Original Article

Comparison of Platelet-Rich Plasma Dressing Versus Normal Saline Dressing for Chronic Non-Healing Ulcers: A Randomized Controlled Trial

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Abstract

Background Chronic non-healing ulcers impose substantial morbidity and healthcare costs. Platelet-rich plasma may accelerate wound healing through growth factors, whereas normal saline provides conventional wound care.

Objective To compare platelet-rich plasma dressing versus normal saline dressing in patients with chronic non-healing ulcers.

Methods A total of 100 patients with chronic non-healing ulcers were randomized equally into platelet-rich plasma dressing and normal saline dressing groups. Diabetic foot ulcers, venous leg ulcers, pressure ulcers, post-traumatic ulcers, and non-diabetic neuropathic ulcers were included. Ulcer area, complete epithelialization, healing time, pain score, wound infection, and surgical intervention were assessed over six weeks. Data were analyzed using SPSS. Independent samples t-test, Mann–Whitney U test, chi-square test, Fisher's exact test, repeated measures analysis, and logistic regression were applied.

Results Follow-up was completed by 46 patients in the platelet-rich plasma group and 44 in the normal saline group; all randomized patients were included in intention-to-treat analysis. Complete epithelialization at week six occurred in 41 (82.0%) patients with platelet-rich plasma and 27 (54.0%) with normal saline (RR: 1.52, 95% CI: 1.14-2.01, *P*=0.005). Mean percentage ulcer area reduction was 93.7±18.2% versus 67.7±41.6% (P<0.001). Median healing time was 24 (IQR 17-27) versus 35 days (IQR 33-40) (P<0.001). Wound infection occurred in 7 (14.0%) versus 17 (34.0%) patients (p=0.035). Platelet-rich plasma dressing remained associated with epithelialization on logistic regression.

Conclusion Platelet-rich plasma dressing was associated with better six-week wound healing response than normal saline dressing. These findings support cautious use as an adjunct to standardized chronic ulcer care.

Keywords Chronic non-healing ulcer; Complete epithelialization; Normal saline dressing; Platelet-rich plasma; Wound healing.

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Introduction

Chronic non-healing ulcers such as diabetic foot ulcers, venous leg ulcers, and pressure ulcers remain a common problem in routine clinical practice. Chronic wounds affect nearly 4% of the global population, while venous leg ulcers are reported in about 1% populations.[1] Diabetic foot ulcers add a major burden, affecting about 18.6 million people yearly, with lifetime risk of 19 to 34% in diabetic patients. Chronic wounds occur at about 86-89 per 10,000 persons yearly, and venous ulcers form 70%

to 90% of chronic leg ulcers.[2]

Non-healing ulcers occur when normal wound repair remains stuck in the inflammatory phase instead of moving toward granulation and closure. Poor arterial flow reduces oxygen supply and new vessel growth, while venous hypertension and edema increase leukocyte trapping, cytokine activity, and continuing tissue injury.[3,4] In diabetic ulcers, neuropathy allows repeated unnoticed trauma, especially when offloading is inadequate. Biofilm-forming bacteria protect themselves from host defenses and antibiotics, keeping protease activity high.[5,6] Excess matrix metalloproteinases, inflammatory cytokines, and oxidative stress damage the wound bed. Hyperglycemia, anemia, malnutrition, smoking, immunosuppression, and fibroblast senescence further weaken collagen formation and delay closure in routine clinical practice daily.[7]

Standard care for chronic non-healing ulcers includes debridement, infection control, moist dressings, pressure relief, compression for venous ulcers, and correction of problems such as diabetes or poor blood flow. Even with care, many ulcers heal slowly and need repeated dressings and long follow-up.[8,9] Platelet-rich plasma has been used as a dressing because it is prepared from the patient's own blood and contains platelets that release growth factors. These factors, including platelet-derived, transforming growth factor beta, vascular endothelial, and epidermal growth factors, help vessel formation, granulation tissue, and epithelial cover.[10]

Previous studies on platelet-rich plasma dressings have shown variable results. Some reported faster ulcer closure, while others found limited difference from standard care. Many studies were limited to one ulcer type, small samples, different PRP preparation methods, or unclear application schedules. In reports, the control treatment was not clearly defined, making comparison difficult. Local evidence using a fixed protocol and normal saline dressing as the comparative is still limited. A randomized study including diabetic, venous, pressure, post-traumatic, and non-diabetic neuropathic ulcers with the same wound bed care in both groups was therefore needed. The objective was to compare platelet-rich plasma dressing versus normal saline dressing in patients with chronic non-healing ulcers.

