

## Effectiveness of Platelets Rich Plasma Regimen in Diabetic Foot Ulcer Management

Muhammad Rehan Khan, Waqas Hanif\*, Afzal Saeed Awan\*\*, Usama Akhter\*\*\*, Syed Munim Hussain\*\*\*\*, Syed Mukarram Hussain\*\*\*\*\*

Department of Surgery, Combined Military Hospital, Bannu/National University of Medical Sciences (NUMS) Pakistan, \*Department of Pathology, Combined Military Hospital, Bannu/National University of Medical Sciences (NUMS) Pakistan, \*\*Department of Surgery, Combined Military Hospital, Attock/National University of Medical Sciences (NUMS) Pakistan, \*\*\*Department of Surgery, Pakistan air force Hospital, Kamra attock Pakistan, \*\*\*\*Department of Surgery, Rawalpindi Medical University, Rawalpindi Pakistan, \*\*\*\*\*Department of Surgery, Combined Military Hospital, Peshawar/National University of Medical Sciences (NUMS) Pakistan

### ABSTRACT

**Objective:** To determine effectiveness of autologous platelet-rich plasma gel versus conventional therapy regimen in the diabetic foot ulcers management based on the number of days required for granulation tissue growth and wound healing time.

**Study Design:** Cross sectional study.

**Place and Duration of Study:** Combined Military Hospital, Bannu Pakistan, from Aug 2021 to Jan 2022.

**Methodology:** In this study we enrolled 60 patients with diabetic foot ulcers and categorized them into two groups: those who got PRP (Group 1) and those who received conventional therapy regimen for wound (Group 2). The PRP group received gel based autologous PRP as a dressing, whereas the control group received no treatment. Consent was taken from every participant and study was conducted with the approval of Ethical Review Board of the institution.

**Results:** Out of 60 patients with diabetic foot ulcer, 30 patients were given PRP therapy. Mean age with SD of patients were 57+9 years. In these 30 patients, 23(77%) were male and 7(23%) were female. Other 30 were managed with conventional regimen of therapy. Mean age with SD of these 30 patients were 58+11. In these 30 patients, 23(77%) were male and 7(23%) were female. Our study revealed that the healing rate of the PRP group was significantly higher than that of the conventional therapy regimen group. The PRP group experienced much faster healing rates each week (0.65) than the conventional therapy regimen group (0.50). Compared to the PRP group, healing occurred at 12th week was 7.84 cm, with a significantly higher rate as compared to group 2, which showed healing 5.31 cm at 12th week.

**Conclusion:** Autologous platelet-rich plasma (PRP) is an effective and safe treatment for diabetic foot ulcers as compared to conventional treatment.

**Keywords;** Platelet-rich plasma, Conventional therapy, Diabetic foot ulcer Effectiveness of Platelets rich plasma regimen in diabetic foot ulcer management.

**How to Cite This Article:** Khan MR, Hanif W, Awan AS, Akhter U, Hussain SM, Hussain SM. Effectiveness of Platelets Rich Plasma Regimen in Diabetic Foot Ulcer Management. *Pak Armed Forces Med J* 2025; 75(Suppl-6): S878-S882. DOI: <https://doi.org/10.51253/pafmj.v75iSUPPL-6.8182>

This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by-nc/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

### INTRODUCTION

Diabetic foot ulcer is a forbidding obstacle of diabetes mellitus.<sup>1</sup> Moreover, the cases of diabetes mellitus patients expeditiously escalate to 439 million at the end of 2030. It frequently develops into nonhealing wounds in 15 % patients. The findings of Alvarsson *et al.*<sup>2</sup> revealed that diabetic foot ulcers were responsible for up to 88 percent of all amputations of lower limb in the United States in 2012. Diabetic foot ulcer (DFU) is the consequence of peripheral vascular disease and diabetic neuropathy.<sup>3</sup> The peripheral vascular disease decreases the blood flow to tissues causing the ischemia, diminished oxygen supply and nutrients to wound. Epithelial cells present at wound cannot be able to produce vital factors necessary for remedial such as VEGF and PDGF due to Insufficiency

of oxygen and nutrients.<sup>4</sup> These changes exhibit hinderance in the healing activity and shatter the customary healing process and finally land into lower leg amputation. As matter of fact, DFUs are always difficult and challenging to treat with multidisciplinary approach. Conventional therapy regimen for DFUs alone does not always result in complete healing and often needs more avant-garde therapies.<sup>5</sup>

