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Original Article

To Study the Effectiveness of Application of Topical Insulin and Normal Saline Dressings in Diabetic Foot Ulcer Management

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ABSTRACT

Background: Diabetic foot ulcer (DFU) is a common and debilitating complication of diabetes mellitus, frequently associated with prolonged hospitalization, increased healthcare costs, and risk of lower-limb amputation. Effective wound care plays a crucial role in DFU management. Topical insulin has been proposed as a cost-effective adjunct that may enhance wound healing through its effects on cellular proliferation, angiogenesis, and collagen synthesis. This study aimed to compare the effectiveness of topical insulin dressing with conventional normal saline dressing in the management of diabetic foot ulcers.

Methods: A hospital-based randomized controlled trial was conducted in the Department of General Surgery, Teerthanker Mahaveer Medical College and Research Centre, Moradabad. Seventy patients with diabetic foot ulcers were randomly allocated into two groups: Group A (topical insulin dressing, n=35) and Group B (normal saline dressing, n=35). Ulcer size, ulcer depth, granulation tissue formation, and overall healing outcomes were assessed at baseline, Day 6, and Day 12. Statistical analysis was performed using appropriate inferential tests, with $p<0.05$ considered statistically significant.

Results: Baseline demographic and clinical characteristics were comparable between the two groups. By Day 12, the insulin group demonstrated significantly greater wound healing than the saline group. Mean ulcer size decreased from 12.3 ± 3.5 cm² to 4.6 ± 2.5 cm² in the insulin group compared with 13.8 ± 3.9 cm² to 8.7 ± 2.8 cm² in the saline group ($p<0.001$). Mean ulcer depth decreased from 6.9 ± 1.8 mm to 2.5 ± 1.1 mm in the insulin group versus 7.1 ± 1.9 mm to 4.5 ± 1.3 mm in the saline group ($p<0.001$). Healthy granulation tissue developed more rapidly in the insulin group (85.7% vs. 71.4% on Day 6; $p<0.05$). More patients achieved >50% ulcer healing in the insulin group than in the saline group (85.7% vs. 42.9%; $p<0.001$).

Conclusion: Topical insulin dressing is a safe, effective, and economical modality for diabetic foot ulcer management. Compared with conventional normal saline dressing, it significantly accelerates wound healing by reducing ulcer size and depth and promoting earlier granulation tissue formation. These findings support the routine use of topical insulin dressing, particularly in resource-limited settings.

Keywords*: Diabetic foot ulcer; Topical insulin; Normal saline dressing; Wound healing; Granulation tissue; Diabetes mellitus; Randomized controlled trial.*

INTRODUCTION

Diabetes mellitus represents one of the most rapidly growing global health crises of the twenty-first century, with an estimated 537 million adults living with the condition worldwide and projections suggesting this figure will exceed 780 million by 2045 [1]. Among its most debilitating complications, diabetic foot ulcers (DFUs) impose a disproportionate clinical and socioeconomic burden, affecting approximately 15–25% of diabetic individuals over their lifetime [2]. DFUs are associated with prolonged hospitalization, significant healthcare expenditure, impaired quality of life, and remain the leading precipitant of non-traumatic lower limb amputations globally [3]. The pathophysiology underlying poor wound healing in diabetic patients is multifactorial, encompassing peripheral neuropathy, peripheral vascular disease, immune dysregulation, impaired angiogenesis, and reduced growth factor activity and collectively creating a hostile microenvironment that renders conventional wound care strategies frequently inadequate [4,5].

Standard wound management protocols for DFUs have traditionally relied on normal saline (NS) dressings, which maintain a moist wound environment and facilitate mechanical debridement. While NS dressings are widely accessible, cost-effective, and safe, they are largely inert in their biological activity and do not actively address the underlying cellular and molecular deficiencies that characterize diabetic wound healing [6]. This limitation has driven increasing interest in adjunctive and alternative topical therapies capable of modulating the wound microenvironment more effectively.

Insulin, a well-established anabolic hormone, has emerged as a promising topical wound-healing agent beyond its classical metabolic role. Preclinical studies have demonstrated that topical insulin promotes keratinocyte proliferation and migration, stimulates fibroblast activity, enhances angiogenesis, and reduces local inflammatory cytokine expression through activation of the PI3K/Akt signaling pathway [7,8]. These mechanisms collectively facilitate granulation tissue formation, re-epithelialization, and overall wound closure processes that are characteristically impaired in diabetic foot ulcers. Several small-scale clinical studies and case series have reported accelerated wound healing with topical insulin application; however, the existing evidence base remains heterogeneous in methodology, sample size, and outcome measurement, limiting the strength of conclusions that can be drawn [9,10].

