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Original Article

Autologous Platelet-rich Fibrin Matrix in Non-healing Trophic Ulcers in Patients with Hansen's Disease

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Hansen's disease, also known as leprosy, often results in trophic ulcers due to peripheral neuropathy. These non-healing ulcers are challenging to treat, particularly in resource-limited settings. Autologous platelet-rich fibrin matrix (PRFM), a regenerative therapy rich in growth factors, offers a potential solution by promoting tissue repair and angiogenesis in chronic wounds. This study aimed to assess the effect of serial PRFM sessions on the healing of non-healing trophic ulcers in patients with Hansen's disease. The prospective interventional study was conducted at the dermatology outpatient department of Chigateri General Hospital and Bapuji Hospital, affiliated with JJM Medical College, Davangere. Twenty-six patients with non-healing trophic ulcers were enrolled based on inclusion criteria. PRFM was prepared from autologous blood and applied to the ulcer site once a week for up to four sessions. Ulcer size, including length, width, and depth, was measured at each session to assess changes in wound area and volume. Significant reductions in ulcer dimensions were observed after four PRFM sessions, with many cases demonstrating notable re-epithelialization and reduced ulcer size. While healing varied among patients, the majority exhibited improvement, with minimal adverse effects reported. PRFM is a promising, effective therapy for accelerating healing in non-healing trophic ulcers among Hansen's disease patients. This treatment could improve wound management in chronic leprosy-related ulcers, enhancing patient outcomes in settings with limited resources.

Keywords: Hansen's Disease, Trophic Ulcers, Autologous Platelet-rich Fibrin Matrix, Chronic Wound, Healing, Regenerative Therapy

Introduction

Hansen's disease, commonly known as leprosy, is a chronic infectious condition caused by *Mycobacterium leprae*, affecting the skin, peripheral nerves, and mucosa of the upper respiratory tract. One of the most disabling complications of this disease is the development of trophic ulcers, which occur due to peripheral neuropathy and resultant loss of sensation in the extremities, making patients prone to repeated trauma and subsequent ulcer formation. Despite global efforts toward leprosy eradication, its complications, including non-healing trophic ulcers, continue to pose significant clinical challenges, especially in resource-limited settings (Britton & Lockwood 2004).

Chronic wounds, such as trophic ulcers, are notoriously difficult to manage due to their delayed healing response, which is often compounded by underlying comorbidities and poor blood supply. In leprosy, the loss of protective sensation in the affected areas

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further contributes to prolonged wound healing, recurrent infections, and potential amputations in severe cases. Conventional treatments for trophic ulcers include wound debridement, topical antimicrobial therapy, and pressure offloading, yet the outcomes are frequently suboptimal. This has spurred the exploration of advanced wound care modalities aimed at enhancing tissue regeneration and promoting faster healing (Schreuder et al 2016, Scollard et al 2006).

In recent years, autologous Platelet-rich Fibrin Matrix (PRFM) has emerged as a promising regenerative therapy in the management of chronic wounds, including diabetic ulcers, venous ulcers, and more recently, leprosy-associated trophic ulcers. PRFM, a second-generation platelet concentrate, is derived from the patient's own blood and contains a high concentration of growth factors, such as platelet-derived growth factor (PDGF), transforming growth factor-beta (TGF-β), and vascular endothelial growth factor (VEGF), which are essential for tissue repair and angiogenesis (Marx 2004). The unique fibrin matrix structure of PRFM acts as a scaffold for cell migration and new tissue formation, facilitating wound healing in previously non-healing ulcers (de Carvalho et al 2020).

Several studies have demonstrated the efficacy of PRFM in accelerating wound healing in various chronic ulcer types, showing significant reductions in ulcer size and faster re-epithelialization compared to conventional treatments (O'Connell et al 2008).

In diabetic foot ulcers, for example, PRFM has been shown to reduce healing times and improve patient outcomes, with some studies reporting complete ulcer closure within weeks of initiating treatment (Driver et al 2006). These findings have prompted further investigations into its use in other chronic ulcer conditions, including leprosy-related trophic ulcers, which share many of the same pathophysiological mechanisms as other neuropathic wounds (Lacci & Dardik 2010). Given the chronicity and refractory nature of trophic ulcers in Hansen's disease, this study aims to assess the improvement in trophic ulcer dimensions after serial sessions of autologous PRFM. By leveraging the regenerative properties of PRFM, we hypothesize that this treatment can promote faster healing and reduce ulcer size, ultimately improving the quality of life for patients suffering from this debilitating complication. The current study is a prospective interventional analysis designed to evaluate the effectiveness of PRFM in a cohort of patients with non-healing trophic ulcers secondary to Hansen's disease. Objective of this study was to assess the improvement in the trophic ulcer dimensions after serial sessions of autologous Platelet-rich fibrin matrix (PRFM)

Materials and Methods

Study Design and Setting:

This was a prospective interventional study conducted at the outpatient department of dermatology, Chigateri General Hospital and Bapuji Hospital, affiliated with JJM Medical College, Davangere, from November 2022 to August 2024.

