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Original Research

Efficacy Of Platelet Rich Fibrin For Treating Chronic Ulcers

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ABSTRACT

Aim: To evaluate the clinical efficacy of Platelet Rich Fibrin (PRF) in the treatment of chronic ulcers of various etiologies with a focus on wound healing outcomes, microbial clearance, and overall patient response.

Material and Methods: This single-centre, single-group, pre-post, prospective observational study was conducted in the Department of Surgery, LN Medical College, Bhopal, over a period of 6 months. A total of 30 patients aged ≥18 years with chronic leg ulcers (>4 weeks duration) of diabetic, venous, pressure, or traumatic origin were included. Patients with malignancy, autoimmune disorders, systemic infections, or on anticoagulant therapy were excluded. PRF was prepared using 20 ml of the patient's venous blood centrifuged at 3000 rpm for 10 minutes. The PRF membrane was applied weekly under aseptic conditions for a maximum of 12 weeks. Wounds were evaluated weekly for reduction in size, granulation, epithelialization, and microbial presence.

Results: Of the 30 enrolled patients, 22 (73.3%) were male and 8 (26.7%) female, with a mean age of 48 years. Diabetic ulcers were the most common (43.3%), followed by traumatic (23.3%), venous (20.0%), and arterial ulcers (13.3%). The average ulcer duration at baseline was 11 weeks. By the end of 12 weeks, complete wound closure was observed in 24 patients (80%), and 27 patients (90%) achieved >75% reduction in wound size. Two patients (6.7%) showed partial healing (25–50% reduction), while one patient (3.3%) had minimal response (<25% healing). The average healing time for complete epithelialization was 9 weeks. Microbial colonization was initially present in 19 patients (63.3%), but 73.7% of these became culture-negative after PRF application. Six patients with non-healing ulcers had comorbidities and persistent infection, particularly in arterial ulcers.

Conclusion:PRF, with its unique three-layered fibrin-leukocyte matrix, demonstrated effective and well-tolerated healing in chronic ulcers. The treatment led to significant wound closure without the need for additional wound care measures in most cases. Healing outcomes were influenced by ulcer size, microbial burden, and underlying systemic conditions. PRF presents a clinically feasible, cost-effective, and biologically active approach in the management of chronic leg ulcers.

Keywords: Platelet Rich Fibrin, Chronic Ulcers, Wound Healing, Diabetic Ulcers, Autologous Therapy

Introduction

Chronic ulcers represent a significant healthcare challenge due to their prolonged healing time, high recurrence rates, and risk of complications, such as infection and tissue necrosis leading to amputation. These ulcers are typically defined as wounds that do not show measurable signs of healing within 4 to 6 weeks despite appropriate care. They often result in prolonged morbidity, reduced quality of life, and a substantial burden on healthcare resources. Common etiologies include diabetic foot ulcers, venous leg ulcers, arterial ulcers, and pressure ulcers. The persistent nature of these wounds is frequently attributed to poor vascularity, persistent inflammation, bacterial colonization, and impaired tissue regeneration [1,2].

Platelet-rich fibrin (PRF), an autologous blood derivative enriched with platelets and growth factors, has emerged as a promising option in wound care. PRF has shown potential in accelerating tissue repair and reducing infection rates, thereby supporting wound healing through mechanisms of angiogenesis, cell migration, and immune modulation. PRF is an autologous matrix that can be applied as a patch directly onto the wound, providing a biologically active scaffold that promotes cellular proliferation and enhances tissue regeneration. PRF is a second-generation platelet concentrate derived from autologous blood, obtained without the use of

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anticoagulants, and prepared through a single centrifugation process. This technique results in a fibrin-rich matrix containing platelets, leukocytes, cytokines, and growth factors, all of which contribute to tissue healing and regeneration [2,3].

