



## TO EVALUATE THE EFFICACY OF TOPICAL APPLICATION OF PLATELET RICH PLASMA IN TREATMENT OF DIABETIC FOOT ULCERS IN A TERTIARY CARE HOSPITAL

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### ABSTRACT

Diabetes is one among the commonest diseases in the society. Frequent complication of Diabetes Mellitus is foot infection. Diabetic foot ulcer care is a challenge for both providers and patients. Over recent years, great progress has been made in the techniques of wound healing among which autologous platelet rich plasma has attracted the most substantial attention. Platelets are known to start the wound healing process through the release of locally acting growth factors. This study was conducted to evaluate the efficacy of topical application of Platelet rich plasma in treatment of diabetic foot at a Tertiary Care Hospital. This Prospective randomised study included 2 group with 31 patients in control group and 30 patients in test group who were admitted at our hospital from Jan 2021 to June 2022. The control group received ordinary conventional dressing and test group received platelet rich plasma dressing after fulfilling the inclusion criteria. Dressing was done twice weekly for 8 weeks. In our study of 61 patients, most patients were in the age group of 51- 70 years and 74% were males. The reduction of slough was as early as 2nd week in the test group than the control group. The number of patients with 75-100% wound filled with granulation tissue was as early as 3rd week in test group than the control group where it took more than 4 weeks. Test group has experienced less pain and reduced malodour from the ulcer site than the control group. In conclusion, this study shows more favorable results for Platelet Rich Plasma dressing as compared to Conventional dressing in healing of diabetic foot ulcers which was statistically significant in terms of early appearance of granulation tissue, epithelialization, rapid decrease in wound size.

**KEYWORDS :** Platelet Rich Plasma, Diabetic foot ulcers, Granulation tissue.

### INTRODUCTION

India is the second most affected country in the world with Diabetes mellitus, after China.<sup>(1)</sup> Foot infection is the most common reason for hospitalization accounting to up to 25% of admissions. Diabetic foot ulcers should be treated aggressively to improve the quality of life, maintain patient's health and prevent amputations and to reduce healthcare costs. No single dressing fulfills all the requirements of a patient with an infected ulcer. Apart from conventional methods to facilitate wound healing, newer methods like PRP dressing is emerging. PRP is obtained by Double spin method. PRP involves taking 10ml patient's blood before procedure, centrifugation, and activating the platelets, application of the gel to the site. The healing is improved 2 to 3 times. PRP contains platelet-derived growth factor, transforming growth factor beta, fibroblast growth factor, insulin-like growth factor 1, insulin-like growth factor 2, vascular endothelial growth factor, epidermal growth factor, Interleukin 8 and keratinocyte growth factor. Upon activation of platelets, platelet degranulation occurs leading to release of Growth Factors which bind to their respective transmembrane receptors expressed over adult mesenchymal stem cells, fibroblasts epidermal cells, endothelial cells. This study was done to evaluate the efficacy of topical application of Platelet rich plasma in treatment of diabetic foot at the tertiary care hospital and to analyze the time required for wound healing by topical application of Platelet rich plasma versus conventional dressings for diabetics foot ulcers. Severity of diabetic foot ulcers are graded according to **Meggitt-Wagner** classification.

#### **Meggitt-Wagner Grading system of Diabetic Ulcer**<sup>26</sup>

Grade 1: Superficial Diabetic ulcer

Grade 2: Ulcer Extension

- i. Involves ligament, tendon, joint capsule or fascia
- ii. No abscess or osteomyelitis

Grade 3: Deep ulcer with abscess or osteomyelitis

Grade 4: Gangrene to portion of forefoot

Grade 5: Extensive gangrene of foot

Activated PRP can be prepared by Manual double Spin method or Automated method.

### MATERIAL AND METHODS

The study included 61 patients aged 18 to 80 years diagnosed with Type 2 Diabetes mellitus with Ulcer grade – Wagner Grade 0 to Grade 2 Diabetic foot ulcer classification after taking written informed consent in the tertiary care hospital from January 2021 to June 2022. Patients with age greater than 80 years; with venous, trophic ulcers; Ulcer grade – Wagners Grade III, IV, V; with known or suspected osteomyelitis; with immunocompromised status, steroid therapy and malignancies were excluded.