Study Population:

Patients diagnosed with Hansen's disease presenting with non-healing ulcers were recruited based on specific eligibility criteria. Non-healing ulcers were defined as those persisting for more than six weeks. Patients aged over 18 years who provided informed consent were included.

Inclusion criteria used was: patients aged 18 years or above, non-healing trophic ulcers of more than 6 weeks duration in Hansen's disease and patients willing to participate in the study. Patients with a history of bleeding

disorders, patients with anaemia or platelet counts < 150,000/cu mm, those on anticoagulant therapy (aspirin, warfarin, heparin), patients with uncontrolled diabetes mellitus or malignant ulcers, pregnant or lactating females and patients with other hematological disorders were excluded.

Sampling and Sample Size:

Convenient sampling was done, and 26 patients meeting the inclusion and exclusion criteria and those who gave consent from this eligible pool were recruited for the study

Data Collection:

After obtaining approval from the institutional ethics committee (Ref No- JJMMC/IEC-64-2022), informed written consent was acquired from all participants. Data collection involved a detailed interview and physical examination using a pre-structured proforma to document demographic details, history, and dermatological findings. Key variables included age, gender, residence, and clinical presentation. Dermatological examination encompassed a thorough assessment of the skin, nails, and mucosa in adequate daylight. Clinical diagnosis was based on established features and relevant investigations.

Intervention Procedure:

After aseptic precautions, 10ml of venous blood from the patient (Autologous) was withdrawn to a plane vacutainer and processed by centrifugation at 3000 rpm (3824g, centrifuge REMI R4C) for 10 minutes, yielding three distinct layers: platelet-poor plasma (PPP), the red blood cell fraction, and platelet-rich fibrin matrix (PRFM) in the middle (Fig. 1). The PPP was discarded, and the PRFM was gently separated from the RBC layer (Figs. 2 and 3) The PRFM was compressed between sterile gauze and applied directly to the ulcer, followed by a secondary non-absorbable dressing. This dressing was removed after 7 days,

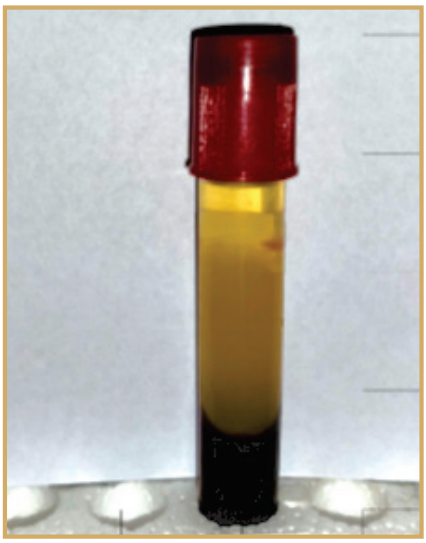


Fig. 1: PRFM prepared from plane vacutainer after centrifugation in Remi centrifuge R-4C at 3824g for 10 minutes.

Fig. 2: PRFM clot taken out from the sterile plane vacutainer.

and the procedure was repeated weekly for up to 4 sittings as required.

Outcome Measurements:

The size of the ulcer was recorded in terms of length, width, and depth using standardized

wound measurement techniques.

The wound area was calculated using the formula for an ellipse (Raju et al 2020): Wound area calculated using the formula for an ellipse: Length x Width x 0.7854

Wound volume calculated using the formula: Length x Width x Depth x 0.7854

Ethical Considerations:

The study was conducted following ethical guidelines, with approval obtained from the institutional ethics committee. Digital photographs were taken with the patients' consent for documentation purposes.

Statistical Analysis:

Data were analyzed using descriptive statistics. Continuous variables, such as wound area and volume, were expressed as mean ± standard deviation (SD). Categorical variables were presented as frequencies and percentages.

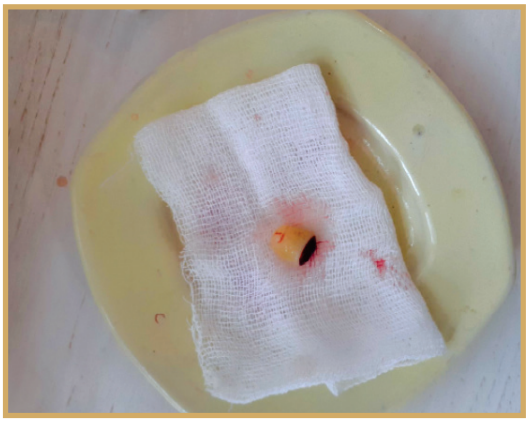


Fig. 3: PRFM clot obtained from the process.

