprised 17 males (56.7%) and 13 females (43.3%), with no statistically significant difference (p = 0.196). Similarly, residential address between the two groups also did not show any significant difference (p = 0.588), with group A having 21 (70.0%) participants and group B having 18 (60.0%) participants from urban areas, while rural residents comprised 9 (30.0%) and 12 (40.0%) of groups A and B respectively (p = 0.588). With regards to education, 27 (90.0%) of group A participants and 29 (96.7%) of group B participants were educated, against only 3 (10.0%) and 1 (3.3%) uneducated participants respectively (p = 0.605). However, a statistically significant difference was observed in socioeconomic status (p = 0.041), with group A showing higher proportion of middle-class participants, that was 20 (66.7%) as compared to group B that was 15 (50.0%). While group B had a higher proportion of lower-class participants, 8 (26.7%) versus only 1 (3.3%) in group A. The upper-class participants numbered 9 (30.0%) in group A and 7 (23.3%) in group B.

Regarding impaction characteristics, the distribution of impaction type differed significantly between the two groups (p = 0.023). Mesioangular impaction was the most common pattern in both groups, occurring in 16 out of 30 (53.3%) in Group A and 17 out of 30 (56.7%) in Group B. Distoangular impaction was equally distributed at 7 (23.3%) in each group. Notably, vertical impaction was entirely absent in Group A (0/30, 0.0%) but present in 5 patients in Group B (16.7%), while horizontal impaction was recorded in 7 (23.3%) of Group A compared to only 1 (3.3%) in Group B. Impaction side showed no significant difference (p = 1.000), with left mandible involvement in 13 (43.3%) of Group A and 14 (46.7%) of Group B, and right mandible in 17 (56.7%) and 16 (53.3%) respectively, as shown in Table I.

Preoperatively, the vast majority of patients in both groups reported only mild pain, 28 out of 30 (93.3%) in Group A and 25 out of 30 (83.3%) in Group B and reported with moderate pain in only 2 (6.66%) of Group A and 5 (16.7%) of Group B, and no patients reporting severe or worst possible pain in either group. This difference was not statistically significant (p = 0.228), confirming adequate baseline homogeneity. At 48 hours post-operatively, pain levels escalated in both groups as expected. Mild pain was reported in 3 (10.0%) of Group A and none in Group B. Moderate pain was most prevalent, affecting 23 (76.6%) of Group A and 20 (66.6%) of Group B. Group B showed a tendency toward higher pain levels, with 8 patients (26.7%) reporting severe pain versus 4 (13.3%) in Group A, and 2 (6.67%) of Group B reporting worst possible pain compared to none in Group A, though this did not reach statistical significance (p = 0.088).

A statistically significant divergence emerged at 72 hours post-operatively (p = 0.022), where 20 out of 30 (66.7%) of Group A reported no pain compared to only 11 out of 30 (36.7%) of Group B. Mild pain persisted in 10 (33.3%) of Group A and 15 (50.0%) of Group B, while moderate pain was reported in 4 (13.3%) of Group B patients but none in Group A. By the 7th post-operative day, the analgesic advantage of PRF was even more pronounced (p = 0.007), with 26 out of 30 (86.7%) of Group A reporting no pain versus only 15 out of 30 (50.0%) of Group B. Mild pain was still present in 4 (13.3%) of Group A and 12 (40.0%) of Group B, while moderate pain persisted in 3 (10.0%) of Group B patients compared to none in Group A, as shown in Table III.

The Mann-Whitney U test further confirmed PRF's analgesic superiority across all three post-operative time points. At 48 hours, Group A (PRF, n=30) had a mean rank of 26.37 compared to 34.63 in Group B (Non-PRF, n=30), with a Mann-Whitney U value of 326.00 (Z = -2.321, p = 0.021). This advantage widened at 72 hours, with mean ranks of 25.33 for Group A and 35.67 for Group B (U = 295.00, Z = -2.579, p = 0.010). By the 7th post-operative day, the difference was most

pronounced, with Group A achieving a mean rank of 24.80 versus 36.20 in Group B (U = 279.00, Z = -3.107, p = 0.002), indicating that PRF's analgesic effects became progressively stronger through the first post-operative week, as shown in Table IV.

