Section: General Surgery

Original Research Article

A RANDOMIZED CONTROLLED STUDY TO DETERMINE THE EFFECT OF TOPICAL INSULIN ON DIABETIC WOUND HEALING

P.Sakthivadivan Palanivelu[1], Yuvarani Prabakaran[1], A.S.Yaser Arafat[2]

[1]Assistant Professor, Department of General Surgery, KAPV Government Medical College, Trichy, Tamil Nadu, India
[2]Senior Resident, Department of General Surgery, KAPV Government Medical College, Trichy, Tamil Nadu, India

Received : 26/04/2026
Received in revised form : 05/06/2026
Accepted : 19/06/2026

Corresponding Author:
Dr. P.Sakthivadivan Palanivelu,
Professor, Department of General Surgery, KAPV Government Medical College, Trichy, Tamil Nadu, India.
Email: mivniel@outlook.com

DOI: 10.70034/ijmedph.2026.3.5

Source of Support: Nil,
Conflict of Interest: None declared

Int J Med Pub Health
2026; 16 (3); 24-30

ABSTRACT

Background: One dangerous consequence of diabetes mellitus is diabetic foot ulcers (DFUs), which can lead to prolonged hospital admissions, infections, and even amputations. Topical insulin has emerged as a viable treatment for enhancing wound healing due to its angiogenic and proliferative properties. The aim is to evaluate the effectiveness of topical insulin dressings against conventional normal saline dressings in promoting wound healing in people with persistent diabetic ulcers.
Materials and Methods: Fifty diabetic patients with chronic foot ulcers were enrolled at the Department of Surgery, Mahatma Gandhi Memorial Government Hospital, Trichy. Patients were randomly assigned to two equal groups: Group A received topical insulin dressings, while Group B received conventional normal saline dressings. Participants were followed for 21 days, with assessments on wound size reduction, granulation tissue formation, slough disappearance, and microbiological findings.
Results: Significant improvements were observed in Group A in terms of earlier granulation tissue appearance, faster slough disappearance, and greater reduction in wound area by Day 21 ($p < 0.05$). The pus culture findings also showed a higher rate of sterile cultures in the insulin group, suggesting improved wound cleanliness.
Conclusion: For diabetic foot ulcers, topical insulin dressing is a safe and efficient way to promote wound healing. It is advised that more multicentric studies be conducted to confirm these results.
Keywords: Topical insulin, Diabetic foot ulcer, Wound healing, Granulation tissue, Normal saline dressing, Chronic wounds.

INTRODUCTION

Diabetes mellitus (DM) is one of the most prevalent non-communicable diseases worldwide and is associated with substantial morbidity and mortality. The global burden of diabetes continues to rise, with an estimated 537 million adults living with the disease in 2021, a number projected to increase significantly in the coming decades.[1] Chronic hyperglycemia in diabetes leads to microvascular and macrovascular complications, including peripheral neuropathy and peripheral arterial disease, which predispose patients to diabetic foot ulcers (DFUs).[2]
The World Health Organization defines the diabetic foot as infection, ulceration, or destruction of deep tissues of the foot associated with neurological abnormalities and varying degrees of peripheral vascular disease in the lower limbs.[3] Diabetic foot ulcers affect approximately 15–25% of patients with diabetes during their lifetime and represent one of the most common causes of hospitalization among diabetic individuals.[4] The development of DFUs is multifactorial, involving peripheral neuropathy, ischemia, foot deformities, repetitive trauma, and impaired wound healing.[5] These ulcers significantly increase the risk of infection, lower extremity amputation, reduced quality of life, and healthcare expenditure.[6]
Early identification and appropriate management of diabetic foot ulcers are essential for limb salvage and prevention of complications. Several

classification systems, including the Wagner-Meggitt classification, University of Texas classification, PEDIS classification, and Diabetic Ulcer Severity Score (DUSS), have been developed to assess ulcer severity and predict outcomes.[7,8] More recently, the M.A.I.D. score, based on four simple clinical parameters—presence of multiple ulcers (M), ulcer area (A), palpable pedal pulses indicating ischemia (I), and ulcer duration (D)—has been proposed as an easy-to-use clinical tool for predicting wound healing and treatment outcomes.[9]

Wound healing is a complex biological process involving hemostasis, inflammation, proliferation, angiogenesis, extracellular matrix formation, and tissue remodelling.[10] In patients with diabetes, these processes are impaired due to reduced growth factor activity, endothelial dysfunction, impaired leukocyte function, and altered collagen synthesis, resulting in delayed wound healing.[11] Therefore, the search for effective adjunctive therapies to accelerate healing remains a major focus in diabetic wound management.