Table 1: Socio-demographic characteristics of Hansen's disease patients (N=26).

Variable	Category	Frequency N=26	Percentage (%)
Age (years)	20-30	3	11.54
	30-40	6	23.08
	40-50	6	23.08
	50-60	5	19.23
	60-70	6	23.08
Sex	Male	22	84.62
	Female	4	15.38
Occupation	Unemployed	8	30.77
	Labourer	14	53.85
	Homemaker	4	15.38
Addictive Habits	Alcohol	3	11.54
	Smoking	3	11.54
	None	20	76.92
Associated Systemic Disease	Hypertension (HTN)	2	7.69
	Diabetes Mellitus (DM)	2	7.69
	None	22	84.62

Results

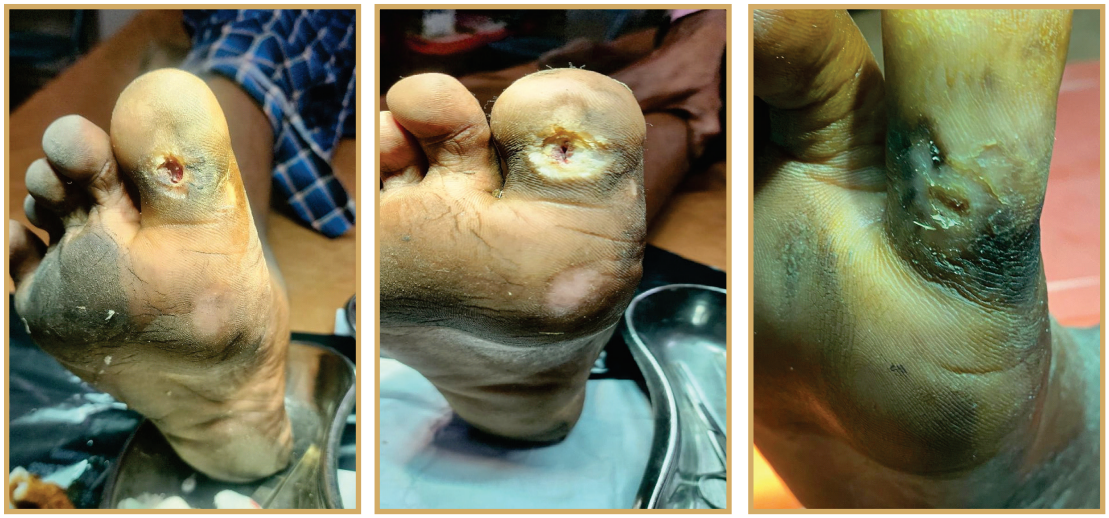
The study analyzed a total of 26 patients diagnosed with various types of Hansen's disease. Among the patients, the majority fell within the borderline spectrum, with 7 cases (26.9%) of borderline lepromatous (BL) and 6 cases (23.1%) of borderline tuberculoid (BT) leprosy. An additional 6 cases (23.1%) were diagnosed as pure neuritic leprosy (PNL), a form characterized by nerve involvement without visible skin lesions. Lepromatous leprosy (LL), the most severe and infectious form, accounted for 5 cases (19.2%). Among them, two patients were old cases of Hansen's disease.

Table 1 presents the distribution of age, sex, occupation, addictive habits, and associated systemic diseases among the Hansen's disease patients included in the study. The majority of patients were between the ages of 30-40 and 40-50 years (each contributing 23.08%), while the smallest age group was 20-30 years (11.54%). Males comprised 84.62% of the study population, with only 15.38% female representation. Most of the patients (53.85%) were laborers, while 30.77% were unemployed and 15.38% were homemakers. Notably, 76.92% of the patients reported no addictive habits, and 84.62% had no associated systemic diseases, such as hypertension or diabetes mellitus.

Table 2 presents data about the age, sex, Hansen's disease classification, wound duration before Platelet-rich Fibrin Matrix (PRFM) treatment, and multi-drug therapy status. The mean age of the patients was approximately 46 years, and the majority of the cases were still undergoing multi-drug therapy at the time of the study. Wound duration before PRFM treatment varied from 2 to 24 months, with 53.85% of patients having wounds for 6 weeks -4 months.