Unlike Platelet-Rich Plasma (PRP), which releases growth factors in a burst, PRF allows for the sustained release of bioactive molecules over several days due to its dense fibrin structure. This characteristic makes PRF more biologically suitable for the treatment of chronic ulcers, where prolonged stimulation of tissue repair is essential [3,4]. The fibrin matrix also serves as a scaffold for cellular migration and angiogenesis, both of which are critical processes in wound healing. Furthermore, PRF is simple to prepare, cost-effective, and biocompatible, with minimal risk of immune reaction, as it is derived from the patient's own blood [4,5].

The biological basis of PRF's efficacy lies in the central role that platelets and leukocytes play in wound repair. Platelets contain a range of growth factors, such as vascular endothelial growth factor (VEGF), platelet-derived growth factor (PDGF), transforming growth factor-beta (TGF-β), and epidermal growth factor (EGF), which are known to promote tissue regeneration, angiogenesis, and epithelialization [5,6]. In addition, leukocytes present in PRF contribute to the control of infection and modulate the inflammatory response, thereby creating a more favorable wound healing environment [6].

Several clinical studies have demonstrated the beneficial effects of PRF in chronic wound management. The application of PRF has shown to significantly reduce wound size, promote faster epithelialization, and improve granulation tissue formation in chronic non-healing leg ulcers [1,2]. These outcomes have been consistent across various etiologies of ulcers, including diabetic, venous, and pressure ulcers. Moreover, patients receiving PRF treatment have reported greater comfort and less need for additional interventions, making it a patient-friendly therapy [2,3].

Comparative evaluations have further strengthened the evidence for PRF's therapeutic potential. Studies comparing PRF with other advanced wound care modalities, such as epidermal cell suspensions or synthetic dressings, have found PRF to be equally or more effective in terms of healing rates and patient outcomes [4]. In particular, PRF offers the advantage of being a one-time, chair-side preparation that does not require laboratory processing, unlike some other cellular or tissue-engineered products [3,4].

The role of platelets in regenerative medicine has been well established through experimental and clinical studies. Platelets not only serve a hemostatic function but also act as reservoirs of bioactive molecules critical for tissue healing. These growth factors are released in a sustained manner when embedded in the fibrin matrix of PRF, allowing for extended biological activity at the wound site [5]. Furthermore, interactions between platelets, endothelial cells, and fibroblasts stimulate angiogenesis, collagen deposition, and re-epithelialization, which are essential steps in wound closure [6].

A notable benefit of PRF is its ability to support healing even in wounds that are refractory to standard treatments. Its fibrin scaffold facilitates cellular migration and neovascularization, while its leukocyte content contributes to antimicrobial activity and immune modulation [5,6]. These combined actions not only enhance tissue regeneration but also reduce the likelihood of secondary infections, a common complication in chronic wounds.

In addition to being compared with PRP, PRF has also been evaluated against other topical treatments such as zinc oxide and phenytoin paste. These comparisons have consistently shown that PRF offers superior healing outcomes, often with faster response times and better tissue quality [7-9]. While PRP has shown benefits in acute and surgical wounds, PRF's more sustained release profile and superior mechanical properties give it an edge in treating chronic, long-standing ulcers [7].

Alternative methods, such as hirudotherapy, have also been explored for chronic wound healing. Although beneficial in specific scenarios, these techniques lack the reproducibility and broad-spectrum efficacy demonstrated by PRF [8]. Furthermore, the preparation and application of PRF require minimal equipment and training, making it a practical option even in low-resource healthcare settings.

Material and Methods

This study was designed as a single-centre, single-group, pre-post, prospective observational study aimed at evaluating the efficacy of Platelet Rich Fibrin (PRF) in the treatment of chronic ulcers.The study was conducted over a period of 6 months.The research was carried out in the Department of Surgery at LN Medical College, Bhopal.The primary outcome assessed was wound healing, evaluated through clinical parameters such as reduction in wound size, improvement in wound bed condition, and the time taken for complete epithelialization.A total of 30 patients with chronic leg ulcers persisting for more than 4 weeks were included in the study after meeting the eligibility criteria.Patients were followed up weekly for a total duration of 12 weeks. At each follow-up visit, the wound was assessed for changes in size, granulation tissue formation, presence of exudate, and signs of infection.