Insulin, traditionally used for glycemic control, has demonstrated potential local effects on wound repair. Experimental studies have shown that insulin promotes keratinocyte migration, fibroblast proliferation, collagen synthesis, angiogenesis, and granulation tissue formation, all of which are crucial components of wound healing.[12,13] Topical insulin administration has emerged as a promising therapeutic strategy that directly targets the wound microenvironment without causing significant systemic hypoglycaemia.[14]

Several clinical studies have reported improved wound healing rates, enhanced granulation tissue formation, and reduced ulcer size following topical insulin application in chronic diabetic wounds.[15,16] Compared with conventional dressings such as normal saline, topical insulin may accelerate epithelialization and tissue regeneration through activation of insulin receptors and downstream cellular signaling pathways involved in repair processes.[17]

Normal saline dressings remain a widely accepted standard wound care modality because they maintain a moist wound environment, facilitate autolytic debridement, and are non-toxic to fibroblasts and keratinocytes.[18] However, despite their widespread use, healing outcomes remain suboptimal in many diabetic patients, highlighting the need for effective adjunctive treatments.

Given the increasing burden of diabetic foot ulcers and the need for cost-effective interventions that improve wound healing, topical insulin has attracted growing interest as a therapeutic option. This study was therefore undertaken to evaluate the effectiveness and safety of topical insulin in promoting wound healing among diabetic patients. The findings of this study may provide evidence regarding the utility of topical insulin as an adjunctive treatment in diabetic wound management.

MATERIALS AND METHODS

This prospective randomized controlled study was conducted in the Department of General Surgery, Mahatma Gandhi Memorial Government Hospital (MGMGH), Tiruchirappalli, affiliated with K.A.P. Viswanatham Government Medical College, over a period of 12 months from December 2023 to November 2024. The study aimed to evaluate the effectiveness of topical insulin in promoting wound healing among patients with diabetic foot ulcers. A total of 50 patients were enrolled and randomly allocated into two equal groups comprising 25 patients each. Patients admitted with diabetic foot ulcers of more than one month's duration, aged between 18 and 70 years, of either sex, and classified as Wagner Grade 1 or Grade 2 ulcers were included in the study. Patients younger than 18 years or older than 70 years, pregnant women, individuals with immunocompromised states such as HIV, hepatitis B surface antigen (HBsAg) positivity, or hepatitis C virus (HCV) infection, patients with significant systemic illnesses including cardiac, hepatic, or renal failure, those with malignancy, and patients with Wagner Grade 3 or higher ulcers were excluded.

Institutional Ethics Committee approval was obtained prior to commencement of the study, and written informed consent was obtained from all participants. Following enrolment, detailed clinical history, physical examination findings, and baseline investigations including fasting blood sugar (FBS), postprandial blood sugar (PPBS), random blood sugar (RBS), HIV and HBsAg screening, radiographs of the affected limb, and pus culture and sensitivity testing were recorded. Pus cultures were repeated every five days during the study period.

Participants were randomly assigned to either the study group (Group A) or the control group (Group B). Patients in Group A received topical insulin dressings, whereas those in Group B received conventional normal saline dressings. For topical insulin therapy, 10 units (0.1 mL) of regular insulin were mixed with 1 mL of 0.9% normal saline for every 10 cm² of wound surface area. The prepared solution was applied topically to the wound using an insulin syringe twice daily. The wound was allowed to dry for approximately 30 minutes before being covered with sterile gauze. Patients in the control group received normal saline dressings using a similar dressing protocol twice daily. Following wound debridement, any bleeding was controlled using sterile gauze packing. Strict glycemic control was maintained in all patients throughout the study period. Wound assessment was performed on Day 1 (baseline) and subsequently on Days 3, 7, 14, and 21. Parameters evaluated included wound surface area, granulation tissue formation, slough reduction, and overall wound healing progress. Granulation tissue and slough were graded using standardized scoring systems ranging from 0 to 3. Clinical findings, laboratory parameters, wound measurements, radiological findings, and microbiological reports were systematically recorded in structured case record forms. The collected data were entered into Microsoft Excel and analyzed using Statistical Package for the Social Sciences (SPSS) software. Continuous variables were expressed as mean ± standard deviation, while categorical variables were presented as frequencies and percentages. Comparisons between groups were performed using Student's t-test for continuous variables and Chi-square test for categorical variables. A p-value of less than 0.05 was considered statistically significant.