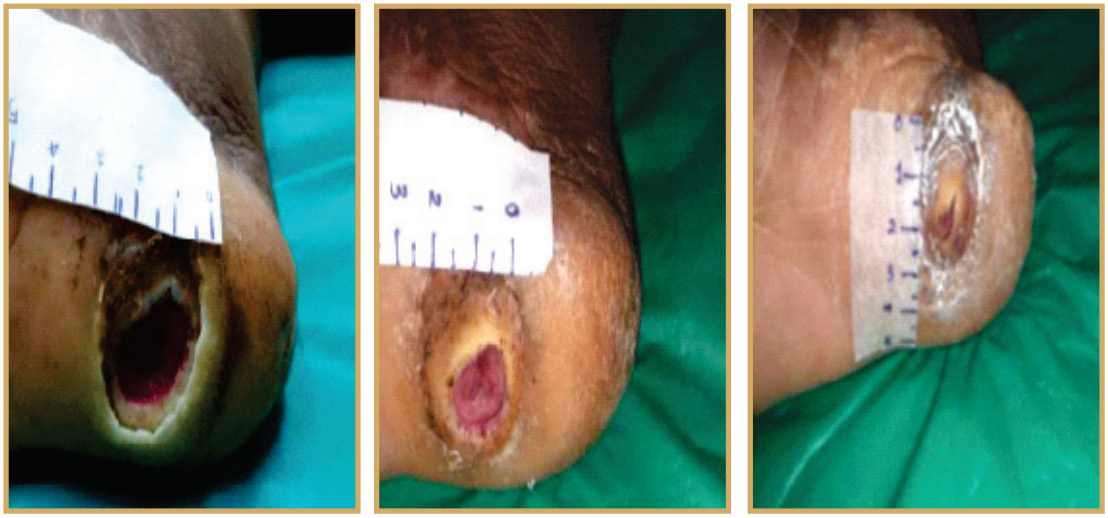
Most patients (14/26) had wound duration ranging from 6 weeks to 4 months, accounting for 53.85% of the cases, while no cases had wounds lasting between 15-19 months. Overall, duration ranged from six weeks up to 24 months (Table 3).

Follow-up of some representative cases is shown in Figs. 4 to 8.



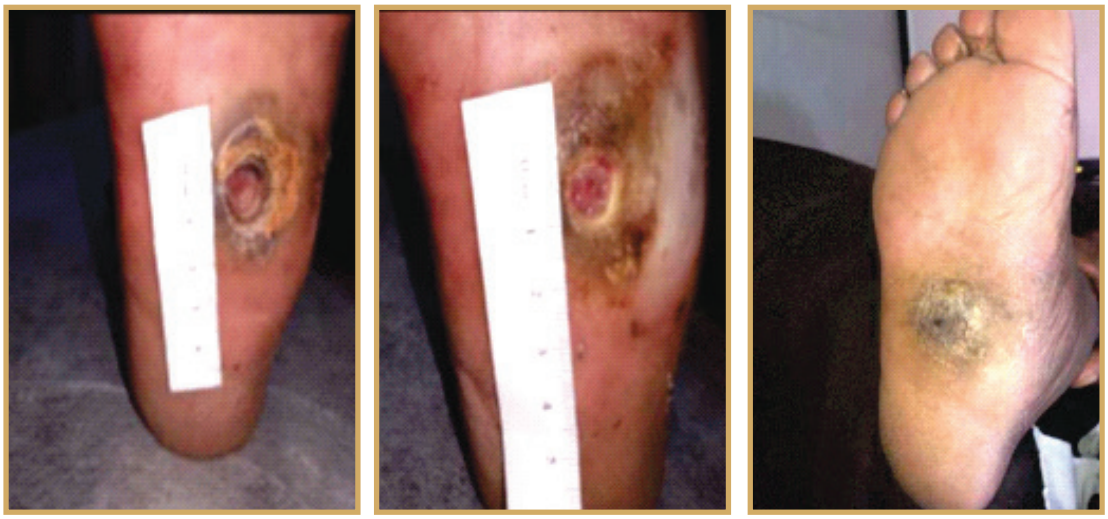
(a) Baseline ulcer (b) After 2 sessions (c) After 4th session

Fig. 4: Progress of case #3, at baseline (a), after two sessions(b) and after 4 sessions (c).



(a) Baseline ulcer (b) After 2nd sessions (c) After 4th session

Fig.5: Progress of healing of case #8, baseline, 2 weeks and 4 weeks of therapy.