Given this evidence gap, a rigorously designed randomized controlled trial comparing topical insulin dressing with conventional normal saline dressing is warranted to generate high-quality evidence capable of informing clinical practice. This study aimed to compare the effectiveness of topical insulin dressing and conventional normal saline dressing in diabetic foot ulcer management by evaluating changes in ulcer size, ulcer depth, granulation tissue formation, and overall wound healing outcomes.

Objective: This study aimed to compare the effectiveness of topical insulin dressing and conventional normal saline dressing in diabetic foot ulcer management by evaluating changes in ulcer size, ulcer depth, granulation tissue formation, and overall wound healing outcomes.

MATERIALS AND METHODS

Study Design and Setting: This hospital-based randomized controlled trial (RCT) was conducted in the Department of General Surgery, Teerthanker Mahaveer Medical College and Research Centre, Moradabad, Uttar Pradesh, India, over a period of 18 months following approval from the Institutional Ethics Committee (IEC).

Study Population: Patients presenting with diabetic foot ulcers (DFUs) to the outpatient and inpatient services of the Department of General Surgery during the study period were screened for eligibility. A total of 70 patients fulfilling the inclusion criteria were enrolled and randomly allocated into two equal groups of 35 patients each.

Inclusion Criteria: Patients aged 18 years or older with a confirmed diagnosis of diabetes mellitus and DFUs classified as Wagner grade I or II who provided written informed consent were included in the study.

Exclusion Criteria: Patients with Wagner grade III–V ulcers, osteomyelitis, gangrene, severe peripheral arterial disease, malignancy-associated ulcers, immunocompromised states, pregnancy, known insulin hypersensitivity, or those unwilling to participate were excluded.

Randomization: Eligible patients were randomized into two treatment groups using serial allocation numbers.

Intervention: There are two groups for intervention

Group A (Topical Insulin Dressing): Patients received topical insulin dressing comprising 4 units (0.1 mL) of human Mixtard insulin diluted in 1 mL of normal saline per 10 cm^2 of wound surface area, applied once daily following wound cleansing and debridement as required.

Group B (Normal Saline Dressing): Patients received conventional sterile normal saline dressing once daily following standard wound care protocols.
All participants in both groups received standard diabetic foot care, including glycemic control, infection management, debridement when clinically indicated, and pressure off-loading measures throughout the study period.

Data Collection and Outcome Assessment: Baseline demographic and clinical data including age, sex, body mass index (BMI), duration of diabetes, glycated hemoglobin (HbA1c), and ulcer characteristics were recorded using a structured proforma. Ulcer assessment was performed at baseline (Day 0), Day 6, and Day 12. Ulcer size was measured in square centimeters (cm^2) using the transparent acetate sheet and graph paper method. Ulcer depth was measured in millimeters (mm) using a Vernier caliper. Granulation tissue formation was assessed clinically and categorized as healthy or poor.
The primary outcome was overall wound healing at the end of the study period. Secondary outcomes included changes in ulcer size, ulcer depth, and granulation tissue formation at each assessment point.

Statistical Analysis
Data were entered and managed in Microsoft Excel and analyzed using appropriate statistical software. Continuous variables were expressed as mean ± standard deviation (SD). A p-value of <0.05 was considered statistically significant.

Ethical Considerations
The study was approved by the IEC of Teerthanker Mahaveer Medical College and Research Centre prior to commencement. Written informed consent was obtained from all participants before enrollment. Patient confidentiality was maintained throughout the study. The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki [11].

RESULTS
A total of 70 patients with diabetic foot ulcers were enrolled in this study and randomly assigned to two equal groups: an insulin group (n = 35) and a saline control group (n = 35). The study population comprised 44 males (62.9%) and 26 females (37.1%). The majority of patients 47 out of 70 (67.1%) belonged to the 30–49 year age group, reflecting the predominance of working-age adults in the diabetic foot ulcer burden. The two groups were well-matched at baseline with no statistically significant difference in ulcer size (12.3 ± 3.5 cm^2 vs 13.8 ± 3.9 cm^2) or ulcer depth (6.9 ± 1.8 mm vs 7.1 ± 1.9 mm) between the insulin and saline groups, respectively ($p > 0.05$) (Table 1, Table 2).