Inclusion Criteria:

Patients were eligible if they were:

- Aged 18 years or older
- Diagnosed with chronic leg ulcers of various etiologies, including:
  - Venous leg ulcers (VLUs)
  - Diabetic foot ulcers (DFUs)

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- Pressure ulcers (PUs)

Exclusion Criteria:
Patients were excluded from the study if they had:

- Active malignancy
- Autoimmune disorders
- Severe infections requiring systemic antibiotics
- Ongoing anticoagulant therapy
- Known allergy to PRF components
- Poor general health status unsuitable for study participation

Study Procedure
Platelet Rich Fibrin (PRF) was prepared individually for each patient using an autologous blood sample. A total of 20 ml of venous blood was collected from a peripheral vein under sterile conditions. Importantly, no anticoagulants were added to the blood sample to maintain the natural clotting cascade.(Figure A) The blood was then immediately subjected to centrifugation at a speed of 3000 revolutions per minute (rpm) for a duration of 10 minutes.(Figure B) This centrifugation process facilitated the separation of blood components, resulting in two distinct layers: a red blood cell-rich layer at the bottom and a platelet- and leukocyte-rich fibrin clot forming the upper layer.(Figure C)

Following centrifugation, the PRF clot was carefully extracted and gently compressed using sterile gauze to form a thin, pliable membrane approximately 1–2 mm in thickness. This membrane was designed to facilitate easier handling and ensure effective coverage of the wound surface..(Figure D) Under strict aseptic conditions, the ulcer area was first cleaned thoroughly with normal saline to remove debris and contaminants. The prepared PRF membrane was then applied directly onto the cleaned wound bed, ensuring complete coverage of the ulcer area.(Figure E)
Once the PRF membrane was positioned, it was secured using a non-adherent primary dressing to prevent displacement. This was followed by additional layers of secondary dressings to maintain a moist wound environment, which is crucial for optimal healing, and to provide protection against external contamination. (Figure F)
This standardized protocol was consistently followed for all patients enrolled in the study. Wound healing was monitored weekly over a 12-week follow-up period. During each visit, clinical assessments were made to evaluate wound size reduction, granulation tissue formation, and epithelialization. The overall efficacy of PRF was determined based on the extent and speed of wound healing observed throughout the follow-up duration. (Figure G)

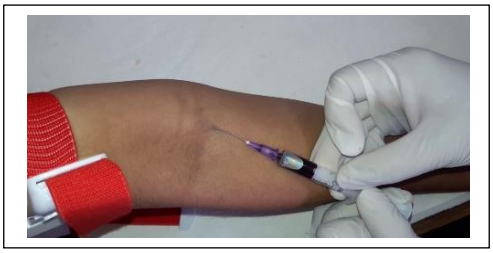
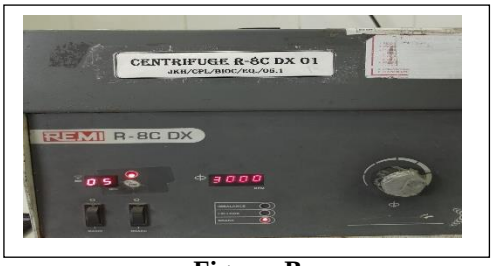


Figure: A



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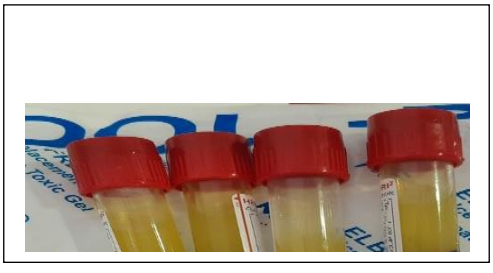