Methods

This parallel-group randomized controlled trial was conducted in the Department of Dermatology, Multan Medical and Dental College, from March 2025 to February 2026 after approval from the Institutional Review Board through letter number C-93-1053-A dated 14.03.2025. The trial was registered as NCT07420868. Written informed consent was obtained from all patients. Patients were recruited consecutively from outpatient wound clinic and inpatient dermatology services. Sample size was based on reported healing rates of 91.0% with PRP and 66.7% with normal saline. With 5% significance, 80% power, and equal allocation, 90 patients were required; 100 were enrolled for possible follow-up loss.[11]

Patients aged 18 years or above, of either sex, with a chronic cutaneous ulcer present for at least six weeks were included. Diabetic foot, venous, pressure, post-traumatic, and non-diabetic neuropathic ulcers suitable for dressing care were included. If multiple ulcers were present, one measurable index ulcer was selected for serial photography and planimetry. Patients were excluded for suspected malignant, vasculitic, or pyoderma gangrenosum ulcers; critical limb ischemia; osteomyelitis; exposed bone; spreading infection or sepsis; severe anemia, thrombocytopenia, platelet dysfunction, bleeding disorder, pregnancy, lactation, concurrent wound trial treatment, or inability to complete follow-up

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visits.

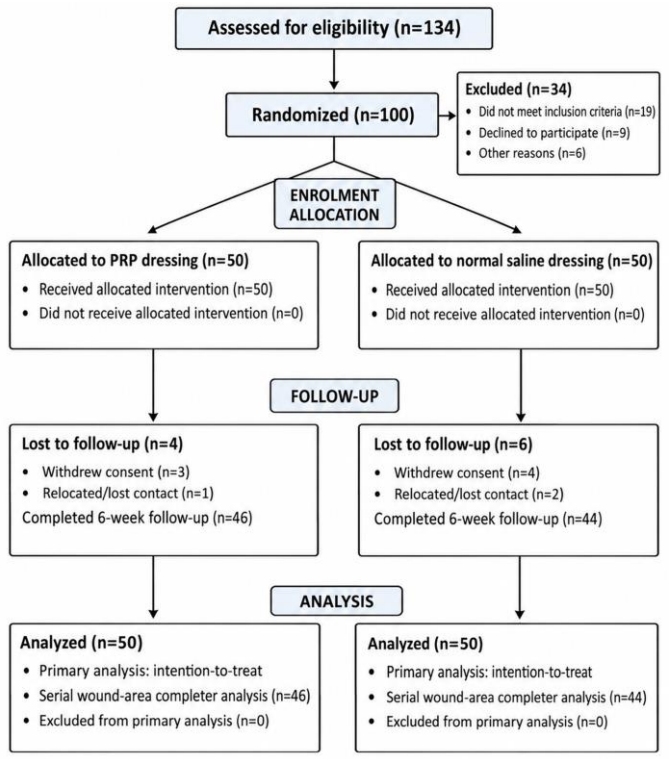
Baseline information included age, gender, smoking status, ulcer duration, ulcer type and site, initial ulcer area, pain score, need for debridement, hemoglobin, platelet count, serum albumin, ankle-brachial index, and HbA1c in diabetic foot ulcer patients. Eligible patients were assigned in a 1:1 ratio to PRP or normal saline dressing by computer-generated randomization. The trial was open-label; patients and treating staff were not blinded because the dressings were visibly different. Both groups received the same basic wound care: cleansing, infection treatment when required, non-adherent dressing, padding, and bandage fixation. Pressure relief was used for pressure ulcers, offloading for diabetic foot ulcers, and compression for venous ulcers after excluding significant arterial disease and reduce imbalance in care delivery.