Table 1. Comparison of Mean Ulcer Size Between Groups

Time Point	Insulin (Mean ± SD, cm^2)	Saline (Mean ± SD, cm^2)	p-value
Day 0	12.3 ± 3.5	13.8 ± 3.9	>0.05
Day 6	8.5 ± 2.9	10.2 ± 3.2	<0.05
Day 12	4.6 ± 2.5	8.7 ± 2.8	<0.001

Regarding ulcer size reduction, a progressive and statistically significant improvement was observed in the insulin group over the 12-day observation period. Mean ulcer area decreased from 12.3 ± 3.5 cm^2 at baseline to 8.5 ± 2.9 cm^2 by Day 6 ($p < 0.05$) and further to 4.6 ± 2.5 cm^2 by Day 12 ($p < 0.001$). In contrast, the saline group demonstrated a comparatively modest reduction, from 13.8 ± 3.9 cm^2 at Day 0 to 10.2 ± 3.2 cm^2 at Day 6 and 8.7 ± 2.8 cm^2 at Day 12. The between-group difference at Day 12 was highly significant ($p < 0.001$) (Table 1).

A similar pattern was observed for ulcer depth. The insulin group showed a reduction from 6.9 ± 1.8 mm at baseline to 4.2 ± 1.5 mm at Day 6 ($p < 0.05$) and 2.5 ± 1.1 mm at Day 12 ($p < 0.001$), while the saline group demonstrated lesser improvement, reaching 5.5 ± 1.7 mm and 4.5 ± 1.3 mm at Day 6 and Day 12, respectively. The inter-group difference was statistically significant at both follow-up time points (Table 2).

Table 2. Comparison of Mean Ulcer Depth Between Groups

Time Point	Insulin (Mean ± SD, mm)	Saline (Mean ± SD, mm)	p-value
Day 0	6.9 ± 1.8	7.1 ± 1.9	>0.05
Day 6	4.2 ± 1.5	5.5 ± 1.7	<0.05
Day 12	2.5 ± 1.1	4.5 ± 1.3	<0.001

Assessment of granulation tissue formation revealed that at Day 6, healthy granulation tissue was present in 30 patients (85.7%) in the insulin group, compared to 25 patients (71.4%) in the saline group, a statistically significant difference ($p < 0.05$). By Day 12, all patients in both groups (100%) had achieved healthy granulation tissue, with no significant difference between the groups at that time point (Table 3). This finding suggests that topical insulin accelerates early-phase tissue repair without affecting the final granulation outcome.

Table 3. Comparison of Granulation Tissue Formation

Time Point	Insulin Healthy n (%)	Saline Healthy n (%)	p-value
Day 0	0 (0)	0 (0)	—
Day 6	30 (85.7)	25 (71.4)	<0.05
Day 12	35 (100)	35 (100)	NS

Analysis of key outcome measures at Day 12 further confirmed the superiority of topical insulin therapy (Table 4). Ulcer area below 5 cm² was achieved in 25 patients (71.4%) in the insulin group compared to only 10 patients (28.6%) in the saline group ($p < 0.001$). Superficial depth of less than 3 mm was attained in 30 insulin-treated patients (85.7%) versus 15 saline-treated patients (42.9%) ($p < 0.001$). Similarly, greater than 50% healing was recorded in 30 patients (85.7%) in the insulin group compared to 15 patients (42.9%) in the saline group ($p < 0.001$). No significant difference was noted between groups in the proportion achieving healthy granulation tissue at Day 12, as both reached 100% (Table 4).

Table 4. Summary of Key Day-12 Outcomes

Outcome Measure	Insulin Group	Saline Group	p-value
Ulcers <5 cm², n (%)	25 (71.4)	10 (28.6)	<0.001
Superficial ulcers (<3 mm), n (%)	30 (85.7)	15 (42.9)	<0.001
Healthy granulation tissue, n (%)	35 (100)	35 (100)	NS
>50% Healing, n (%)	30 (85.7)	15 (42.9)	<0.001