Figure: C

Figure: D

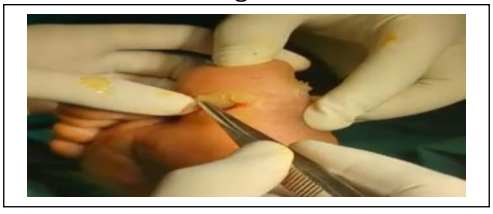

Figure: E

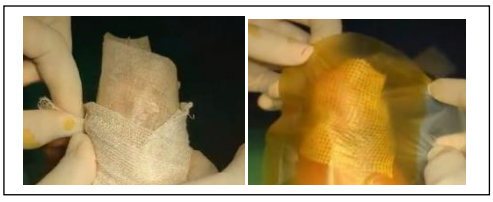

Figure: F

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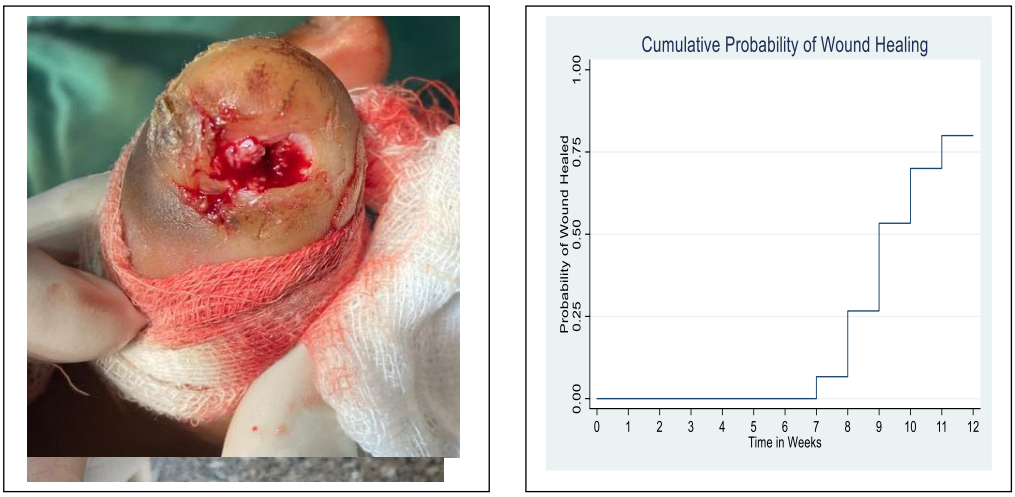

Figure: G

Results

Demographic Characteristics

A total of 30 patients were enrolled in the study. The majority of the participants were males, accounting for 22 patients (73.3%), while females constituted 8 patients (26.7%) (Table 1). The age of participants ranged from 34 to 62 years, with a mean age of approximately 48 years.

Ulcer Aetiology and Duration

Ulcers of varying etiologies were observed among the participants. Diabetic ulcers were the most prevalent, seen in 13 patients (43.3%), followed by traumatic ulcers in 7 patients (23.3%). Venous ulcers were noted in 6 patients (20.0%) and arterial ulcers in 4 patients (13.3%) (Table 2). The duration of ulcers at the time of PRF treatment ranged from 6 to 16 weeks, with the mean duration being approximately 11 weeks.

Wound Healing Outcomes

By the end of the 12-week follow-up period, 24 patients (80%) demonstrated complete wound closure, which was defined as 100% epithelialization with no visible granulation tissue or drainage. Furthermore, 27 patients (90%) showed significant healing with a reduction in wound size exceeding 75%. Two patients (6.7%) achieved partial healing, marked by a 25% to 50% reduction in wound size. One patient (3.3%) had minimal healing (<25%) and was classified as a non-healer (Table 3).Among the 24 patients who achieved complete wound closure, the **mean time to healing** was approximately **9 weeks**. It was observed that ulcers of diabetic and venous origin required longer healing times as compared to traumatic ulcers.