Early wound closure is the ultimate objective of diabetic foot ulcer management. Conventional therapy regimen for diabetic foot ulcers includes appropriate wound debridement, pressure relief over wound, suitable antiseptic dressings (e.g., saline soaked dressings), administration of antibiotics for infection, ischemia management, management of medical comorbidities (e.g., Chronic renal disease).<sup>6</sup> Great advancement has been made to find the strategies for wound healing in recent years, out of which

**Correspondence:** Dr Muhammad Rehan Khan, Department of Surgery, Combined Military Hospital, Bannu Pakistan  
Received: 17 Feb 2022; revision received: 17 Apr 2022; accepted: 31 May 2022

autologous platelet-rich gel appear more fascinating.<sup>7</sup> Autologous PRP is a fraction of one's own venous blood with platelet concentration above baseline ( $1 \times 10^9$  platelets per ml of plasma) obtained following peculiar centrifugation.<sup>8</sup> PRP contains growth factors, cytokines, chemokines, and fibrin scaffold.<sup>9</sup> The growth factors enhance epithelialization by the formation of neo-vessels, enticement of mesenchymal cells and fibroblasts, production of collagen fibres, and by multiplication of keratinocytes to give rise granulation tissue. PRP may also suppress inflammation by controlling cytokine release.<sup>18</sup> PRP has also been showed antimicrobial activities against pathogens including some bacteria (*Escherichia coli*, MRSA), *Candida albicans*, and *Cryptococcus neoformans*. Scientific literature shows encouraging results by applying PRP for the diabetic foot ulcer management.<sup>10</sup>

Rationale of our study to find the effectiveness of autologous PRP gel versus standard wound care in the management of DFUs based on the number of days required for granulation tissue growth and the wound healing time.

## METHODOLOGY

A cross-sectional study conducted in Surgical and Pathology department of Combined Military Hospital Bannu from August 21 to January 22 after the approval of Ethical Review Board of our Hospital (Combined Military Hospital, Bannu: 02/07/ER), Sample size is 60, calculated by using 95 % confidence interval. Non-probability, consecutive sampling technique was used. 60 diabetic patients with foot ulcers are incorporated in our study. A written consent was received from every participant and baseline characteristics with complete medical history and laboratory examinations were measured.

**Inclusion Criteria:** Diabetic Patients with foot ulcers greater than 1 cm diameter that have not healed three months after surgical wound debridement and treatment were included in our study.

**Inclusion Criteria:** Patients with obvious illness or gangrene on a local level (no redness, no hotness, no purulent discharge, no osteomyelitis in X-ray with a negative probe to bone test, and negative C-reactive protein), patients who had reached the later stages of organ failure, such as hepatic or renal failure, patients on anticoagulant-treatment, patients receiving antiplatelet therapy, patients suffering from thrombocytopenia, patients who were receiving steroid therapy, patients with ulcers with a diameter

of less than 1cm or greater than 8 cm with ulcers that were deeper than 2 cm and patients with lower limb ischemia (acute or chronic) and the absence of distal limb pulsations with a greater than 0.9 ankle-brachial index ruled out limb ischemia were excluded from the study.

Diabetic patients with foot ulcer disease, fulfilling the inclusion and exclusion criteria and gave consent to participate in the study, were enrolled in our study. Patients were appraised by adequate history and detailed examination. All patients were investigated for complete blood count, haematocrit, renal function tests, liver function test, serum albumin, plasma glucose, HbA1C and Doppler ultrasound scan of the leg and X-ray of the foot at time of admission by respective specialists. The size of DFUs had also been recorded before treatment. Then, patients were categorized to grades as per Texas University classification. Patients were also showed to medical specialist for strict plasma glucose control.