61 patients were randomized into 2 groups with 31 patients in control group – Conventional Dressing Group (Group A) and 30 patients in Test group – Platelet Rich Plasma Dressing Group (Group B). Group A received bed side surgical debridement with conventional dressing for 8 weeks. Group B received PRP application over the ulcer. Dressing was done twice weekly upto 8 weeks. The amount of nonviable tissue, degree of wound granulation and overall wound area was evaluated weekly using a visual score.

The visual scores are as follows The score for the percentage of wound covered by slough and nonviable (necrotic) tissue are

- 1 = 76-100% wound covered with nonviable tissue.
- 2 = 51-75% wound covered with nonviable tissue
- 3 = 26-50% wound covered with nonviable tissue.
- 4 = 11-25% wound covered with nonviable tissue.
- 5 = 0-10% wound covered with nonviable tissue.
- 6 = No necrotic tissue

The score for the percentage of wound covered by granulation tissue are

- 1 = No granulation present
- 2 = < 25% of wound covered by granulation tissue
- 3 = 25-74% of wound covered by granulation tissue
- 4 = 75-100% of wound covered by granulation tissue.

The reduction of wound size and area measured in cm<sup>2</sup>.

The final parameters and wound characteristics of the two randomized groups were analyzed and compared.

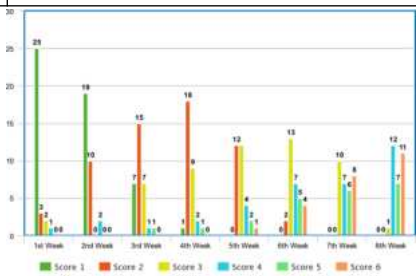
### RESULTS

Most of the patients fell in the age group between 50 years to 70 years. In both the groups, male gender preponderance was seen. The mean size of the ulcer was 14.68 cm to 14.83 cm. Most of the patients had Grade II ulcers in both test and control groups.

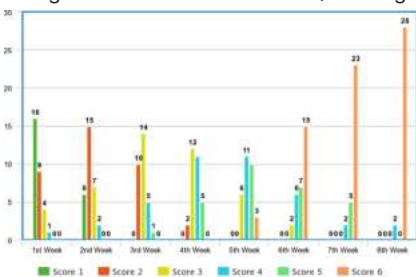
**Table 1: Presence of necrotic tissue or slough**

Study Period	Control group (n=31) visual score covering the ulcer						Test group (n=30) visual score covering the ulcer					
	1	2	3	4	5	6	1	2	3	4	5	6
1 <sup>st</sup> week	25	3	2	1	0	0	16	9	4	1	0	0
2 <sup>nd</sup> week	19	10	0	2	0	0	6	15	7	2	0	0
3 <sup>rd</sup> week	7	15	7	1	1	0	10	14	5	1	0	0
4 <sup>th</sup> week	1	18	9	2	1	0	2	12	11	5	0	0
5 <sup>th</sup> week	0	12	12	4	2	1	0	6	11	10	3	0
6 <sup>th</sup> week	0	2	13	7	5	4	0	2	6	7	15	0
7 <sup>th</sup> week	0	0	10	7	6	8	0	0	2	5	23	0
8 <sup>th</sup> week	0	0	1	12	7	11	0	0	2	0	28	0

Inference: Number of patients with less necrotic tissue are significantly higher in Test group at 2<sup>nd</sup> week follow up (P<0.05), 3<sup>rd</sup> week follow up (P < 0.05), at 4<sup>th</sup> week (P < 0.001), at 5<sup>th</sup> week (P < 0.001), at 6<sup>th</sup> week (P < 0.05) and at the 7<sup>th</sup> week (P <0.01) when compared to control group as per the chi-square / Fisher Exact test.