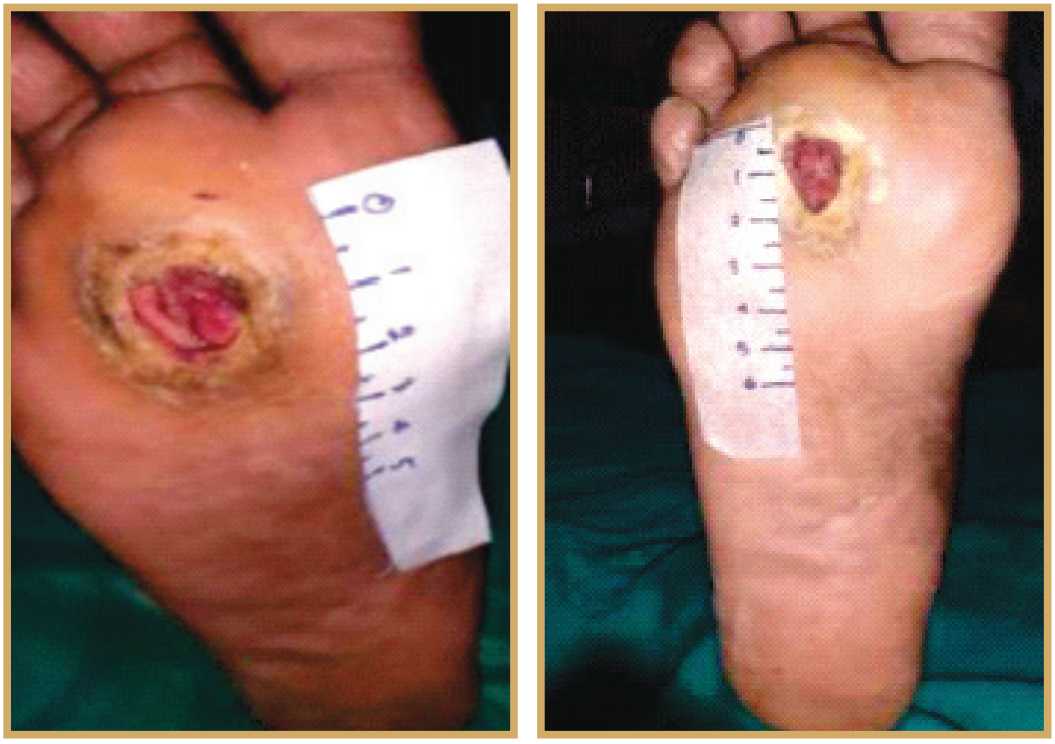


(a) Baseline ulcer (b) After 1st sessions (c) After 4th session

Fig. 6: Progress of case # 13 at baseline, after one sitting (one week) and after 4 sittings (4 weeks).

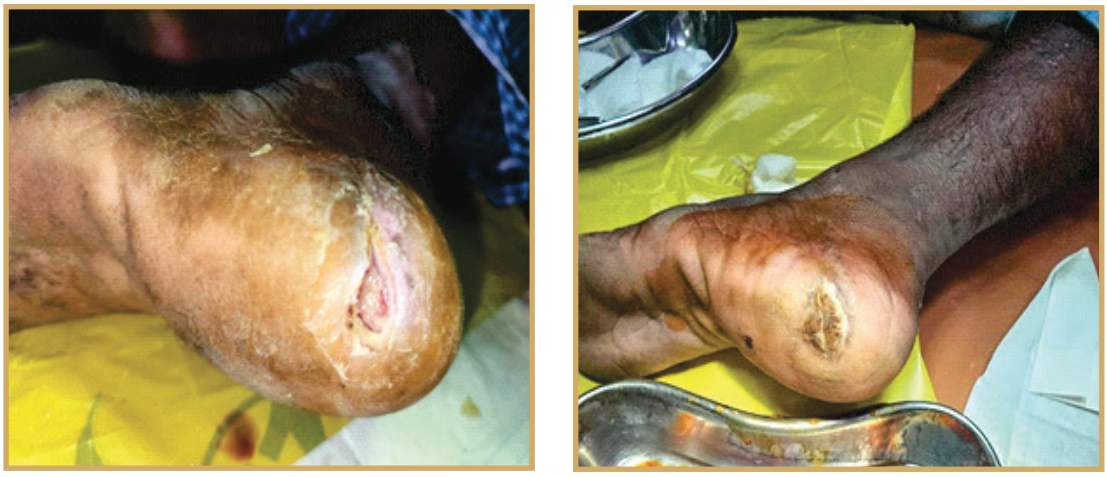
Overall, average percentage reduction in the area of ulcer is shown in Fig. 9.

The bar graph (Fig. 9) shows that by the 4th sitting of Platelet-rich Fibrin Matrix (PRFM) treatment, the majority i.e 12 patients' ulcer areas were reduced by 91-100%, whereas 5 of them even had undergone re-epithelialisation by the end of 4th sitting of PRFM.