RESULTS

The baseline demographic and clinical characteristics were comparable between the two study groups. The mean age of participants was similar in both groups, with Group A (Topical Insulin) having a mean age of 55.08 ± 8.43 years and Group B (Normal Saline) 59.72 ± 9.42 years. The distributions of gender, onset of ulcer, site of ulcer, X-ray findings, and smoking status did not differ significantly between the groups (all $p > 0.05$). The baseline laboratory parameters, including fasting blood sugar, postprandial blood sugar, urea, and creatinine levels, were comparable between the two groups. Although Group B showed slightly higher mean fasting blood sugar and urea levels than Group A, these differences were not statistically significant ($p > 0.05$). Similarly, postprandial blood sugar and creatinine values were comparable between the groups.

Table 1: Baseline Demographic and Clinical Characteristics of the Study Population

Variable	Group A (Topical Insulin)	Group B (Normal Saline)	Total (N=50)	P value
Age (years), Mean ± SD	55.08 ± 8.43	59.72 ± 9.42	57.40 ± 9.15	-
Gender, n (%)				0.152
Male	12 (48.0)	17 (68.0)	29 (58.0)	
Female	13 (52.0)	8 (32.0)	21 (42.0)	
Onset of Ulcer, n (%)				0.294
Spontaneous	12 (48.0)	16 (64.0)	28 (56.0)	
Traumatic	13 (52.0)	9 (36.0)	22 (44.0)	
Site of Ulcer, n (%)				0.771
Dorsum	9 (36.0)	10 (40.0)	19 (38.0)	
Plantar	16 (64.0)	15 (60.0)	31 (62.0)	
X-ray Findings, n (%)				0.714
Soft tissue swelling	6 (24.0)	8 (32.0)	14 (28.0)	
No significant findings	19 (76.0)	17 (68.0)	36 (72.0)	
Smoking Status, n (%)				0.508
Smoker	20 (80.0)	18 (72.0)	38 (76.0)	
Non-smoker	5 (20.0)	7 (28.0)	12 (24.0)	
Baseline Laboratory Parameters (Mean ± SD)				
Fasting Blood Sugar (mg/dL)	143.36 ± 32.02	159.44 ± 28.79	151.40 ± 30.41	0.069
Postprandial Blood Sugar (mg/dL)	212.56 ± 52.46	220.16 ± 48.68	216.36 ± 50.57	0.589
Urea (mg/dL)	25.44 ± 6.89	29.44 ± 7.56	27.44 ± 7.23	0.059
Creatinine (mg/dL)	0.91 ± 0.17	0.89 ± 0.15	0.90 ± 0.16	0.661

The pus culture findings among the study participants revealed a range of microbial growth patterns. In the Normal Saline group, the most commonly isolated organism was Staphylococcus aureus in 10 patients (40%), followed by E. coli in 5 patients (20%), mixed flora in 4 patients (16%), Klebsiella in 2 patients (8%), Pseudomonas in 1 patient (4%), and no growth in 3 patients (12%). In the Topical Insulin group, Staphylococcus aureus was isolated in 4 patients (16%), E. coli in 5 patients (20%), Klebsiella in 3 patients (12%), Pseudomonas in 3 patients (12%), mixed flora in 1 patient (4%), and no growth was observed in 9 patients (36%). Overall, among the 50 patients, Staphylococcus aureus was the most frequently identified organism (28%), followed by E. coli (20%), no growth (24%), and smaller proportions of other organisms.