Microbial Flora and Response to PRF

At baseline, wound swabs revealed microbial growth in 19 out of 30 patients (63.3%). The most commonly isolated organisms were *Staphylococcus aureus* and *Pseudomonas aeruginosa*. Upon reassessment at the 12th week, follow-up swabs indicated that 14 of the 19 initially culture-positive patients (73.7%) had negative cultures, reflecting a marked reduction in microbial colonization, which may be attributed to the local immunomodulatory effect of PRF (Table 4).

Characteristics of Non-Healing Ulcers

Of the 30 patients, six were categorized as having non-healing ulcers based on incomplete or minimal healing response. Regarding ulcer etiology, 3 patients (50%) had arterial ulcers, 2 patients (33.3%) had diabetic ulcers, and 1 patient (16.7%) had a venous ulcer. All six patients (100%) had multiple comorbidities, most commonly involving hypertension and diabetes mellitus. Additionally, two patients (33.3%) were found to be immunocompromised due to chronic steroid use or underlying immunosuppressive disorders.Clinically, non-healing ulcers were generally larger in size at baseline, had longer durations before initiation of PRF therapy, and displayed signs of chronic inflammation and tissue fibrosis. Moreover, microbial cultures from these wounds continued to show persistent colonization with pathogenic organisms such as *Staphylococcus aureus* and *Pseudomonas aeruginosa* despite regular PRF applications (Table 5).

Table 1: Demographic Characteristics of Participants

Parameter	Number	Percentage (%)
Male	22	73.3%
Female	8	26.7%
Mean Age (years)	–	~48 years

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Table 2: Aetiology and Duration of Ulcers

Aetiology of Ulcers	Number	Percentage (%)
Diabetic Ulcers	13	43.3%
Traumatic Ulcers	7	23.3%
Venous Ulcers	6	20.0%
Arterial Ulcers	4	13.3%
Mean Duration	–	~11 weeks

Table 3: Wound Healing Outcomes at 12 Weeks

Healing Outcome	Number	Percentage (%)
Complete Wound Closure (100%)	24	80.0%
Significant Healing (>75%)	27	90.0%
Partial Healing (25–50%)	2	6.7%
Minimal Healing (<25%)	1	3.3%

Table 4: Microbial Flora Before and After Treatment

Microbial Status	Number	Percentage (%)
Positive Culture at Baseline	19	63.3%
Negative Culture at Week 12 (among those 19)	14	73.7%

Table 5: Characteristics of Non-Healing Ulcers

Non-Healing Factors	Number	Percentage (%)
Arterial Ulcers	3	50.0%
Diabetic Ulcers	2	33.3%
Venous Ulcers	1	16.7%
Multiple Comorbidities (e.g., Hypertension, Diabetes)	6	100.0%
Immunocompromised Status	2	33.3%
Large Size & Chronic Inflammation at Baseline	6	100.0%
Persistent Microbial Colonization	6	100.0%

Discussion

In our study, the majority of patients were male (73.3%) with a mean age of 48 years. This trend is supported by Naik et al. (2013), who observed a higher incidence of chronic ulcers in middle-aged male patients, likely due to increased exposure to trauma, occupational risks, and a higher prevalence of comorbid conditions such as diabetes and peripheral vascular disease [10]. Rayner et al. (2009) also reported that leg ulcers often present atypically and are commonly associated with multiple systemic comorbidities, reinforcing the need for early and advanced interventions in such populations [11].

The most common ulcer type in our study was diabetic foot ulcer (43.3%), followed by traumatic (23.3%), venous (20.0%), and arterial ulcers (13.3%). These findings are consistent with the clinical observations by Madhu et al. (2022), who highlighted diabetic ulcers as the predominant type of chronic non-healing wound in Indian patients [12]. Similarly, Agale (2013) emphasized that diabetic ulcers are often slow to heal due to poor vascularization and neuropathy, requiring biologically active therapies to promote tissue repair [13]. The average duration of ulcers in our study was 11 weeks, indicating chronicity. Dorjay et al. (2021) noted that longer ulcer durations often correlate with greater tissue damage and delayed healing, further justifying the application of advanced therapies like PRF [14].