(a) Baseline ulcer (b) After 4th session

Fig.7: Results of healing seen in case # 18 after 4 sittings (4 weeks); a= baseline; b= After 4 sessions.



(a) Baseline ulcer (b) After 4th session

Fig. 8: Re-epithelization in case #22 after 4 sessions (4 weeks) of therapy.

Table 2: Information about age, sex, and wound duration among Hansen's disease patients included in the study (N=26).

Case	Age (yrs)	Sex	Hansen disease	Wound duration before Platelet-rich fibrin (months)	Multi-drug therapy
1.	49	M	OLD BL	4 Months	Completed
2.	39	M	BT	3 Months	On Therapy
3.	55	M	BT	2 Months	On Therapy
4.	35	M	PNL	3 Months	On Therapy
5.	48	M	BT	2 Months	On Therapy
6.	34	M	LL	3 Months	On Therapy
7.	42	M	BL	7 Months	On Therapy
8.	55	M	PNL	13 Months	On Therapy
9.	42	M	PNL	5 Months	On Therapy
10.	52	M	LL	6 Months	On Therapy
11.	65	M	BT	3 Months	On Therapy
12.	42	M	PNL	4 Months	On Therapy
13.	22	M	LL	12 Months	On Therapy
14.	65	M	LL	7 Months	On Therapy
15.	44	M	BT	6 Months	On Therapy
16.	38	M	PNL	3 Months	On Therapy
17.	26	F	BT	3 Months	On Therapy
18.	57	M	OLD PNL	24 Months	Completed
19.	74	M	PNL	7 Months	On Therapy
20.	35	M	BT	3 Months	On Therapy
21.	27	M	BL	3 Months	On Therapy
22.	32	M	BL	4 Months	On Therapy
23.	42	M	BL	9 Months	On Therapy
24.	58	M	Old case	24 Months	Completed
25.	41	M	BL	3 Months	On Therapy
26.	68	M	Old case	11 Months	Completed

Table 4 summarizes the ulcer area and volume reduction across four PRFM sessions. The percentage reduction in both areas and volume was significant in most patients, with many achieving re-epithelialization (RE) after the second or third session. By the fourth sitting, 84.62% of the patients showed complete healing or significant improvement in ulcer size.

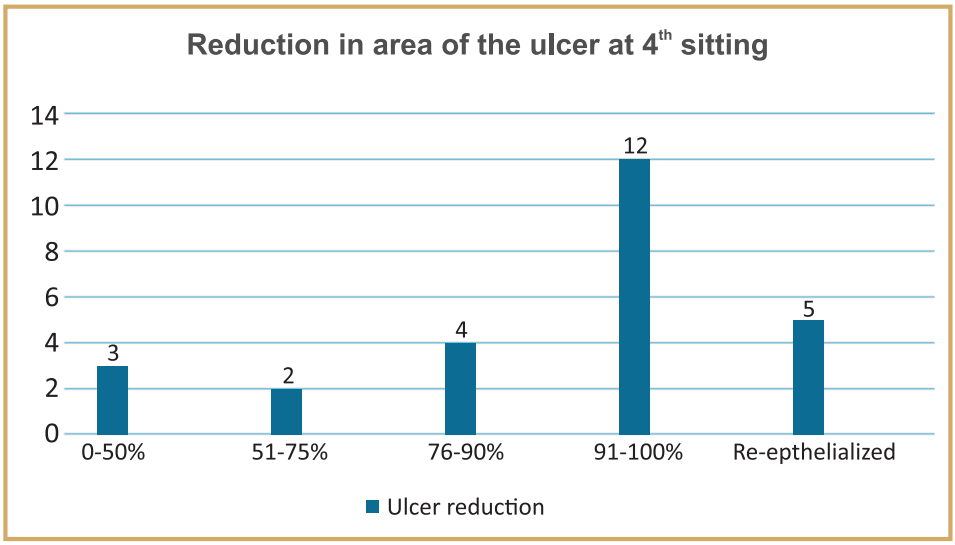


Fig 9: Percentage reduction in the area of the ulcer at 4th sitting.

Table 3: Distribution of wound duration among Hansen's disease patients (N=26) included in the study.

Wound Duration (Months)	No. of Patients, N= 26	(%)
6 weeks-4	14	53.85
5-9	6	23.08
10-14	3	11.54
15-19	0	0.00
20-24	3	11.54

Table 4: Changes in area and volume of ulcers after 1, 2, 3, 4 PRFM applications.