FIGURE 1 — PATIENT DEMOGRAPHICS

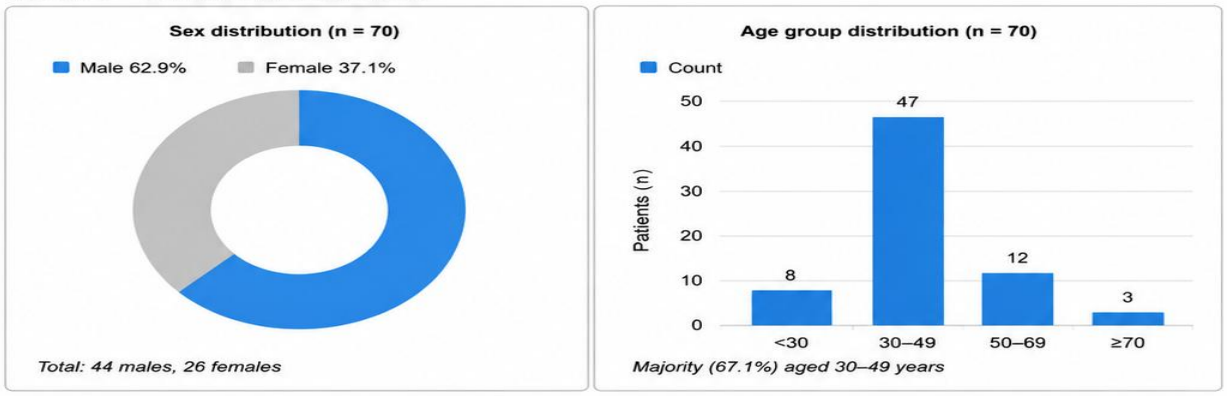


FIGURE 2 — ULCER HEALING OVER TIME

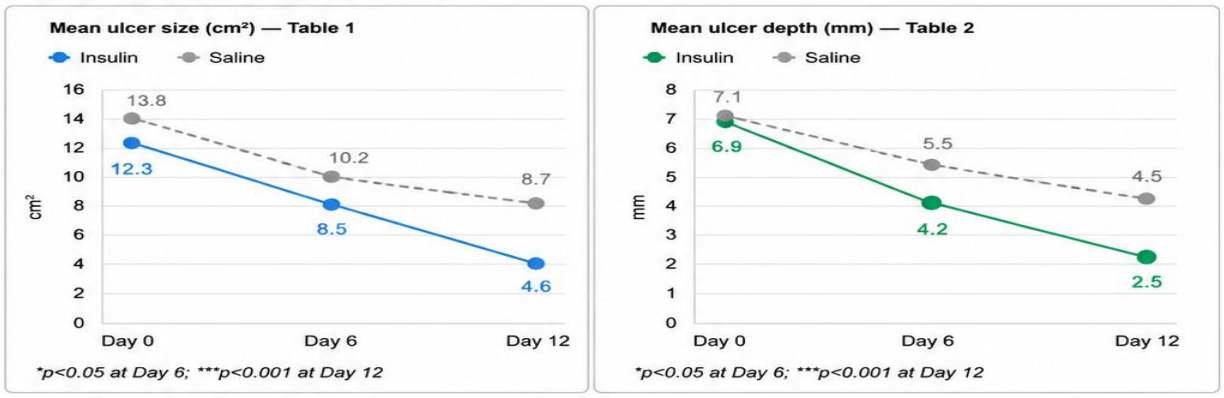
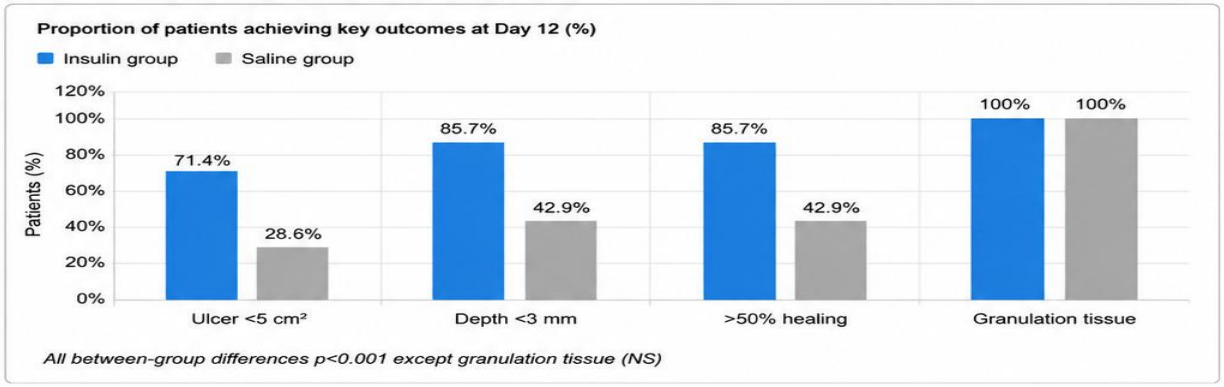


FIGURE 3 — DAY-12 OUTCOME COMPARISON — TABLE 4



DISCUSSION

This study demonstrated that topical insulin application produces significantly greater improvement in diabetic foot ulcer healing compared to normal saline across all measured parameters, including ulcer size, depth, granulation tissue formation, and overall healing rate.