In the PRP group, autologous platelet-rich plasma was prepared from venous blood under aseptic precautions by a standardized double-centrifugation method. Venous blood was collected into two sterile 10-mL tubes containing 3.2% sodium citrate making it up to 20 ml and processed immediately. A Hettich EBA 20 benchtop centrifuge (Andreas Hettich GmbH & Co. KG, Tuttlingen, Germany; rotor radius 86 mm) was used. The first spin was performed at 1500 rpm (approximately 216 ×g) for 10 minutes and the second at 3500 rpm (approximately 1178 ×g) for 10 minutes. After the second spin, the upper platelet-poor plasma was discarded and approximately 5 mL of PRP was retained. Immediately before application, PRP was activated with 10% calcium chloride at 0.1 mL per 1 mL of PRP, and 5 mL of activated PRP was spread evenly over the cleaned index ulcer after debridement when required. A non-adherent secondary dressing, absorbent padding, and fixation bandage were then applied. PRP dressing was repeated twice weekly for six weeks. In the normal saline group, ulcers were cleaned with sterile normal saline and covered with saline-moistened sterile gauze, followed by the same secondary dressing and fixation method.

The primary outcome was complete epithelialization at week six, defined as full surface closure of the index ulcer with epithelial cover and no open raw area or active discharge. Ulcer area was measured at baseline and weekly by transparent grid tracing. Percentage area reduction was calculated from baseline and follow-up areas. Secondary outcomes were week-six area reduction, time to complete healing, pain score change, wound infection, and surgical intervention. Pain was recorded on a 0-10 Visual Analogue Scale at each scheduled weekly follow-up visit. Wound infection was assessed clinically at each weekly visit and was recorded when purulent discharge was present or when at least two local inflammatory signs (erythema, warmth, swelling or induration, and increasing pain or tenderness) were identified; wound culture was obtained when clinically indicated.

Patients were followed weekly for six weeks. At each visit, ulcer area, wound bed status, granulation, epithelialization, exudate, pain score, infection signs, dressing details, offloading or compression compliance, and complications were recorded. Patients who did not complete the week 6 visit were recorded as lost to follow-up. All randomized patients were included in intention-to-treat analysis, and completer analysis was used for serial ulcer area assessment.

Data were analyzed using SPSS version 26. Normality was assessed using the Shapiro–Wilk test. The Shapiro–Wilk p-values in the PRP and normal saline groups, respectively, were 0.960 and 0.112 for age, 0.528 and 0.076 for baseline pain VAS, 0.193 and 0.601 for hemoglobin, and 0.587 and 0.366 for serum albumin. Ulcer duration (p=0.0002 and 0.007), baseline ulcer area (p=0.048 and 0.006), and platelet count (p=0.002 and 0.017) were non-normally distributed. Qualitative variables were reported as frequency and percentage. Baseline comparison was performed using independent samples t-test for normally distributed continuous



CONSORT 2025 Flow Diagram

Table 1 Baseline demographic and clinical characteristics of study participants.

Variable	*PRP group n=50*	*Normal saline group n=50*	*P-value*
Age, years	50.8 ± 12.8	53.5 ± 11.6	.270[T]
Male	33 (66.0%)	28 (56.0%)	.412[C]
Female	17 (34.0%)	22 (44.0%)	
Smoking status			.181[C]
Never	27 (54.0%)	18 (36.0%)	
Former	12 (24.0%)	15 (30.0%)	
Current	11 (22.0%)	17 (34.0%)	
Ulcer etiology			.979[C]
Diabetic foot ulcer	22 (44.0%)	24 (48.0%)	
Venous leg ulcer	14 (28.0%)	13 (26.0%)	
Pressure ulcer	8 (16.0%)	7 (14.0%)	
Other chronic ulcers (post-traumatic/non-diabetic neuropathic)	6 (12.0%)	6 (12.0%)	
Ulcer duration, weeks	14.9±8.6	16.7±8.8	.321[M]
Baseline ulcer area, cm²	9.22±5.87	8.51±6.59	.570[M]
Baseline pain VAS	5.1±2.2	5.7±2.0	.106
Hemoglobin, g/dL	11.8±2.0	11.8±2.1	.950[T]
Platelet count, ×10⁹/L	222±59	235±67	.277[M]
Serum albumin, g/dL	3.29±0.55	3.23±0.48	.538[T]
Baseline debridement required	34 (68.0%)	33 (66.0%)	1[F]
Lost to follow-up	4 (8.0%)	6 (12.0%)	.739[C]

