

Outcomes of Wound Healing after Plasma-Rich Platelet Therapy

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ABSTRACT

OBJECTIVE: To identify outcomes of wound healing after using Plasma rich platelet therapy

METHODOLOGY: A prospective cross-sectional study was conducted at ISRA University Hospital, Hyderabad, from July to December 2022, with a sample size of 50 and a non-probability sampling technique. Both genders aged 45 to 75 years, Diabetes mellitus type II, Chronic or Non-healing wounds/ulcers for 3 to 6 months, and Wound size 2cm to 6cm were included. Participants who were not willing to study, Patients on steroid and Anticoagulant therapy and Immunosuppressive drugs, Pregnant females, those with Cardiovascular Disorders, and Associated Lymphoedema were excluded. Data was analyzed by SPSS version 21.

RESULTS: Fifty patients were enrolled after matching the inclusion and exclusion criteria. The age range was 40 years to 70 years. Thirty-one were males, and 19 were females. Co-morbid conditions included were diabetes mellitus type II and hypertension. The most common cause of lower limb ulcers was diabetic foot, and the most common site was the dorsum of the foot. 52% of patients had <2cm size ulcers, and they responded well to plasma-rich platelet therapy in a single session. PRP is a cost-effective, advanced therapy and safe procedure to manage wound healing. It improves quality of life, reduces hospitalization, and decreases hospital visits, which would lessen the patient burden. It works on cellular regeneration, so it helps in faster recovery and avoidance of old traditional methods and excessive or misuse of antibiotics.

CONCLUSION: Plasma Rich Platelet therapy is a safe method for treating chronic and non-healing ulcers.

KEYWORDS: chronic wound, non-healing wound, Plasma-rich platelet therapy, outcomes after therapy, wound management

INTRODUCTION

The wound disrupts the skin's normal anatomical and functional integrity, a barrier to various mechanical and physical pathogens. Subsequently, the wound-healing process is integrated with the coordination of different growth factors, chemokines and cytokines at multiple cellular levels. However, any distortion in this dynamic homeostatic tissue repair mechanism will result in chronic non-healing wound¹.

Furthermore, Chronic ulcers are non-healing and categorized as spontaneous or traumatic lesions, typically in the lower extremities, that are unresponsive to initial therapy or persist despite appropriate care². There are 3 phases of wound

healing: inflammation, tissue formation, and tissue remodelling. Various non-healing ulcers include venous, arterial, diabetic, pressure and traumatic ulcers³.

As explained, the complexity of wound healing mechanisms is organized under various cellular and molecular course involvement for tissue regeneration. Hence, chronic non-healing wounds have remained a challenge for a few years, in contempt of numerous therapeutically approached proposals to intensify healing⁴. Undoubtedly effectively, non-healing compromised wounds and skin wounds are specified under crucial public health issues. Due to its prolonged and complicated treatments, there is also an unrationalized rise in healthcare expenditure⁵. Moreover, non-healing wounds or chronic ulcers play a significant role in health problems, and approximately 2-6 million people are affected in the United States by chronic ulcers⁶. The overall prevalence of diabetic foot ulcers was 16.83%⁷. While its prevalence globally ranges from 1.9 to 13.1%. It is estimated that almost 10% of the population would develop a chronic wound during a lifetime, with a wound-related mortality rate of 2.5%⁸.

Despite medicinal and nutritional care advancements, various challenges exist in achieving optimal wound healing outcomes. In this regard, specific medicinal evolution is progressing towards numerous cost-efficient minimal to non-invasive methods, which

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would result in accelerated good functional recovery and reduced morbidity in patients to facilitate quality of life¹.

Platelet-rich Plasma (PRP) is a new alternative technique in different medical fields (i.e., dentistry, traumatology, cosmetic surgery, ophthalmology, and dermatology). The advantages of PRP are that it is a simple, low-cost procedure with good results compared to other standard treatments with better results. Chronic ulcers not only heal with PRP but also PRP prevent lower extremity complications and amputations⁹. The cytokines and growth factors in autologous/homologous PRP play a crucial role in the healing process¹⁰.

Platelet-rich Plasma is an autologous blood-derived product that contains a high concentration of platelets in Plasma derived from whole blood by centrifugation. Activated platelets in PRP release multiple growth factors and cytokines, including platelet-derived growth factor (PDGF), basic fibroblast growth factor (bFGF), vascular endothelial growth factor (VEGF), insulin-like growth factor1 (IGF-1) and transforming growth factor- β (TGF- β), and others that are involved in promoting tissue repair and regeneration¹¹.

Therefore, for all the reasons mentioned above, this research article aims to rationalize the role and significance of PRP in wound healing, focusing on the therapeutic approach and cost-effectiveness to lower the healthcare burden.