**Fig 1a** showing Presence of necrotic tissue (control group)



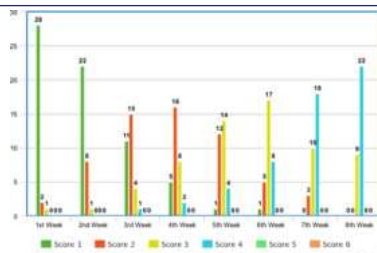
**Fig 1b** showing Presence of necrotic tissue (test group)

**Presence of granulation tissue**

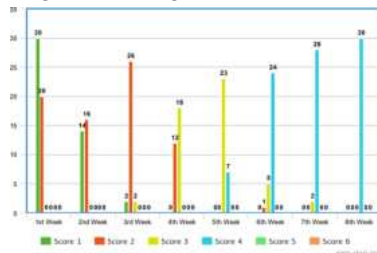
**Table 2: Presence of granulation tissue**

Study Period	Control group (n=31)						Test group (n=30)					
	1	2	3	4	5	6	1	2	3	4	5	6
1 <sup>st</sup> week	28	2	1	0	0	0	30	0	0	0	0	0
2 <sup>nd</sup> week	22	8	1	0	0	0	14	16	0	0	0	0
3 <sup>rd</sup> Week	11	15	4	1	0	0	2	26	2	0	0	0
4 <sup>th</sup> Week	5	16	8	2	0	0	0	12	18	0	0	0
5 <sup>th</sup> Week	1	12	14	4	0	0	0	0	23	7	0	0
6 <sup>th</sup> Week	1	5	17	8	0	0	0	1	5	24	0	0
7 <sup>th</sup> Week	0	3	10	18	0	0	0	0	2	28	0	0
8 <sup>th</sup> Week	0	0	9	22	0	0	0	0	0	30	0	0

Inference: Number of patients with 75-100% wound filled are significantly higher in Test group at 3<sup>rd</sup> week follow up (P<0.05), at 4<sup>th</sup> week (P < 0.05), at 5<sup>th</sup> week (P < 0.001), at 6<sup>th</sup> week (P<0.001) at the 7<sup>th</sup> week (P<0.05), and at the 8<sup>th</sup> week (p<0.001) when compared to control group as per the Chi- square / Fisher Exact test.



**Fig 2a.** showing Presence of granulation tissue (control group)



**Fig 2b.** showing Presence of granulation tissue (test group)

**Wound Surface Area**

**Table 3 wound surface area**

Wound surface area in weeks	Test group		Control group	
	Mean	SD	Mean	SD
SA 1 <sup>st</sup> week	14.500	1.341	13.903	1.978
SA 2 <sup>nd</sup> week	13.400	1.273	12.742	1.891
SA 3 <sup>rd</sup> week	12.467	1.264	11.903	1.889
SA 4 <sup>th</sup> week	11.233	1.135	10.935	1.847
SA 5 <sup>th</sup> week	10.367	1.159	9.871	1.804
SA 6 <sup>th</sup> week	9.700	1.230	8.290	1.772
SA 7 <sup>th</sup> week	7.033	1.424	6.065	1.532
SA 8 <sup>th</sup> week	4.000	1.163	5.581	1.550
F test (df) P-value	78.213 p-value<0.001		35.27 p-value<0.001	

A one-way repeated measures ANOVA was conducted to determine whether there were statistically significant differences in surface area of the wound over the course of 8 weeks after the initiation of treatment. The treatment elicited statistically significant changes in wound healing both in the control group as well as the test group over time with p < 0.001. The surface area level showed a decreasing trend across different time points. Post hoc analysis with a Bonferroni adjustment revealed that there was a statistically significant decrease between pairs of wound healing surface area with p-value <0.001.

**Inference-** the reduction in wound surface area is significantly higher in test group when compared to the control group and p value is <0.001 which is statistically significant.



**Patient-1 PRP group (test group)**  
**Fig 3b Patient-1 Day 4-covered with slough with appearance of granulation tissue**



**Fig 3b Patient-1 Day 7-ulcer with Granulation tissue with Minimal slough**



**Fig 3c Patient-1 Day-14 ulcer covered with good granulation tissue**



**Fig4a - Patient-2 Day 1-post debrided ulcer with minimal slough**



**Fig4b - Patient-2 Day 21 ulcer with wound contraction and epithelialization**



**Fig 5a Patient-3 Day 1-ulcer with slough**



**Fig 5b Patient-3 Day 14-ulcer covered with granulation tissue**

**DISCUSSION**

The number of patients studied was 61 and randomly divided into test group (30) and control group (31).