variables and Mann–Whitney U test for non-normal variables. Chi-square test or Fisher's exact test was used for categorical variables. In **Tables 1** and **2**, T, M, C, F, and L denote independent-samples t-test, Mann–Whitney U test, chi-square test, Fisher's exact test, and log-rank test, respectively; * denotes a statistically significant result ($p<0.05$), while unstarred values are non-significant. Percentage ulcer area reduction, week 6 ulcer area, and pain score change were non-normally distributed and were compared between groups using the Mann–Whitney U test. Serial ulcer area was assessed by repeated measures analysis. Complete epithelialization was reported as risk ratio with 95% confidence interval. Logistic regression was used to identify factors associated with complete epithelialization after adjustment for ulcer duration, baseline ulcer area, albumin, hemoglobin, ulcer etiology, and smoking status. A P-value <0.05 was considered statistically significant.

Result

The mean age was 50.8±12.8 years in the platelet-rich plasma group and 53.5±11.6 years in the normal saline group. Male patients constituted 33, 66.0%, and 28, 56.0%, respectively. Diabetic foot ulcer was the most frequent ulcer type in both groups, followed by venous leg ulcer. Baseline demographic, clinical, wound-related, and laboratory characteristics were statistically comparable between the two groups, as shown in **Table 1**.

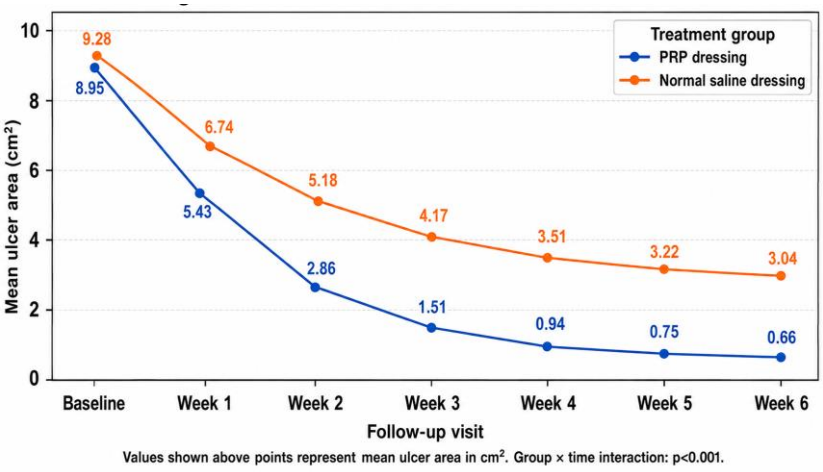


Figure 1 Serial change in mean ulcer area from baseline to week 6 in platelet-rich plasma and normal saline dressing groups