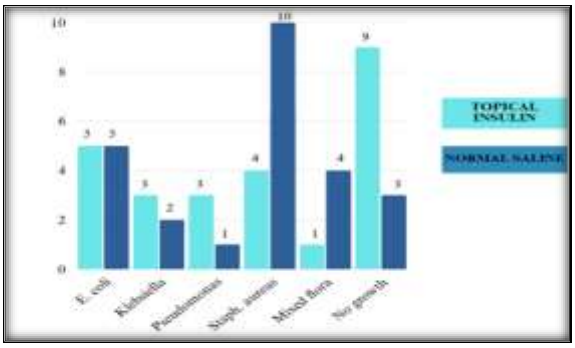

Figure 1: Pus culture finding

Table 2: Disappearance of slough

Day	Slough Disappearance Code	Group		Total	P Value
		A Topical Insulin	B Normal Saline		
Day - 1	2	8	6	14	0.529
	3	17	19	36	
Day - 3	1	4	2	6	0.304

	2	18	16	34	
	3	3	7	10	
Day - 7	0	2	0	2	0.061
	1	15	8	23	
	2	7	15	22	
	3	1	2	3	
Day - 14	0	15	2	17	<0.001
	1	9	12	21	
	2	1	11	12	
Day - 21	0	24	11	35	<0.001
	1	0	14	14	
	2	1	0	1	

The disappearance of slough in the wound bed was monitored at multiple time intervals to compare the wound-cleansing effect of the two treatment modalities. On Day 1, most patients in both groups exhibited a slough score of 3, indicating heavy slough presence17 patients in Group A (Topical Insulin) and 19 in Group B (Normal Saline), with no significant difference (*p* = 0.529). By Day 3, a shift toward lower slough scores were observed, though not statistically significant (*p* = 0.304). Group A had more patients progressing to scores 1 and 2 compared to Group B. By Day 7, improvements were more evident. In Group A, 15 patients had reduced slough to a score of 1, and 2 patients had complete disappearance (score 0), while Group B still had a higher proportion of patients at scores 2 and 3. Although the difference was not yet statistically significant (*p* = 0.061), the trend favoured the Topical Insulin group. By Day 14, the difference became statistically significant ($p < 0.001$), with 15 patients in Group A achieving a score of 0 (no slough), compared to only 2 patients in Group B. The majority of patients in Group B remained at higher slough scores. On Day 21, 24 out of 25 patients in Group A had complete disappearance of slough, compared to just 11 patients in Group B, further reinforcing a significant difference in slough clearance between the two groups ($p < 0.001$). These results indicate a markedly faster and more effective reduction in slough in the Topical Insulin group, suggesting superior wound bed preparation and potential for faster healing.

Table 3: Appearance of Granulation Tissue

Day	**Granulation Tissue Code**	**Group**		**Total**	**P Value**
		A Topical Insulin	**B Normal Saline**		
Day - 1	0	19	22	41	0.269
	1	6	3	9	
Day - 3	0	10	17	27	0.060
	1	12	8	20	
	2	3	0	3	
Day - 7	0	0	5	5	0.043
	1	16	14	30	
	2	6	6	12	
	3	3	0	3	
Day - 14	1	4	13	17	0.013
	2	13	10	23	
	3	8	2	10	
Day - 21	1	0	2	2	0.002
	2	9	19	28	
	3	16	4	20	

The appearance and progression of granulation tissue in the wound bed were assessed at multiple time points during the study to evaluate the healing response in both groups. On Day 1, the majority of patients in both groups showed no granulation tissue, with 19 patients in Group A (Topical Insulin) and 22 patients in Group B (Normal Saline) scoring 0. The difference was not statistically significant (p = 0.269). By Day 3, early signs of granulation began to appear, with 12 patients in Group A and 8 in Group B showing a score of 1, while 3 patients in Group A showed a score of 2; the difference approached significance (p = 0.060). On Day 7, granulation had improved notably in Group A, where 16 patients scored 1, 6 scored 2, and 3 had developed healthy granulation tissue (score 3), compared to Group B, where 14 patients scored 1, 6 scored 2, and none reached score 3. This difference was statistically significant (p = 0.043). By Day 14, further improvement was seen, with 8 patients in Group A achieving a score of 3 compared to only 2 in Group B. Group A also had a higher number of patients scoring 2 (13 vs. 10), and the difference in granulation status was statistically significant (p = 0.013). On Day 21, 16 patients in Group A had well-formed, healthy granulation tissue (score 3) compared to only 4 in Group B, and 9 patients in Group A scored 2 versus 19 in Group B. This significant difference in granulation tissue formation between the two groups by Day 21 (p = 0.002) suggests a superior wound healing response in the Topical Insulin group.