Our results showed that 80% of patients achieved complete wound closure, and 90% showed more than 75% reduction in wound size. This outcome is in agreement with findings from Somani et al. (2017), who reported a significantly higher healing rate in chronic venous ulcers treated with PRF compared to conventional dressings [15]. Madhu et al. (2022) also reported a comparable healing rate of over 70% in chronic ulcers treated with PRF within a 10-week period [12].

Moreover, we observed a mean healing time of 9 weeks, particularly longer in diabetic and venous ulcers. These results align with those of Suryanarayan et al. (2014), who demonstrated slower epithelialization in diabetic ulcers due to impaired angiogenesis and prolonged inflammation [16]. Naik et al. (2013) similarly confirmed that delayed healing is more common in diabetic patients, necessitating multiple sessions of PRF application for effective wound management [10].

Despite these overall positive outcomes, one patient (3.3%) showed minimal healing. This aligns with observations by Steenvoorde et al. (2008), who reported variable responses to PRF, particularly in cases with compromised blood flow and complex comorbidities [17].

At baseline, 63.3% of patients had positive wound cultures, primarily with *Staphylococcus aureus* and *Pseudomonas aeruginosa*. By the 12th week, 73.7%

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of these patients converted to culture-negative status. This microbial improvement is likely due to the antimicrobial and immunomodulatory properties of PRF. Choukroun et al. (2000) were among the first to suggest that leukocytes present in PRF play a critical role in controlling wound colonization through cytokine release [18]. Davis et al. (2014) further supported this, noting that PRF creates a local immune-rich environment that reduces microbial burden while promoting regeneration [19].

Our findings corroborate those of Suresh et al. (2014), who demonstrated that PRF application significantly reduced microbial colonization and supported granulation in diabetic foot ulcers [20]. Thus, PRF not only promotes tissue regeneration but also plays a pivotal role in creating a biologically clean wound bed.

Despite the overall success of PRF, six patients in our study (20%) did not achieve complete healing. Arterial ulcers comprised 50% of these non-responders, and all six had multiple comorbidities such as diabetes and hypertension. Additionally, 33.3% were immunocompromised. These factors are well-documented barriers to wound healing. Rayner et al. (2009) emphasized the negative impact of systemic illness and immunosuppression on ulcer recovery [11]. Steenvoorde et al. (2008) similarly observed poor healing outcomes in ischemic and immunocompromised cases despite PRF use [17].

Clinically, these non-healing ulcers were larger at baseline, showed signs of chronic inflammation and fibrosis, and continued to show microbial colonization despite repeated PRF applications. Dorjay et al. (2021) noted that ulcers with extensive tissue fibrosis and biofilm formation often require adjunctive treatments along with PRF for successful healing [14]. Agale (2013) also underlined that chronicity and ulcer size are significant predictors of poor outcomes, particularly in cases involving arterial insufficiency [13].

Persistent infection in these ulcers is another limiting factor. Although PRF has demonstrated antimicrobial potential, its efficacy may be reduced in biofilm-dense wounds. As observed by Suresh et al. (2014), combining PRF with debridement and antimicrobial therapy may be more effective in such cases [20].

Conclusion

Healing is mediated by distinct three layered composition of leucocytes & PRF, is well tolerated treatment feasible to clinical practice and has potential armamentarium of chronic ulcer. In the present study, progressive reduction in ulcer surface area was observed over a maximum follow-up period of 12 weeks. Notably, many patients achieved complete wound closure characterized by 100% epithelialization, absence of exudate or granulation tissue, and no further requirement for dressing or additional wound care interventions. The need for multiple PRF sessions varied among patients and was largely influenced by the initial size of the ulcer and the regularity of follow-up. While some ulcers responded completely after just two applications, others especially larger or more complex wounds required up to four sessions to achieve full epithelialization.

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