The demographic profile of our cohort — predominantly male (62.9%) and concentrated in the 30–49 year age group (67.1%) — reflects the working-age burden of diabetic foot disease documented globally. Boulton et al. [3] emphasized that diabetic foot complications disproportionately affect individuals in their productive years, carrying profound socioeconomic consequences. Armstrong et al. [2] further noted that diabetic foot ulcers carry a high risk of recurrence and amputation, underscoring the critical importance of achieving rapid and complete wound closure. Sun et al. [1] projected that global diabetes prevalence will reach 783 million by 2045, highlighting the urgency of identifying effective and accessible wound care strategies.

The pathobiological basis of impaired healing in diabetes was described by Brownlee [5] as a consequence of chronic oxidative stress, mitochondrial dysfunction, and disrupted intracellular signaling. Falanga [4] further characterized the diabetic wound microenvironment as one marked by a prolonged inflammatory phase, deficient angiogenesis, and reduced growth factor bioavailability, collectively preventing orderly progression through the healing cascade. Dumville et al. [6], in a Cochrane systematic review, confirmed that topical antimicrobial agents address wound infection but do not correct this underlying biological healing deficit, reinforcing the rationale for growth-factor-directed therapies such as topical insulin.

The significantly greater reductions in ulcer size and depth observed in the insulin group at Day 6 and Day 12 ($p < 0.001$) (Table 1, Table 2) are consistent with established molecular mechanisms. Lima et al. [8] demonstrated in a double-blind placebo-controlled clinical trial that topical insulin accelerates wound healing by enhancing AKT and ERK signaling pathways, promoting keratinocyte and fibroblast proliferation, and attenuating pro-inflammatory cytokine activity. Chen et al. [7] similarly reported that topical insulin modulates the wound inflammatory response, facilitating earlier transition from the inflammatory to the proliferative healing phase. The accelerated granulation tissue formation in the insulin group at Day 6 — 85.7% versus 71.4% in the saline group ($p < 0.05$) — directly corroborates these mechanistic findings (Table 3).

The present results are consistent with prior clinical evidence. Rezvani et al. [9] reported significantly faster wound healing with topical insulin in a randomized double-blind placebo-controlled trial. Stephen et al. [10] confirmed comparable benefits in a randomized controlled trial evaluating topical insulin versus normal saline in pressure ulcer management, lending cross-wound-type validity to the current findings. Geetha et al. [12] reported that topical insulin significantly reduced healing time in chronic wounds compared to conventional dressings. Bhansali et al. [13] observed accelerated epithelialization and granulation in diabetic foot ulcers treated with topical insulin, with no systemic hypoglycemic adverse effects, affirming its safety profile for clinical use.

The convergence of both groups to 100% healthy granulation tissue by Day 12 suggests that topical insulin primarily accelerates early-phase repair rather than altering the ultimate healing potential (Table 3, Table 4). As Armstrong et al. [2] and Falanga [4] have both noted, earlier granulation reduces wound exposure time, infection risk, and the likelihood of progression to osteomyelitis or limb-threatening complications. This study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki as adopted by the World Medical Association [11].
Limitations of this study include the short 12-day follow-up period, single-center design, and modest sample size. Larger multi-center randomized controlled trials with longer observation periods, standardized wound grading using the Wagner or University of Texas classification systems, and biochemical wound assessments are warranted to confirm these findings and to establish the optimal insulin concentration, vehicle formulation, and frequency of application.

Limitations

This study was conducted at a single center with a relatively small sample size (n=70), which may limit the generalizability of the findings. The follow-up period was short (12 days), preventing assessment of long-term healing outcomes and recurrence rates. Only patients with Wagner grade I and II diabetic foot ulcers were included; therefore, the results may not be applicable to advanced ulcers. Additionally, blinding was not performed, which may have introduced observer bias.

CONCLUSIONS

Topical insulin dressing was significantly more effective than conventional normal saline dressing in the management of diabetic foot ulcers. Patients treated with topical insulin demonstrated greater reductions in ulcer size and depth, earlier granulation tissue formation, and superior overall healing outcomes. Given its safety, low cost, and ease of application, topical insulin dressing represents an effective and practical treatment option for diabetic foot ulcers, particularly in resource-limited settings. Further large-scale studies with longer follow-up are warranted to validate these findings.

Human Subjects
Consent was obtained or waived by all participants in this study. The study was approved by the Institutional Ethics Committee of Teerthanker Mahaveer Medical College and Research Centre, Moradabad, Uttar Pradesh, India.

Conflicts of Interest
The authors have declared that no competing interests exist.

Financial Relationships
All authors have declared that they have no financial relationships, either currently or within the previous three years, with any organizations that might have an interest in the submitted work.

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