DOI: https://doi.org/10.3126/njdvl.v24i1.84140

Topical Insulin: A Game-Changer for Non-Healing Leprosy Ulcers – A Case Series

Aniket Anil Ratnaparkhi[1], Purvesh Pramod Fale[1], Vishwas Vinay Rahangdale[1], Mahesh M. Unni[1]

[1]Department of Dermatology, Maharashtra Institute of Medical Sciences & Research (MIMSR), Latur, India

Abstract

Leprosy, caused by *Mycobacterium leprae*, frequently leads to neuropathic trophic ulcers and ulcerative lesions associated with type II lepra reactions. These ulcers are difficult to treat due to sensory loss, repeated trauma, and poor vascularity, often responding inadequately to conventional therapies. Topical insulin has recently gained attention for its potential to enhance local wound healing by stimulating angiogenesis, collagen deposition, and re-epithelialization without systemic adverse effects. This case series included five male patients with Hansen's disease who presented with chronic trophic ulcers or ulcerative lesions of lepra reaction. A solution of 0.1 ml Actrapid insulin diluted with 0.9 ml normal saline was irrigated directly to the ulcer surface twice daily and covered with sterile gauze for five minutes. The intervention was continued for four to six weeks. Ulcer size, depth, tissue quality, and granulation were assessed clinically and documented photographically at baseline and follow-up. All patients showed significant improvement within two weeks, with marked reduction in ulcer dimensions and healthy granulation tissue formation. Complete epithelization was achieved in four to six weeks. No local or systemic adverse effects were observed, and compliance was excellent. Topical insulin is a safe, economical, and effective therapeutic option for leprosy-associated ulcers, meriting further evaluation in larger controlled studies.

Key words: Leprosy, Skin Ulcer, Insulin; Topical, Wound healing

Introduction

Leprosy, caused by *Mycobacterium leprae*, is a chronic granulomatous infection that primarily affects the skin and peripheral nerves. The disease displays a broad clinical spectrum classified by the Ridley–Jopling system into five types: tuberculoid, borderline tuberculoid, mid-borderline, borderline lepromatous, and lepromatous leprosy. This classification reflects the host immune response and bacillary load, with tuberculoid disease showing robust cellular immunity and low bacterial counts, while lepromatous leprosy is characterized by immunosuppression and extensive bacillary proliferation. A rare form, pure neuritic leprosy, involves nerve trunks in the absence of overt cutaneous lesions, further demonstrating the neurotropic nature of the bacillus.[1]

Hansen's disease ulcers represent one of the most disabling sequelae of leprosy, particularly involving the plantar surface of the feet. They result from sensory impairment, repeated trauma, motor dysfunction, and autonomic changes, all of which compromise protective reflexes and tissue viability. Chronicity is often perpetuated by scar tissue formation, vascular insufficiency, recurrent reactions, and in some cases, direct bacterial impact. Management generally includes protective footwear, pressure offloading, antimicrobial therapy, surgical debridement, and reconstructive

Funding: None
Conflict of Interest: None

Corresponding Author:
Dr. Vishwas Vinay Rahangdale
Junior resident, Department of Dermatology, Maharashtra Institute of Medical Sciences & Research (MIMSR), Latur, India
Email: vishwasrahangdale@gmail.com
ORCID ID: 0000-0002-4861-3725

Date of Submission: 2025-09-05
Date of Acceptance: 2025-03-11
Date of Publication: 2026-05-01

How to cite this article
How to cite the article: Ratnaparkhi A, Fale P, Rahangdale V, Unni M. Topical Insulin: A Game-Changer for Non-Healing Leprosy Ulcers – A Case Series. NJDVL 2026;24(1):54-57

https://doi.org/10.3126/njdvl.v24i1.84140

procedures such as free tissue transfer or metronidazole plaster boots.[2] Despite these approaches, recurrence rates remain high and definitive healing elusive.

Emerging therapies have explored biological agents to stimulate local tissue repair. Insulin, conventionally known for its metabolic role, has gained recognition as a local wound-healing enhancer. Topical application of insulin exerts beneficial effects on angiogenesis, collagen synthesis, re-epithelialization, and inflammatory modulation without systemic complications like hypoglycaemia or hypokalaemia. This makes it a cost-effective, accessible, and safe adjunct in chronic wound management.[3]

Experimental studies in animals and clinical data in both diabetic and non-diabetic populations support the use of insulin in enhancing wound closure, improving pressure ulcer healing, reducing burn injury complications, and accelerating epithelial recovery in ophthalmologic and otologic injuries. Mechanistically, insulin modulates macrophage polarization via P13K/Akt–STAT3 pathways, promoting the transition to reparative M2 macrophages, which secrete IL-4, IL-10, and IL-13, thereby reducing inflammation and supporting angiogenesis. Additional benefits include upregulation of VEGF and TGF-β1, enhanced fibroblast activity, and improved extracellular matrix deposition.[4-7]

This paper presents a case series of five patients with Hansen's disease complicated by ulcers or ulcerative lesions of type II lepra reaction, all treated with topical insulin. Their clinical courses, therapeutic responses, and outcomes are described, followed by an overall analysis of efficacy.