Both the test and control groups were matched regarding their age, sex, duration of diabetes, diabetic status, grade of ulcer and baseline ulcer size there was no significant difference between the two groups.

The mean age of patients in the study was 58.6 ± 10.46 years, 74% of patients were male. The mean size of the ulcer in the study was 14.7 cm and most of the patients (66%) had grade II ulcers.

Number of patients with less necrotic tissue are significantly higher in Test group at 2<sup>nd</sup> week follow up (P<0.05), 3<sup>rd</sup> week follow up (P < 0.05), at 4<sup>th</sup> week (P < 0.001), at 5<sup>th</sup> week (P < 0.001), at 6<sup>th</sup> week (P < 0.05) and at the 7<sup>th</sup> week (P < 0.01) when compared to control group as per the chi-square / Fisher Exact test.

Number of patients with 75-100% wound filled are significantly higher in Test group at 3<sup>rd</sup> week follow up (P<0.05), at 4<sup>th</sup> week (P < 0.05), at 5<sup>th</sup> week (P < 0.001), at 6<sup>th</sup> week (P<0.001) at the 7<sup>th</sup> week (P<0.05), and at the 8<sup>th</sup> week (p<0.001) when compared to control group as per the Chi-square / Fisher Exact test.

For wound surface area, the treatment elicited shows statistically significant changes in wound healing both in the control group as well as the test group over time with p < 0.001. The surface area level showed a decreasing trend across different time points. Post hoc analysis with a Bonferroni adjustment revealed that there was a statistically significantly decrease between pairs of wound healing surface area with p-value < 0.001.

In addition to the above observation test group has experienced less pain and reduced Malodour from the ulcer site compared to that of control group.

The patients treated with PRP dressing had faster reduction of slough / necrotic tissue and increased granulation tissue, compared to studies in the literature.

Driver et al conducted a prospective randomized- controlled, blinded, multicentre clinical study in 129 patients to evaluate the safety and efficacy of autologous platelet-rich plasma gel for the treatment of non healing diabetic foot ulcers. It was found that significantly more autologous platelet-rich plasma gel (81.3%) than control gel (42.1%) treated wounds healed<sup>52</sup>.

Knighton DR et al conducted a prospectively randomized, blinded trial in 32 patients in 1990 at Minnesota, Minneapolis to test whether or not platelet derived wound healing factors accelerate repair. In the study group, 81% of patients had epithelialization compared to 15% in the control group. Results from this study demonstrate a highly statistically significant effect of topically applied platelet derived growth factors on the repair of chronic non healing cutaneous ulcers<sup>53</sup>.

Robert G Frykberg et al used autologous PRP gel on 49 patients with chronic, non healing wounds and found that 97% of wounds improved, for all wound etiologies. The results of this study suggest that the application of PRP gel can reverse non healing trends in chronic wounds<sup>54</sup>.

In this study test group patients had increased growth of the granulation tissue along with epithelisation which is generally correlated with the development of a granulating wound bed. All this are done with visual score so it cannot be determined whether there was an increase in granulation tissue production resulting from the treatment or that more granulation was visible after debridement.

But patients in test group produced better results than the control group. The test group patients under went skin grafting, secondary suturing and flap as early as 4th week than control group because of faster wound bed preparation. The wound also healed faster this is due to increased epithelisation.

## CONCLUSION

This prospective study was done to compare the Efficacy of Platelet Rich Plasma with Conventional dressing in the management of Diabetic foot ulcers.

This study shows more favorable results for Platelet Rich Plasma as compared to Conventional dressing in healing of diabetic foot ulcers which are statistically significant. In patients treated with Platelet Rich Plasma comparatively we found that there was:

1. Early appearance of granulation tissue.
2. Early appearance of epithelialization.
3. Rapid decrease in wound size.

This study confirms that Platelet Rich Plasma with its moistening effects and cost effectiveness is safe, has faster response in wound healing and gives better results compared to the conventional dressing for use in wound care in management of Diabetic foot ulcers. Hence it is a good choice for management of Diabetic foot ulcers.

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