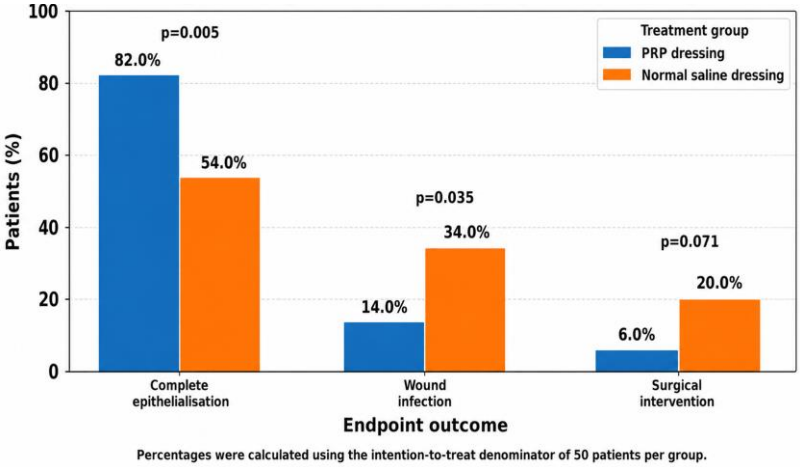


Figure 2 Comparison of complete epithelialization, wound infection, and surgical intervention between platelet-rich plasma and normal saline dressing groups.

At week 6, complete epithelialization on intention-to-treat analysis was achieved in 41 patients (82.0%) in the platelet-rich plasma group and 27 patients (54.0%) in the normal saline group (RR: 1.52, 95% CI: 1.14–2.01, P=0.005). Among completers, ulcer area reduction was greater with platelet-rich plasma (93.7±18.2% vs. 67.7±41.6%, P<0.001), and residual ulcer area was lower (0.66±2.42 cm² vs. 3.04±4.87 cm², P=0.002). Median healing time was shorter with platelet-rich plasma (24 [IQR 17-27] vs. 35 [IQR 33-40] days, P<0.001), while pain reduction was greater and wound infection was less frequent. Surgical intervention did not differ significantly between groups (P=0.071).

Serial wound area measurements showed a progressive reduction in ulcer area in both groups during follow-up. Among completers, mean ulcer area decreased from 9.28±5.96 cm² at baseline to 0.66±2.42 cm² at week 6 in the platelet-rich plasma group. In the normal saline group, mean ulcer area decreased from 8.95±6.90 cm² at baseline to 3.04±4.87 cm² at week 6. Repeated measures analysis showed a statistically significant group-by-time interaction, *P*<.001. The weekly ulcer area values are presented in **Figure 1**.

As shown in **Figure 2**, complete epithelialization was higher in the platelet-rich plasma group than in the normal saline group (82.0% vs. 54.0%, *P*=.005), while wound infection (14.0% vs. 34.0%, *P*=0.035) and surgical intervention (6.0% vs. 20.0%, *P*=0.071) were lower.

Among venous leg ulcers, healing was observed in 11/14 (78.6%) patients in the PRP group and 7/13 (53.8%) in the normal saline group (P=0.178). Among pressure ulcers, healing occurred in 6/8 (75.0%) and 3/7 (42.9%) patients, respectively (P=0.297). For other chronic ulcers (post-traumatic and non-diabetic neuropathic), healing was recorded in 5/6 (83.3%) patients in the PRP group and 4/6 (66.7%) in the normal saline group (P=0.549). On multivariable logistic regression, PRP dressing remained associated with complete epithelialization after adjustment for ulcer duration, baseline ulcer area, albumin, hemoglobin, ulcer etiology, and smoking status (adjusted OR: 4.82, 95% CI: 1.78-13.06, *P*=0.002).

Table 3 presents the unadjusted and adjusted logistic regression results for complete epithelialization by

Table 2 Primary and secondary outcome measures.

Outcome measure	*PRP group*	*Normal saline group*	*Effect measure*	*p/test*
Complete epithelialization by week 6, ITT	41/50 (82.0%)	27/50 (54.0%)	RR 1.52, 95% CI 1.14–2.01	0.005[C*]
Risk difference			28.0%, 95% CI 10.6–45.4	
Percentage ulcer area reduction at week 6, completers	93.7 ± 18.2	67.7 ± 41.6	MD 26.1%, 95% CI 24.1–40.3	<0.001
Week 6 ulcer area, cm², completers	0.66 ± 2.42	3.04 ± 4.87	MD −2.38 cm²	0.002[M*]
Time to complete healing, healed patients only	24 (17–27) days	35 (33–40) days	Log-rank test	<0.001
Pain VAS change from baseline to week 6	−3.11 ± 0.94	−1.63 ± 0.49	MD −1.48, 95% CI −2.1 to −0.7	<0.001
Wound infection during follow-up, ITT	7/50 (14.0%)	17/50 (34.0%)	RR 0.41, 95% CI 0.19–0.88	0.035[C*]
Surgical intervention required, ITT	3/50 (6.0%)	10/50 (20.0%)	RR 0.30, 95% CI 0.09–1.01	0.071[F]