Case	Site of Ulcer	Measurement Category	Baseline	1st Sitting	2nd Sitting	3rd Sitting	4th Sitting
1	R-Heel	Area (cm^2)	1.02	44.62%	67.69%	88.46%	90.77%
		Volume (cm^3)	0.51	44.62%	80.62%	93.08%	94.46%
2	R-Sole	Area (cm^2)	0.94	16.67%	79.17%	90.00%	100.00%
		Volume (cm^3)	0.75	37.50%	89.58%	95.00%	100.00%
3	R-great toe	Area (cm^2)	0.79	70.00%	98.00%	100.00%	100.00%
		Volume (cm^3)	0.79	85.00%	99.80%	100.00%	RE
4	L-Heel	Area (cm^2)	1.76	19.64%	78.57%	100.00%	RE
		Volume (cm^3)	1.41	19.64%	91.96%	100.00%	RE

5	R-fore foot	Area (cm^2)	0.35	52.00%	100.00%	RE	RE
		Volume (cm^3)	0.04	80.80%	100.00%	RE	RE
6	R-Fore Foot	Area (cm^2)	0.79	52.00%	84.00%	100.00%	RE
		Volume (cm^3)	0.39	80.80%	93.60%	100.00%	RE
7	L-fore Foot	Area (cm^2)	4.81	26.47%	64.05%	81.37%	94.02%
		Volume (cm^3)	3.85	44.85%	82.03%	93.01%	95.75%
8	R-Heel	Area (cm^2)	3.93	20.00%	46.00%	74.00%	84.00%
		Volume (cm^3)	3.14	30.00%	66.25%	83.75%	96.00%
9	L-Heel	Area (cm^2)	0.31	20.00%	40.00%	80.00%	100.00%
		Volume (cm^3)	0.13	20.00%	70.00%	90.00%	100.00%
10	R-Fore Foot	Area (cm^2)	0.63	40.00%	70.00%	95.00%	100.00%
		Volume (cm^3)	0.31	52.00%	76.00%	98.00%	100.00%
11	L-Great Toe	Area (cm^2)	0.79	52.00%	70.00%	85.00%	96.00%
		Volume (cm^3)	0.63	64.00%	81.25%	94.38%	99.50%
12	R-fore foot	Area (cm^2)	2.51	53.13%	100.00%	RE	RE
		Volume (cm^3)	1.26	53.13%	100.00%	RE	RE
13	R-mid Foot	Area (cm^2)	3.14	28.75%	75.00%	93.75%	100.00%
		Volume (cm^3)	2.51	28.75%	84.38%	98.44%	100.00%
14	L-Great Toe	Area (cm^2)	3.14	43.75%	73.00%	92.00%	100.00%
		Volume (cm^3)	1.57	55.00%	78.40%	96.80%	100.00%
15	L-Heel	Area (cm^2)	2.54	25.93%	48.15%	69.14%	95.37%
		Volume (cm^3)	2.29	83.54%	82.72%	89.71%	99.49%
16	R-Sole	Area (cm^2)	2.54	25.93%	66.05%	87.65%	100.00%
		Volume (cm^3)	2.04	53.70%	91.51%	96.91%	100.00%
17	R-Great Toe	Area (cm^2)	3.53	37.78%	66.67%	86.67%	100.00%
		Volume (cm^3)	1.77	50.22%	86.67%	94.67%	100.00%
18	R-fore foot	Area (cm^2)	4.54	27.34%	48.10%	61.94%	72.32%
		Volume (cm^3)	3.63	27.34%	61.07%	76.21%	86.16%
19	R-Sole	Area (cm^2)	5.37	23.25%	47.37%	61.99%	82.46%
		Volume (cm^3)	4.30	23.25%	53.95%	76.24%	95.61%
20	L-Sole	Area (cm^2)	5.50	37.14%	59.29%	76.00%	100.00%
		Volume (cm^3)	4.40	45.00%	69.46%	88.00%	100.00%
21	L-Fore Foot	Area (cm^2)	4.52	30.43%	70.78%	82.61%	100.00%
		Volume (cm^3)	4.06	38.16%	80.52%	90.34%	100.00%
22	L-sole	Area (cm^2)	4.24	46.67%	52.59%	72.22%	100.00%
		Volume (cm^3)	3.82	81.48%	85.19%	93.42%	100.00%