We took 2.5 ml of blood in EDTA tube and analyzed platelets count by Sysmex X 100. We proceeded further when platelets count was within normal limit. Now we took 20 ml of blood in CPDA syringe and transfer it equally (5ml) into 4 glass tubes. Centrifuged these 4 glass tubes in Biomed-20 centrifuge at 1000 RPM for 10 min. This spin separated the cellular content from plasma. After that plasma of these tubes transferred into a single glass tube. Then, the plasma was centrifuged at 3500 rpm for 15 minutes in Biomed-20 centrifuge. After this spin supernatant was removed to other tube and remaining plasma was platelet rich plasma (PRP).<sup>11</sup>

The wound was being debrided. To begin, the margins and floor of the incision were debrided, and any callosities in the surrounding area were eliminated. When callosities returned around the wound, this process was repeated if necessary. This treatment was used to convert a chronic wound into an acute wound.

Half of PRP, prepared, was used to cover diabetic foot ulcer and remaining half PRP was injected inside and around the periphery of the wound/ ulcer subcutaneously. After that, Anti-septic dressing applied.

During the treatment, patients were advised to use antidiabetics, antibiotics, NSAID, and vitamin.

Procedure for dressing: The wound toilet was done with normal saline before being covered with

normal saline soaked gauze. If the wound does not heal fully after two weeks, repeat the procedure.<sup>12</sup> 30 patients were given this regimen

The first step is termed as debridement of the wound. To begin, the incision's margins and floor were debrided, as well as any callosities in the area. This technique was repeated if callosities surrounding the wound returned. This technique converted the chronic wound into an acute one.

Conventional therapy regimen: The wound toilet was done with normal saline and then coated in Vaseline gauze and a sterile dressing. After 20 weeks, if the wound does not heal, the dressing should be replaced every two days and 30 patients were given this management

Data was analyzed with SPSS version 21 Kolmogorov smirnov test was used to find nature of data. The paired t-test was used to compare the mean of data obtained before and after management, and the independent t-test was used to compare the means of two groups. Qualitative data was provided as frequency and percentage while quantitative data was represented by mean and standard deviation. The two-sample t test or Fisher's exact test were used to compare them, depending on the situation. The result was considered statistically significant if the *p*-value was less than 0.05.

## RESULTS

Out of 60 patients with diabetic foot ulcer, 30 patients were given PRP therapy. Mean age with SD of

had history of hypertension and 14(47%) had history of smoker. 8(27%) patients had HbA1c level of 8.90% to 9.20%. 14(47%) were with right foot affected. 20(66%) patients had ulcer length of 3.90 to 4.30 cm and 23(77%) patient had width of 1.60 to 2.30 cm. 6 (20%) had ulcer area of 6.80 to 6.90 cm<sup>2</sup>. Other 30 were managed with conventional regimen of therapy. Mean age with SD of these patients were 58±11 years. In these 30 patients, 23(77%) were male and 7(23%) were female. 9(30%) had history of hypertension and 10(33%) had history of smoking. 11(37%) patients had HbA1c level of 8.90% to 9.50%. 21(70%) out 30 patients were with right foot affected. 15(50%) patients had ulcer length of 3.90 to 4.50 cm and 9(30%) patient had width of 1.80 to 1.90 cm. 8(27%) had ulcer area of 6.80 to 6.90 cm<sup>2</sup>. The baseline demographic characteristics were recorded for every patient. History of hypertension and smoking were taken. While laboratory examinations of HbA1c, hemoglobin level, platelet an albumin count were investigated (Table-I).

The baseline size of ulcer was recorded in every patient. The mean length with SD of ulcer in group 1 and group 2 was 3.87±0.419 cm and 3.81±0.406 cm respectively and the mean width with SD of the ulcer was 1.82±0.321 cm and 1.85±0.29 cm in group 1 and group 2 respectively. The mean area with SD of ulcer taken was 7.13±0.403 cm<sup>2</sup> and 7.25±0.374 cm<sup>2</sup> in group 1 and 2 respectively whereas, the mean volume with SD within group 1 was 1.68±0.43 cm<sup>3</sup> and 1.71±0.457 cm<sup>3</sup> in group 2 (table-II).