week 6. Normal saline dressing, other ulcer types, and never smoker were used as reference categories for treatment group, ulcer etiology, and smoking status, respectively. Ulcer duration was entered per week, baseline ulcer area per 1 cm², and albumin and hemoglobin per 1 g/dL. Model fit was acceptable, with Hosmer-Lemeshow P=0.612, Nagelkerke R^2=0.381, and AUC=0.791.

Discussion

The present randomized study found that platelet-rich plasma dressing was associated with improved healing outcomes in chronic non-healing ulcers compared with normal saline dressing. Complete epithelialization at six weeks was recorded in 82.0% of patients in the PRP group and 54.0% in the normal saline group. The PRP group also showed greater reduction in ulcer area, shorter documented healing time, greater pain reduction, and lower wound infection frequency. On adjusted analysis, treatment group, ulcer duration, and baseline ulcer area remained associated with complete epithelialization, while surgical intervention showed no statistically significant difference.

The 82.0% complete epithelialization observed with platelet-rich plasma dressing in the present study was close to the healing rates reported in several trials using similar six-week assessment. Local studies from Pakistan reported 91.0% versus 66.7% healing and 92.3% versus 61.5% healing with platelet-rich plasma and normal saline dressing, respectively, which is directionally similar to the present finding of 82.0% versus 54.0%.[11,12] The slightly lower healing rate in the present study is likely related to enrolment of mixed chronic ulcers, including venous and pressure ulcers, rather than diabetic wounds alone, because venous hypertension, tissue edema, pressure-related ischemia, and limited mobility may slow epithelial closure within a fixed six-week period.

A similar result was reported in diabetic foot ulcers, where PRP-soaked dressing achieved 86.7% healing compared with 64.0% with saline dressing, probably because these ulcers were early-grade, non-complex diabetic ulcers with better potential for closure after wound bed preparation.[13] The present finding was also close to the 86.11% versus 63.89% healing reported in chronic diabetic foot ulcers, although that trial used PRP injection with topical gel and followed patients for a longer healing duration, which may explain differences in absolute closure rates.[14] A lower healing rate of 60.87% was reported

Table 3 Crude and adjusted logistic regression for complete epithelialization by week 6.

Variable entered in model	*Adjusted OR*	*95% CI*	*P-value C/a*
Treatment group	3.88 (1.56–9.65)	4.82 (1.78–13.06)	0.004*/0.002*
Ulcer duration	1.00 (0.95–1.04)	0.94 (0.88–1.00)	0.843/0.049*
Baseline ulcer area	1.00 (0.93–1.07)	0.91 (0.83–0.99)	0.984/0.038*
Serum albumin	0.73 (0.32–1.66)	2.14 (0.91–5.03)	0.450/0.082
Hemoglobin	0.85 (0.68–1.05)	1.12 (0.88–1.43)	0.124/0.361
Ulcer etiology	1.14 (0.49–2.66)	1.84 (0.74–4.58)	0.757/0.190
Smoking status	0.25 (0.09–0.69)	0.61 (0.22–1.71)	0.008*/0.349

in mixed chronic wounds, which may reflect inclusion of more heterogeneous and long-standing wounds of at least three months' duration.[15] In contrast, 95% healing was reported in non-ischemic diabetic foot ulcers after vascular assessment, suggesting that exclusion of ischemic ulcers and adequate tissue perfusion can increase the probability of epithelialisation.[16] The much lower complete healing rate of 25% in another saline-controlled trial may be explained by the very small sample size and inclusion of chronic diabetic ulcers assessed over a different outcome framework (Elsaid et al., 2020).[17] Pooled evidence also supports the same direction, with higher complete healing in PRP-treated ulcers in saline-controlled and diabetic foot ulcer meta-analyses.[18,19]