23	R-Heel	Area (cm^2)	4.40	14.29%	35.71%	46.43%	92.86%
		Volume (cm^3)	3.52	73.21%	65.71%	91.43%	98.21%
24	R-Lateral Malleolus	Area (cm^2)	3.77	13.03%	17.29%	13.07%	31.02%
		Volume (cm^3)	1.88	17.30%	20.02%	23.07%	37.07%
25	R-Heel	Area (cm^2)	3.77	41.67%	53.33%	54.17%	87.50%
		Volume (cm^3)	1.88	72.50%	66.25%	79.75%	97.50%
26	R-Fore Foot	Area (cm^2)	4.91	19.04%	32.53%	36.00%	64.00%
		Volume (cm^3)	2.95	68.00%	51.36%	75.68%	88.00%

[RE- Re-epithelialisation]

Discussion

This study evaluated the efficacy of autologous Platelet-rich Fibrin Matrix (PRFM) in the healing of non-healing trophic ulcers among patients with Hansen's disease. The results demonstrate significant ulcer size reduction and complete healing in a substantial number of cases by the fourth PRFM session. This finding aligns with the increasing body of literature that supports the effectiveness of PRFM in chronic wound management, particularly in leprosy, a disease that continues to pose significant public health challenges despite global efforts for its eradication.

A key finding from our study is that 84.62% of patients showed significant improvement in ulcer size, with 53.85% achieving complete re-epithelialization by the third or fourth PRFM sitting. This high rate of ulcer closure is consistent with recent studies, such as the one conducted by Ehrenfest et al (2009) & O'Connell et al (2008), which found that PRFM facilitated faster wound closure due to its rich concentration of growth factors like platelet-derived growth factor (PDGF) and transforming growth factor-beta (TGF-β), which stimulate tissue regeneration and angiogenesis. The role of PRFM in enhancing wound healing has been widely studied in diabetic ulcers, with parallels being drawn to trophic ulcers in leprosy due to their chronic nature and poor healing propensity. In a study by Driver et al (2006), PRFM significantly improved healing outcomes in diabetic foot ulcers, with most patients showing a 70-100% reduction in ulcer area by the fourth week. This mirrors our findings, where 12 patients (46.15%) achieved over 90% reduction in ulcer area by the fourth session, underscoring the broad applicability of PRFM in chronic wound management, including those complicated by peripheral neuropathy, as seen in leprosy.

The study population predominantly consisted of patients with borderline lepromatous (26.9%) and borderline tuberculoid (23.1%) leprosy, with pure neuritic leprosy (PNL) accounting for 23.1% of cases. PNL, characterized by nerve involvement without visible skin lesions, often presents with delayed diagnosis and increased risk of trophic ulcers. In our study, patients with PNL had longer ulcer durations, some exceeding 24 months, consistent with the findings of Bhalla et al (2022), who noted that PNL is often associated with delayed healing due to its neuropathic complications.

The majority of patients (53.85%) in the present study had ulcer durations of 1.5-4 months before starting PRFM therapy, with significant reductions in ulcer size observed early in the

treatment course. This rapid response may be attributed to the early initiation of PRFM, as noted in the work by O'Connell et al (2008), where early intervention with autologous platelet concentrates improved healing times compared to delayed treatment. However, the benefits of PRFM were also evident in patients with longer ulcer durations, supporting its utility across varying stages of wound chronicity.

Despite the positive outcomes observed, our study is limited by the small sample size and short follow-up period. Larger, randomized controlled trials are needed to further validate the efficacy of PRFM in treating leprosy-related ulcers, particularly in comparison with standard care modalities like multi-drug therapy (MDT) alone. Additionally, the cost-effectiveness of PRFM remains a concern in resource-limited settings, as highlighted by Russo et al (2025), who stressed the need for cost-benefit analyses when implementing advanced wound care therapies in developing countries.

Future research should also explore the potential of combining PRFM with other adjunctive therapies, such as hyperbaric oxygen therapy, to optimize wound healing outcomes in this patient population. Moreover, studies investigating the long-term recurrence rates of trophic ulcers post-PRFM treatment are warranted to assess the sustainability of the observed healing outcomes.

Conclusion

The findings of this study suggest that PRFM is a highly effective modality for promoting ulcer healing in patients with Hansen's disease. The significant reductions in both ulcer area and volume, particularly in patients with longstanding ulcers, underscore the potential of PRFM as a valuable adjunctive therapy in the management of chronic trophic ulcers. These results contribute to the growing evidence base for the use of autologous platelet concentrates in wound healing, particularly in resource-constrained settings where traditional therapies may be insufficient.

By adhering to the principles of prospective interventional research, including the systematic assessment of outcomes across multiple sessions and the application of standardized ulcer measurements, this study contributes to the ongoing efforts to improve care for patients with leprosy-related complications. Further studies are encouraged to build on these findings, with a focus on expanding patient cohorts and exploring synergistic therapeutic approaches to enhance healing outcomes.

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