The weekly repair of foot ulcers was assessed. 1<sup>st</sup>

Table-I: Variables with Mean, Standard Deviation and Percentages (n=60)

Demographic Characteristics	Prp (Group 1)	Conventional Management (Group 2)
Age (years)(Mean±SD)	57.20±9.30 years	58.73±11.35 years
Gender (M/F)	23/7 (76%/24%)	22/8(73%/27%)
Hypertension	16 (53.3%)	9 (30%)
Smokers	14 (46.7%)	10 (33.3%)
HbA1c (%) (Mean±SD)	9.19±0.85 %	9.26 ± 0.89 %
Hemoglobin Level (Mean±SD)	11.24±2.14 g/dl	11.78±1.98 g/dl
Platelet Count (Mean±SD)	252.33±10.90 x 10 <sup>9</sup> /L	254.33±10.06 x 10 <sup>9</sup> /L
Albumin Level (Mean±SD)	3.62±0.44 g/dl	3.58±0.39 g/dl
Right Foot Involved	14(53.3%)	9(30.0%)
Left Foot Involved	16(46.7%)	21(70.0%)

Table-II: Dimensions of Diabetic foot ulcers (n=60)

Size of Ulcer	Prp (Group 1) (Mean±SD)	Conventional Management (Group 2) (Mean±SD)
Length	3.87±0.41 cm	3.81±0.40 cm
Width	1.82±0.32 cm	1.85±0.29 cm
Area	7.13±0.40 cm <sup>2</sup>	7.25±0.37 cm <sup>2</sup>
Volume	1.68±0.43 cm <sup>3</sup>	1.71±0.45 cm <sup>3</sup>

these 30 patients were 57±9 years. In these patients, 23(77%) were male and 7(23%) were female. 16(53%)

week, 6<sup>th</sup> and 12<sup>th</sup> week evaluation showed statistical significant difference between two treatments between

group 1 and 2. The resulted *p*-value also concludes the significance of statistical analysis (Table-III).

**Table-III; Healing Time of Diabetic Foot Ulcers (n=60)**

Time Period of Completed Healed Ulcers	PRP (Group 1) (Mean±SD)	Conventional Management (Group 2) (Mean±SD)	<i>p</i> -value
1 <sup>st</sup> week	0.69±0.270 cm	0.25±0.17 cm	<0.001
6 <sup>th</sup> week	5.48±0.51 cm	3.39±0.34 cm	<0.001
12 <sup>th</sup> week	7.84±0.42 cm	5.31±0.20 cm	<0.001



**Figure: Comparison of Healed Foot Ulcer Every Week in Both Groups (n=60)**

The laboratory investigations were repeated at the endpoint of the study after the completion of treatment. Before and after labs showed no significant difference statistically. Hence, it can be concluded that PRP treatment has no effect on blood hematology (Table-IV).

**Table-IV: Parameters after Treatment (n=60)**

After Completion of Treatment	PRP (Group 1) (Mean±SD)	Conventional Management (Group 2) (Mean±SD)
HbA1c (%)	9.38±0.67 %	9.12±0.87 %
Hemoglobin level	10.6±1.88 g/dl	11.53±1.92 g/dl
Platelet Count	253.80±11.44 x 10 <sup>9</sup> /L	255.30±10.13 x 10 <sup>9</sup> /L
Albumin Level	3.56±0.386 g/dl	3.52±0.34 g/dl

## DISCUSSION

Diabetic foot ulcers therapy regimen includes wound debridement, infection management, revascularization where necessary, and ulcer off-loading. As an addition to these treatments, various therapies have been identified as potentially effective adjuncts, including wound healing products, hyperbaric oxygen therapy (HBOT) and negative pressure wound therapy (NPWT).<sup>13</sup>

A complex balance between matrix elements and growth factors is requirement of wound healing. Epithelial cell of diabetic foot ulcer lost ability to produce adequate amount of growth factors including platelet derived vascular endothelial growth factor (VEGF), growth factor (PDGF), epidermal growth factor (EGF), transforming growth factor- $\beta$  (TGF- $\beta$ ), epidermal growth factor (EGF), keratinocyte growth factor (KGF), and insulin-like growth factor (IGF).<sup>14</sup> In 1986, Knighton *et al.*, conducted clinical study which revealed the role of autologous platelet factors in escalating the epithelialization of granulation tissue leading to complete healing of chronic non-healing ulcers.