With respect to osseous regeneration, greyscale values representing bone density within the extraction socket were measured at three time points. At the immediate post-operative period, mean greyscale values were 1632.55 ± 36.54 in Group A and 1716.96 ± 41.09 in Group B (p = 0.764), reflecting fresh blood clot density. By the 3rd post-operative month, values declined to 1145.11 ± 38.50 in Group A and 1422.61 ± 42.16 in Group B (p = 0.390), indicating active socket remodeling in both groups. At the 5th post-operative month, values further decreased to 638.68 ± 185.45 in Group A and 1072.46 ± 312.30 in Group B (p = 0.112). Although Group A consistently showed lower greyscale values across all time points suggesting a trend toward more advanced remodeling although none of these differences reached statistical significance (all p > 0.05), as shown in Table II. This could be attributed to spontaneous surgical healing, or to limitations in imaging sensitivity, sample size, or follow-up duration in detecting subtle PRF-related variations.

The baseline pain scores in the current study were similar, suggesting that both groups were clinically comparable prior to surgery. The idea that PRF can lessen early inflammatory discomfort following third molar surgery is supported by the statistically significant decrease in pain seen in the PRF group at 72hrs and one week after surgery.[14] Our findings are consistent with a 2023 systematic review that found PRF was found to significantly reduce pain by 3rd and 7th seventh postoperative days after mandibular third molar removal.[15] Similarly, a prospective randomized controlled study published in 2025 found that PRF significantly reduced postoperative pain during the first six days after mandibular third molar removal. These results of our investigation showed that PRF's analgesic effects were more noticeable at 72hrs and onwards till the end of the 1st post-op week.[16]

According to a 2023 clinical trial on impacted mandibular third molar extraction, the PRF group experienced less discomfort and swelling, especially in the early stages of recovery. It was suggested that the fibrin matrix offers a favorable healing environment.[17] Prior research by Rodrigues ED et al[18] showed that PRF reduced pain and other immediate postoperative consequences following mandibular third molar surgery. When combined, these findings support the theory that PRF is helpful in pain management following lower 3rd molar extraction.[19]

With respect to osseous regeneration, equivalent radiographic bone changes were found regardless of PRF application. Both groups show progressive improvement in greyscales values at 3rd and 5th post-op months. Intergroup differences in terms of bone healing were not statistically significant in this study. This could be due to either spontaneous surgical healing or inadequate sensitivity of the imaging technique, sample size, or follow-up period to identify minute PRF-related variations.

Randomized trials have shown enhanced radiographic bone regeneration and improved postoperative outcomes following PRF application in mandibular 3rd molar sockets. However, the effectiveness of PRF appears to be influenced by factors such as the length of follow-up, imaging modality and PRF preparation method.[18, 20-21] Similarly, research shows that while PRF enhances early healing, the difference fades with time. According to a meta-analysis, PRF can promote osseous healing and lessen pain, while the authors stressed that the clinical evidence is still sparse and inconsistent.[23] Our findings suggest a more conservative radiographic effect while showing comparatively greater benefits in pain alleviation.

Conclusion:

The PRF significantly decreases postoperative pain by the end of 1st post-op week, especially at 72hrs and beyond, but after that the difference moderated. On the other hand, radiographic analysis through Grayscale value did not show statistically significant difference at the measured time points which indicates that the healing parameters improved over time in both groups.

This suggests that PRF may have a stronger short-term analgesic effect than a clearly observable radiographic bone-healing advantage in this study.

Strengths and Limitations:
This study's strength includes the utilization of various follow-up time points and the comparison of objective radiography data and subjective pain results enabling evaluation of both early and later postoperative alterations. It is important to recognize some restrictions, though. The follow-up period was short in terms of evaluating bone formation, the sample size was small, and grayscale-based radiographic evaluation might not be as sensitive as more sophisticated imaging techniques such as CBCT, for assessing bone regeneration. The results may also have been altered by differences in individual healing responses and the precise features of the impaction.

Conflict of Interest: Authors have no conflict of interest

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