Methodology

This was a prospective, open-label, single-center case series conducted over one month. Five male patients with Hansen's disease presenting with chronic trophic ulcers or type II lepra reaction–associated ulcerations were enrolled.

Inclusion criteria were adults with clinically diagnosed leprosy, presence of chronic ulceration (>4 weeks), and willingness to comply with treatment and follow-up. Exclusion criteria included uncontrolled diabetes, active systemic infection, known hypersensitivity to insulin, or concurrent participation in other clinical trials.

The study protocol was approved by the Institutional Ethics Committee, and written informed consent was obtained from all participants. Topical treatment consisted of 0.1 ml Actrapid insulin diluted with 0.9 ml normal saline, applied directly to the ulcer surface twice daily after wound debridement and covered with sterile gauze for five minutes. Treatment continued for four to six weeks.

Ulcer dimensions (length, width, depth), tissue quality, and granulation were assessed clinically at baseline and weekly intervals, with photographic documentation for verification. Data accuracy was confirmed independently by two clinicians to ensure objectivity and consistency. Patients were monitored for local and systemic adverse effects throughout the study period. X-ray to rule out bone involvement and swab cultures were not done.

Case Series

Case 1

A 55-year-old man with biopsy-proven leprosy, who had completed a 12-month course of multi-drug therapy (MDT), presented with a non-healing ulcer over the medial malleolus of the left foot. The ulcer developed two months post-treatment, measured approximately 15 cm^2, and had regular borders with complete loss of sensation in the surrounding area. Previous management with systemic and topical antibiotics failed to achieve improvement. Based on absent sensations and clinical context, the lesion was diagnosed as a trophic ulcer. Topical insulin was initiated. After two weeks, the ulcer showed marked reduction in size with healthy granulation tissue formation. Progressive improvement was noted at follow-up, and by four weeks the ulcer demonstrated substantial contraction and restoration of tissue integrity.

Case 2

A 58-year-old man, a known case of Hansen's disease, presented with erythematous painful nodular lesions and ulcerations measuring 2 cm^2 to 4 cm^2 over the left forearm, thigh, and buttock, persisting for 20 days. Biopsy revealed type II lepra reaction (erythema nodosum leprosum). The patient had not received prior therapy for the reaction. He was started on oral corticosteroids, MDT, and topical insulin therapy for the ulcerated lesions. At two weeks follow-up, significant reduction in ulcer size and pain was observed. By four weeks, the ulcers had completely healed with well-formed scar tissue.

Case 3

A 45-year-old male presented with a persistent deep ulcer over the medial plantar aspect of the left foot, below the great toe, of size 48 cm^2, present for three months. He reported complete loss of sensation in both palms and soles. Examination revealed bilateral ulnar nerve thickening (Grade II), atrophy of thenar and hypothenar eminences, partial claw hand deformity, xerotic hypopigmented patches on the thigh and knee, and associated focal anhidrosis with alopecia. Biopsy confirmed Hansen's disease. MDT was initiated alongside topical insulin therapy. By three weeks, the ulcer showed marked reduction in depth and area, with formation of healthy granulation tissue, indicating significant healing.

Case 4

A 52-year-old male with leprosy presented with a chronic plantar ulcer of approximately 24 cm2 on the right sole, persisting for two months and refractory to antibiotics and conventional dressings. Examination

confirmed sensory loss in the affected area consistent with neuropathic etiology. Topical insulin was commenced. At two weeks, healthy granulation tissue and a decrease in ulcer depth were evident. After six weeks, near-complete epithelialization was achieved, with minimal residual scarring.

Case 5

A 60-year-old male with Hansen's disease presented with recurrent ulcerative lesions due to type II lepra reaction, located over the lateral malleolus and measuring 6 cm2. The patient complained of pain, erythema, and recurrent inflammation despite corticosteroid use. Topical insulin was added to his regimen. By the fourth week, complete epithelization was achieved with scar formation, and no recurrence was observed during six weeks of follow-up.