PRP contains these growth factors, cytokines and inflammatory mediators.<sup>14,30</sup> These growth factors are responsible for the commencement of the inflammatory reaction and the progression of the healing process.

Tang YQ *et al.*<sup>15</sup> reported release of antimicrobial peptides (connective tissue activating peptide 3 (CTAP-3)-related antimicrobial peptides) from human platelets after thrombin stimulation which subsequently, enforced by Krijgsveld *et al.*<sup>16</sup> These platelet polypeptides displayed antimicrobial activities against microorganisms (Staph aureus, Strept sanguis, E coli, Candida albicans, and Cryptococcus neoformans). Moreover, wounds treated with PRP have a lower incidence of infection than wounds treated with other methods.

In contrast to almost all previously reported therapies, we used both PRP and conventional therapy regimen in our study. It was found that the healing rate of the PRP group was remarkably greater than that of the conventional therapy. The PRP group experienced much faster healing rates each week (0.65) than the conventional therapy regimen group (0.50). Compared to the PRP group, healing occurred at 12<sup>th</sup> week was 7.84, with a significantly higher rate as compared to group 2, which showed healing 5.31 at 12<sup>th</sup> week.

Frykberg *et al* conducted study on 65 patients which exhibited Sixty-three (63) of 65 wounds (97%) responded with reductions in area, volume, undermining, and/or Sinus tract/Tunneling in a mean of 2.8 weeks with 3.2 treatments suggesting reversal of the nonhealing trend in chronic wound.

Jeong *et al.*<sup>17</sup> evaluated the effect of blood bank platelet concentrate in managing DFUs and showed

straightforward and effective method for the management of DFUs in term of both healing time and degree of shrinkage of wound. Ahmed and colleagues, on the other hand, revealed that PRP accelerated wound healing in diabetic foot ulcers and achieved complete healing in 86% as compared to 68% of control group (Anti septic ointment dressing). Moreover, the application of PRP exhibited a lesser rate of wound infection.

Elsaid A *et al.*<sup>18</sup> conducted a study to compare the role of PRP gel with regular saline dressing as control to assess the crucial role of platelet-rich plasma (PRP) gel for management of clean non-healing diabetic foot ulcer (DFU). Findings of study showed the application of PRP gel as a dressing for non-healing DFU resulted in considerably decrease in ulcer size in comparison with regular saline dressing in appreciably lesser time.

Singh SP *et al.*<sup>19</sup> studied the comparison of PRP and conventional therapy to find out the function of PRP in treating DFUs in term of rate of healing. Study showed DFUs healed more quickly treated with Platelet rich plasma.<sup>20</sup>

## CONCLUSION

If the conventional bandage fails to heal a persistent diabetic foot ulcer, developing therapeutic options such as recombinant human growth factors and bioengineered skin substitutes may be successful; however, their high cost limits their use. Autologous PRP is valuable and reliable approach of escalating wound healing by stimulating the healing process via local growth factor release in the wound for diabetic foot ulcers.

**Conflic of Interest:** None.

**Funding Source:** None.

## Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

MRK & WH: Data acquisition, data analysis, critical review, approval of the final version to be published.

ASA & UA: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

SMH & SMH: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

## REFERENCES

1. Tran T, Le P, Pham P. Diabetic foot ulcer treatment by activated platelet rich plasma: a clinical study. *Biomed Res Ther* 2014; 1: 37–42.