METHODOLOGY

A prospective cross-sectional study was conducted at ISRA University Hospital Hyderabad from July to December 2022, using a non-probability sampling technique. The study population included both genders aged 45 to 75 years, Diabetes mellitus type II, Chronic or Non-healing wounds/ulcers for 3 to 6 months, and Wound size 2cm to 6cm. Participants who were unwilling to study, Patients on steroid and Anticoagulant therapy and Immunosuppressive drugs, Pregnant females, Cardiovascular Disorders, and Associated Lymphoedema were excluded from the study. The patient was assessed via thorough history and clinical examination. The wound site was noted, and size was measured in cm. Patients received plasma-rich platelet therapy followed by antiseptic dressing with antibiotic cover. On 2 to 4 weeks follow-up, the wound was assessed for healing, and a second session of PRP was given for non-healing ulcers. 2 to 3 sessions of PRP were given to non-healing ulcers. All the data was recorded via study Proforma and was analyzed using SPSS version 21. The descriptive frequencies and percentages were computed for qualitative variables such as gender, co-morbidity, and clinical characteristics of patients such as history, size, site and number of ulcers. P value < 0.5 is taken as statistically significant. The written and informed consent was obtained from patients. The ethical approval was obtained from the ethical review committee.

Platelet-rich Plasma (PRP) Preparation and Therapeutic Applications:

PRP preparation is achieved by obtaining a 5cc blood sample from the patient, which is then centrifuged at 4000 rpm for 10 minutes. After this cycle, the prepared PRP serum was infused through a 1ml insulin syringe into the affected wound area using proper aseptic techniques and protocol. The procedure was repeated every two to four weeks, depending upon the wound's severity and response to the treatment.

RESULTS

Of the total 50 patients enrolled, 62% were male, and 38% were female. The age of patients was generally distributed, with the majority in the age bracket of 48 – 59 years (62%). The majority of patients presented with Type II diabetes (82%). 60% of the participants in the study had hypertension, while 40% did not have hypertension. Among the participants, 56% were smokers, while 44% were non-smokers. HbA1c levels: 38% of the participants had poor control, 44% had fair control, 6% had normal levels, 5% were pre-diabetic, and only 1% had good control. (**Table I**)

74% of patients presented with a history of ulcers for 1 month, 11% had ulcers for three months, and only 2% for six months. Among the participants, 55% had a history of trauma, while 45% did not have a history of trauma. The most common locations of ulcers were on the dorsum of the foot (36%), followed by the plantar of the foot (32%) and between the knee and malleolus (8%). Some ulcers were found at the medial malleolus (6%) and lateral malleolus (6%). 52% of the patients had ulcer size of less than 2 cm, 36% were between 2 to 4 cm, and 12% were between 4 to 6 cm. 86% of the participants had a single ulcer, while 14% had multiple ulcers. Half of the participants received a single PRP (Platelet-Rich Plasma) therapy session, while the other half received various sessions.

The majority of patients took six weeks (40%) or eight weeks (32%) for wound healing, followed by four weeks (16%) and 12 weeks (12%). 86% of the participants had their wounds healed during the follow-up, while 14% had not healed wounds. (**Table II**) Patients with diabetes mellitus have shown a significant ($p < 0.05$) association with the time taken for wound healing after a PRP (Platelet-Rich Plasma) session. At the same time, it had no significant ($p = 0.324$) association with the treatment outcome. There is no significant association between gender and No. A PRP (Platelet-Rich Plasma) session was administered, and time and wound healing on follow-up were taken. The study showed a significant association between HbA1c control and No. Of PRP session administered ($p < 0.001$), time taken for wound healing ($p < 0.05$) and wound healing on follow up ($p < 0.05$). A history of hypertension had no significant association with any of the treatment outcomes. (**Table III**) A single session of PRP was effective for most patients, and wound healing was achieved in 6 weeks. (**Graph I**)

Table I: Socio-demographics and patient characteristics

Variables		N (%)	P values
Gender	Male	31 (62%)	<0.5
	Female	19 (38%)	
Age	42-47 years	6 (12%)	<0.001
	48-53 years	16 (32%)	
	54-59 years	15 (30%)	
	60-66 years	13 (26%)	
Diabetes Mellitus	Type I	1 (2%)	<0.001
	Type II	41 (82%)	
	Non-Diabetic	8 (16%)	
Hypertension	Hypertensive	30 (60%)	<0.001
	Non-Hypertensive	20 (40%)	
Smoking	Smoker	28 (56%)	<0.001
	Non-Smoker	22 (44%)	
HbA1c	Poor control	19 (38%)	<0.001
	Fair control	22 (44%)	
	Normal	3 (6%)	
	Pre-Diabetic	5 (10%)	
	Good	1 (2%)	

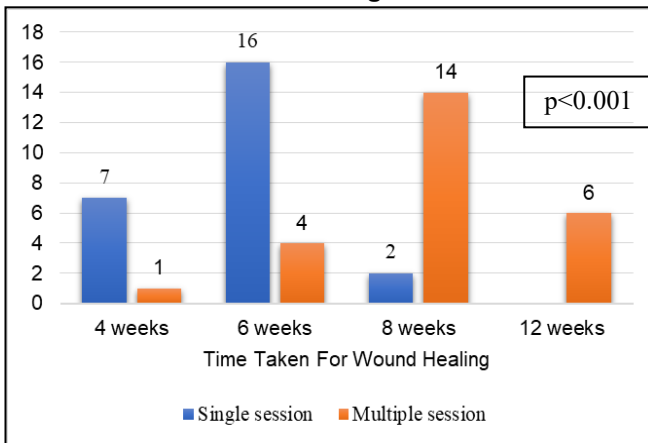
Table II: Clinical characteristics of patients