The greater percentage reduction in ulcer area in the PRP group, 93.7% versus 67.7%, was close to the 86.51±15.71% versus 65.47±30.18% reduction reported in diabetic foot ulcers followed for 12 weeks, showing a similar response despite the shorter six-week follow-up in the present study.[20] A smaller but same-direction response was reported at 14 days, with 63.80±5.75% reduction after PRP and 27.02±4.46% after saline, which is likely because early assessment captures granulation and wound contraction before full epithelial cover develops.[21] Similar area reduction was also reported in chronic leg ulcers, 66.39% versus 28.6%, supporting the finding beyond diabetic ulcers.[22] The larger absolute area change in another six-week study, from 42.90 cm^2 to 9.94 cm^2 with PRP, may reflect larger baseline ulcers, where the same biological response produces a visibly greater fall in cm^2.[23] The present median healing time of 24 days was near the 28.3±6.2 days reported in diabetic ulcers and was consistent with pooled shorter healing time for PRP, MD-3.13 weeks.[13,19]

Wound infection, assessed prospectively using the predefined clinical criteria, was lower in the PRP group than in the normal saline group, which was similar to the lower infection rates reported in earlier trials, including 10% versus 45% and 7.7% versus 23.1% in favor of PRP.[12,16] In contrast, comparable infection rates in some pooled andtertiary-care data may reflect heavier wound contamination, variable wound flora, and different infection definitions during follow-up.[18,24]

The subgroup findings showed a clearer difference among diabetic foot ulcers, while venous, pressure, post-traumatic, and non-diabetic neuropathic ulcers did not show statistically significant differences. This pattern was close to prior Pakistani findings where PRP showed stronger results in diabetic and pressure ulcers, while the venous ulcer difference remained non-significant.[11] The greater pain reduction in the PRP group was consistent with reports showing better pain response or only transient application discomfort, while fewer surgical interventions followed the direction of lower amputation or intervention rates reported previously.[15,19]

The clinical relevance of the present study lies in its assessment of PRP dressing in mixed chronic non-healing ulcers under a practical tertiary-care wound setting, rather than restricting analysis to diabetic foot ulcers alone. The study also adds locally relevant data from Pakistan using serial ulcer area measurement, pain assessment, infection documentation, and adjusted analysis. The inclusion of venous, pressure, diabetic, post-traumatic, and non-diabetic neuropathic ulcers make the findings useful for routine dermatology and wound-care services where mixed ulcer presentations are commonly encountered.

The study had some strengths, including randomized allocation, comparable baseline groups, same wound bed preparation in both arms, objective ulcer area measurement, weekly follow-up, intention-to-treat analysis, and assessment of healing, pain, infection, and surgical intervention. However, it was limited by single-center setting, modest sample size, open-label treatment (blinding of patients and treating staff was not practical because the dressings were visibly different), six-week follow-up, small

numbers in ulcer subgroups, and lack of long-term recurrence, scar, cost, quality-of-life, and detailed microbiology data. Future studies should include larger multicenter samples, longer follow-up, ulcer-specific analysis, standard PRP preparation, and assessment of cost, patient comfort, recurrence, and wound care burden.

Conclusion

Platelet-rich plasma dressing was associated with higher complete epithelialization, greater ulcer area reduction, shorter healing time, and fewer wound infections than normal saline dressing during six weeks of follow-up.

Limitations Our study is subjected to few limitations worth mentioning. First selection bias might be

Declaration of patient consent Authors certify that they have obtained all appropriate patient consent.

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Author's contribution

SA: Substantial contributions to study design, interpretation of data, manuscript writing.

NF: Substantial contributions to concept, analysis of data and critical review of the manuscript.

AB: Substantial contributions analysis and interpretation of data and manuscript writing.

AS: Substantial contributions to study design, analysis of data and critical review of the manuscript.

SUNA: Substantial contributions to study design, interpretation of data, manuscript writing.

ZUN: Substantial contributions to study design, data analysis, manuscript writing.

Every author has given final approval of the manuscript version to be published and agreed to be accountable for all aspects of the work.

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