2. Alvarsson A, Sandgren B, Wendel C, Alvarsson M, Brismar K. A retrospective analysis of amputation rates in diabetic patients: can lower extremity amputations be further prevented? *Cardiovasc Diabetol* 2012; 11:18.
3. Wu SC, Driver VR, Wrobel JS, Armstrong DG. Foot ulcers in the diabetic patient, prevention and treatment. *Vasc Health Risk Manag* 2007; 3(1): 65-76.
4. Lobo R, Kiernan TJ, Jaff MR. Medical therapy for critical limb ischemia and the diabetic foot: an update. *J Cardiovasc Surg (Torino)* 2013; 54(6): 671-678.
5. Steed DL, Attinger C, Colaizzi T, Crossland M, Franz M, Harkless L et al. Guidelines for the treatment of diabetic ulcers. *Wound Repair Regen* 2006; 14(6): 680-692.
6. Driver V, Hanft J, Fylling C, Beriou J, and the AutoloGel™ Diabetic Foot Ulcer Study Group. A prospective, randomized, controlled trial of autologous platelet-rich plasma gel for the treatment of diabetic foot ulcers. *Ostomy Wound Manag* 2006; 52: 68–87.
7. Yang L, Gao L, Yang LV, Wang J. Autologous platelet-rich gel for lower extremity ischemic ulcers in patients with type 2 diabetes. *Int J Clin Exp Med* 2017; 10: 13796–13801.
8. Moreno-Serrano A, García-Díaz JJ, Ferrer-Márquez M, Alarcón-Rodríguez R, Álvarez-García A, Reina-Duarte Á. Using autologous platelet-rich plasma for the treatment of complex fistulas. *Rev Esp Enferm Dig* 2016; 108(3): 123-128.
9. Frykberg RG, Driver VR, Carman D, Lucero B, Borris-Hale C, Fylling CP et al. Chronic wounds treated with a physiologically relevant concentration of platelet-rich plasma gel: a prospective case series. *Ostomy Wound Manage* 2010; 56(6): 36-44.
10. Villela DL, Santos VL. Evidence on the use of platelet-rich plasma for diabetic ulcer: a systematic review. *Growth Factors* 2010; 28(2): 111-116
11. Mishra A, Woodall J Jr, Vieira A. Treatment of tendon and muscle using platelet-rich plasma. *Clin Sports Med* 2009; 28(1): 113-125.
12. Pietramaggiore G, Scherer SS, Mathews JC, Gennaoui T, Lancerotto L, Ragno G et al. Quiescent platelets stimulate angiogenesis and diabetic wound repair. *J Surg Res*. 2010 May 1; 160(1): 169-177.
13. Pietramaggiore G, Scherer SS, Mathews JC, Alperovich M, Yang HJ, Neuwalder J et al. Healing modulation induced by freeze-dried platelet-rich plasma and micronized allogenic dermis in a diabetic wound model. *Wound Repair Regen* 2008; 16(2): 218-225.
14. Beer HD, Longaker MT, Werner S. Reduced expression of PDGF and PDGF receptors during impaired wound healing. *J Invest Dermatol* 1997; 109: 132–138.
15. Tang YQ, Yeaman MR, Selsted ME. Antimicrobial peptides from human platelets. *Infect Immun* 2002; 70: 6524e33.
16. Krijgsveld, J., S. A. J. Zaat, J. Meeldijk, P. A. van Veelen, G. Fang, B. Poolman et al. Thrombocidins, microbicidal proteins from human blood platelets, are C-terminal deletion products of CXC chemokines. *J. Biol. Chem.* 275: 20374–20381.
17. Jeong SH, Han SK, Kim WK. Treatment of diabetic foot ulcers using a blood bank platelet concentrate. *Plast Reconstr Surg* 2010; 125(3): 944-952
18. Elsaid A, El-Said M, Emile S, Youssef M, Khafagy W, Elshobaky A. Randomized Controlled Trial on Autologous Platelet-Rich Plasma Versus Saline Dressing in Treatment of Non-healing Diabetic Foot Ulcers. *World J Surg* 2020; 44(4): 1294-1301.
19. Singh SP, Kumar V, Pandey A, Pandey P, Gupta V, Verma R. Role of platelet-rich plasma in healing diabetic foot ulcers: a prospective study. *J Wound Care* 2018; 27(9): 550-556.
20. Suthar M, Gupta S, Bukhari S, Ponemone V. Treatment of chronic non-healing ulcers using autologous platelet rich plasma: a case series. *J Biomed Sci* 2017; 24(1): 16.