Variables	N (%)	
History of Ulcer	1 month	37 (74%)
	3 months	11 (22%)
	6 months	2 (4%)
History of Trauma	Yes	N=49 27 (55%)
	No	N=49 22 (45%)
Location Of Ulcer	Between knee and malleolus	4 (8%)
	At medial Malleolus	3 (6%)
	At Lateral Malleolus	3 (6%)
	Dorsum of foot	18 (36%)
Size Of Ulcer	Plantar of foot	16 (32%)
	< 2 cm	26 (52%)
	2 to 4 cm	18 (36%)
	4 to 6 cm	6 (12%)
Number of ulcers	Single	43 (86%)
	Multiple	7 (14%)
No. of PRP Sessions administered	Single session	25 (50%)
	Multiple sessions	25 (50%)
Time taken for wound healing (Weeks)	4 weeks	8 (16%)
	6 weeks	20 (40%)
	8 weeks	16 (32%)
	12 weeks	6 (12%)
Wound Healing Outcome	Wound healed	43 (86%)
	Wound not healed	7 (14%)

Table III: χ^2 linear association between clinical characteristics and treatment outcomes

Variables	No. of PRP Sessions administered		Time taken for wound healing (Weeks)		Wound Healing Outcome		
	Linear by linear 2	p-value	Linear by linear 2	p-value	Linear by linear 2	p-value	
Gender	Male (N=31)	2.080	0.149	3.261	0.071	0.080	0.777
	Female (N=19)						
Diabetes Mellitus	Type I ((N=1)	3.055	0.080	5.138	0.023	0.975	0.324
	Type II(N=41)						
	Non-Diabetic(N=08)						
HbA1c	Poor control (N=19)	5.573	0.018	11.456	0.001	4.987	0.026
	Fair control (N=22)						
	Normal (N=3)						
	Pre-Diabetic (N=5)						
Hypertension	Hypertensive (N=30)	0.327	0.568	0.408	0.523	0.027	0.869
	Non-Hypertensive (N=20)						
Smoking	Smoker (N=28)	2.864	0.091	6.049	0.014	0.771	0.380
	Non-smoker (N=22)						

Graph I:
Time taken for wound healing VS PRP sessions



DISCUSSION

Platelets are considered a rich source of growth factors. PRP enhance wound healing by either the barrier effect to prevent bacterial invasion or the growth factors stimulate wound healing. Elsaid in 2020 reported that the mean age in their study was 55.2 ± 6.4 years¹². While Aymen Salem reported that the mean age in their study was 58.6 ± 2.7 ¹³, the findings are consistent with the present study. In the present study, males (31) were more common than females (19), and a study reported the same findings¹⁴. The majority of patients were diabetic, and the duration of their diabetes mellitus was 10 years \pm 2 SD. Similar findings of 13.4 years \pm 4.7 were observed in a study conducted in Lady Reading Hospital, Peshawar, Pakistan¹⁵.

There is a significant association between HbA1c level and wound healing. An international study reported that HbA1c control was achieved after PRP treatment and wound healing improved. In the present study, wound healing was achieved after PRP treatment and HbA1c levels reduced towards normal levels (p Value 0.001)¹⁶. A study reported that wound healing was achieved seven weeks after plasma-rich platelet therapy. These findings are consistent with the present study, as the majority of cases of wound healing were achieved in 6 to 8 weeks¹⁷. A researcher reported in 2020 that there is a strong association between the size of the ulcer and the number of Plasma-rich platelet sessions¹⁸. Based on these advantages, PRP has been widely used to promote skin regeneration, colon anastomosis, and bone formation, as it is cost-effective and has better outcomes¹⁹. Various clinical trials have reported that PRP has significantly played a role in health problems²⁰.

CONCLUSION

Our study has illuminated a path to transformation in treating lower limb ulcers. Lower limb ulcers affect the quality of life. Our study concluded that PRP is a safe

method for treating chronic and non-healing ulcers. It enhances wound healing and improves the patient's quality of life. PRP not only accelerates wound recovery but also rejuvenates the very essence of patient well-being. Further trials are needed on a larger scale for better results and outcomes.

Ethical permission: ISRA University Hospital, Hyderabad Pakistan ERC letter No. IUH/ASST-DEAN (CS)/35/02/23.

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Data Sharing Statement: The corresponding author can provide the data proving the findings of this study on request. Privacy or ethical restrictions bound us from sharing the data publically.

AUTHOR CONTRIBUTION

Memon J: Manuscript writing and data analysis
Mughal S: Data collection and data analysis
Memon S: Research Design and drafting
Kalhor R: Data analysis and interpretation
Qureshi U: Data collection and designing

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