Results

Five male patients aged 45–58 years with Hansen's disease were assessed. Three presented with chronic non-healing trophic ulcers, and two had ulcerative lesions of type II lepra reaction. Ulcer size ranged from 2 cm2 to 48 cm2, at baseline. The chronicity ranged from 20 days to three months. After 6 weeks of topical insulin therapy, all patients exhibited 60–70% reduction in ulcer size and depth, with development of healthy granulation tissue and progressive epithelialization. By the end of 6 weeks, all ulcers achieved complete closure. No adverse events were reported, and compliance was excellent. Patients were followed up till 24 weeks with no recurrence in lesions.

Table-1 Table showing demographic details, comorbidities, ulcer characteristics, baseline measurements, and response to treatment at 6 weeks in five patients.

Case	Age (years)	Comorbidities	Type of lesion	Ulcer site	Baseline size (cm)	Baseline depth (cm)	Size at 6 weeks (cm)	Depth at 6 weeks (cm)	% Reduction	Outcome
1	55	None	Chronic trophic ulcer	Left medial malleolus	5×3	1.5	1.7×1	0.5	65%	Complete epithelization
2	58	None	Type II lepra reaction ulcer	Forearm, thigh, buttock	2×1–2×2	0.5	0.6×0.4	0.2	70%	Complete epithelization
3	45	None	Chronic trophic ulcer	Medial plantar	8×6	2.3	3×2	0.9	60%	Near-complete healing
4	52	Hypertension	Chronic trophic ulcer	Plantar aspect	6×4	1.2	2.1×1.4	0.4	65%	Complete epithelization
5	47	Diabetes mellitus (controlled)	Type II lepra reaction ulcer	Leg	3×2	0.8	1×0.6	0.3	70%	Complete epithelization

Size is given in centimeters (length × width), depth in centimeters, and % Reduction represents the decrease in ulcer size and/or depth from baseline to 6 weeks. Outcome indicates the final healing status.

Discussion

The wound healing process is a complex interplay of haemostasis, inflammation, proliferation, and remodelling phases. Following injury, haemostasis occurs through clot formation and platelet activation. Inflammation ensues, characterized by neutrophil migration, release of proteases, and macrophage recruitment via chemotactic mediators such as MCP-1 and TGF-β. Macrophages, central to wound healing, facilitate angiogenesis, fibrin resolution, and epithelial proliferation [4–7].

Trophic ulcers in leprosy are notoriously resistant to conventional management owing to neuropathy, repeated trauma, and impaired tissue responses. Plantar ulcers affect 15–20% of patients and represent a major cause of disability (8–13). The chronic nature of these ulcers emphasizes the urgent need for effective, affordable, and safe therapeutic adjuncts.

Insulin has been shown to activate the PI3K/Akt–STAT3 pathway, suppress STAT1, and drive macrophage polarization toward an M2 reparative phenotype. These macrophages secrete anti-inflammatory cytokines such as IL-4, IL-10, and IL-13, as well as metabolites like ornithine, which support tissue regeneration. Additionally, insulin enhances production of VEGF and TGF-β1, critical mediators of angiogenesis and granulation tissue formation. Insulin also stimulates fibroblast proliferation and collagen maturation, contributing to wound tensile strength and epithelial stability.[14–16] Oral steroids delay wound healing

and are reserved for inflammatory ulcers, whereas topical insulin enhances granulation, angiogenesis, and epithelialization, making it useful in chronic non-healing ulcers.[17]

In the present case series, topical insulin consistently accelerated wound healing in chronic trophic ulcers and lepra reaction–associated lesions. All patients experienced reduction in ulcer size and depth within weeks, and complete epithelization occurred within four to six weeks. No systemic side effects were observed, confirming the safety of topical application. These findings align with existing literature on insulin's efficacy in diabetic ulcers, pressure sores, and burn wounds, supporting its broader utility in chronic wounds of varied etiologies.

The advantages of topical insulin are manifold: affordability, ease of application, accessibility in resource-constrained settings, and absence of systemic risks. Its integration into routine leprosy ulcer care could significantly improve outcomes, reduce disability, and enhance quality of life for patients in endemic regions. Nonetheless, controlled clinical trials are needed to validate these observations, standardize dosing protocols, and evaluate long-term outcomes.

Limitations include the small sample size, absence of a control group, short follow-up duration. Larger blinded controlled trials with longer follow-up are warranted to validate efficacy, optimize dosing, and establish standardized treatment protocols.

Conclusion

Topical insulin demonstrates substantial promise as a therapeutic option for chronic trophic ulcers and ulcerative lesions in leprosy. It is safe, cost-effective, and capable of accelerating healing with high patient compliance and no observed adverse effects. Combining topical insulin with adjunctive modalities such as platelet-rich fibrin may further enhance efficacy. Future large-scale clinical studies are warranted to confirm its role and to develop standardized treatment guidelines for leprosy-related chronic ulcers.

References

1. Pawar M. Topical insulin in the treatment of nonhealing erosions and ulcers of pemphigus vulgaris. J Am Acad Dermatol. 2021 Nov;85(5):e271-2. https://doi.org/10.1016/j.jaad.2020.05.149
2. Riyaz N, Sehgal VN. Leprosy: Trophic Skin Ulcers. Skinmed. 2017;15(1):45-51
3. Edek YC, Çalışkan Güneş E, Ertugay Aral HN, Adışen E, Aksakal AB. Topical Insulin as an Add-On Therapy for Leg Ulcer: A Case Report. Cureus. 15(6):e39822.
4. Ibrahim HM, Fahmy EAM, Elsayed MM, Elardi A. Role of Insulin in Dermatology: Review Article. The Egyptian Journal of Hospital Medicine. 2022 Oct 1;89(1):4967-9. https://doi.org/10.21608/ejhm.2022.260867
5. Ellis S, Lin EJ, Tartar D. Immunology of Wound Healing. Curr Dermatol Rep. 2018;7(4):350-8. https://doi.org/10.1007/s13671-018-0234-9
6. Su Y, Richmond A. Chemokine Regulation of Neutrophil Infiltration of Skin Wounds. Adv Wound Care (New Rochelle). 2015 Nov 1;4(11):631-40. https://doi.org/10.1089/wound.2014.0559
7. Krzyszczyk P, Schloss R, Palmer A, Berthiaume F. The Role of Macrophages in Acute and Chronic Wound Healing and Interventions to Promote Pro-wound Healing Phenotypes. Front Physiol. 2018;9:419. https://doi.org/10.3389/fphys.2018.00419
8. Gahalaut P, Pinto J, Pai GS, Kamath J, Joshua TV. A novel treatment for plantar ulcers in leprosy: local superficial flaps. Lepr Rev. 2005 Sept;76(3):220-31. https://doi.org/10.47276/lr.76.3.220
9. Rezvani O, Shabbak E, Aslani A, Bidar R, Jafari M, Safarnezhad S. A randomized, double-blind, placebo-controlled trial to determine the effects of topical insulin on wound healing. Ostomy Wound Manage. 2009 Aug 1;55(8):22-8.
10. Lima MHM, Caricilli AM, de Abreu LL, Araújo EP, Pelegrinelli FF, Thirone ACP, et al. Topical insulin accelerates wound healing in diabetes by enhancing the AKT and ERK pathways: a double-blind placebo-controlled clinical trial. PLoS One. 2012;7(5):e36974. https://doi.org/10.1371/journal.pone.0036974
11. Stephen S, Agnihotri M, Kaur S. A Randomized, Controlled Trial to Assess the Effect of Topical Insulin Versus Normal Saline in Pressure Ulcer Healing. Ostomy Wound Manage. 2016 June;62(6):16-23
12. Zeng M, Zhi Y, Liu W, Zhang W, Xu J. Clinical study on local application of low-dose insulin for promoting wound healing after operation for deep burns. Exp Ther Med. 2016 Nov;12(5):3221-6. https://doi.org/10.3892/etm.2016.3749
13. Dionesov SM, Zykov NN. [Insulin therapy of trophic ulcers]. Vestn Dermatol Venerol. 1980 Jan;(1):57-9
14. Mantovani A, Biswas SK, Galdiero MR, Sica A, Locati M. Macrophage plasticity and polarization in tissue repair and remodelling. J Pathol. 2013 Jan;229(2):176-85. https://doi.org/10.1002/path.4133
15. Orliaguet L, Dalmas E, Drareni K, Venteclef N, Alzaid F. Mechanisms of Macrophage Polarization in Insulin Signaling and Sensitivity. Front Endocrinol (Lausanne). 2020;11:62. https://doi.org/10.3389/fendo.2020.00062
16. Schilrreff P, Alexiev U. Chronic Inflammation in Non-Healing Skin Wounds and Promising Natural Bioactive Compounds Treatment. Int J Mol Sci. 2022 Apr 28;23(9):4928. https://doi.org/10.3390/ijms23094928
17. Guo S, Dipietro LA. Factors affecting wound healing. J Dent Res. 2010 Mar;89(3):219-29. https://doi.org/10.1177/0022034509359125