Granulation Tissue Score refers to the quality and amount of healthy granulation tissue in the wound bed and graded as follows

0 – No granulation tissue visible (wound base may be necrotic or covered in slough)

1 – Minimal or pale granulation tissue present

2 – Moderate granulation tissue; pink/red but not fully healthy

3 – Healthy, red, well-vascularized granulation tissue filling the wound bed.

Table 4: Area of the Wound

Time	Group	Mean	Mean Difference	t value	p value#
Day - 1	A	56.0	0.26	0.124	0.902
	B	56.3			
Day - 3	A	53.6	1.54	0.737	0.465
	B	55.1			
Day - 7	A	50.2	3.73	1.825	0.074
	B	53.9			
Day - 14	A	45.1	3.66	1.784	0.081
	B	48.7			
Day - 21	A	40.3	4.81	2.320	0.025
	B	45.1			

The progression of wound healing was assessed by measuring the mean area of the wound at different time points across both groups. On Day 1, the mean wound area in Group A (Topical Insulin) was 56.0 cm², while in Group B (Normal Saline) it was 56.3 cm², with a negligible mean difference of 0.26 cm² ($p = 0.902$), indicating no significant difference at baseline. By Day 3, the mean wound area was 53.6 cm² in Group A and 55.1 cm² in Group B, with a mean difference of 1.54 cm² ($p = 0.465$). On Day 7, the wound area further reduced to 50.2 cm² in Group A and 53.9 cm² in Group B, showing a mean difference of 3.73 cm²; this approached statistical significance ($p = 0.074$). By Day 14, the difference remained similar, with mean wound areas of 45.1 cm² in Group A and 48.7 cm² in Group B (mean difference = 3.66 cm², $p = 0.081$). However, by Day 21, the difference became statistically significant, with Group A showing a greater reduction in wound area (mean = 40.3 cm²) compared to Group B (mean = 45.1 cm²), yielding a mean difference of 4.81 cm² and a p-value of 0.025. These findings suggest that while both groups experienced progressive wound healing, the use of topical insulin was associated with a significantly greater reduction in wound area by the third week.

DISCUSSION

Diabetic foot ulcers (DFUs) continue to represent one of the most difficult complications of diabetes mellitus, due to their chronicity, delayed healing, increased risk of infection, and potential for lower limb amputation. The pathogenesis of diabetic wounds involves multiple factors, including peripheral neuropathy, vascular insufficiency, impaired immune response, and defective cellular mechanisms involved in tissue repair. In the present study, topical insulin dressing was evaluated as an adjunctive therapy for diabetic foot ulcer healing and was compared with conventional normal saline dressing. The results showed that topical insulin significantly improved wound healing, as evidenced by faster slough clearance, earlier granulation tissue formation, and greater reduction in wound area compared with normal saline dressings.

The demographic and baseline characteristics were similar between the two groups, indicating successful randomization and minimal confounding factors. The mean age of the patients in the present study was 57.40 ± 9.15 years and there was no significant difference between the topical insulin and normal saline groups. Likewise, gender distribution, ulcer onset, ulcer location, radiological findings, smoking status, and baseline biochemical parameters including blood glucose, renal function markers, and creatinine were similar between the two groups. These findings are important as factors such as age, glycemic control, vascular status, and smoking are known to influence diabetic wound healing outcomes.[2,5]

The present study demonstrated a significant effect of topical insulin on slough removal. While no significant difference was observed between the groups in the early assessment periods (Day 1, Day 3, and Day 7), a significant difference was observed at Day 14 and Day 21 ($p < 0.001$). Complete disappearance of slough was achieved in 24 of 25 patients (96%) in the topical insulin group by Day 21 as opposed to only 11 of 25 patients (44%) in the normal saline dressing group. This accelerated wound bed preparation suggests that topical insulin may promote the transition from the inflammatory phase to the proliferative phase of wound healing.

Previous experimental studies have described the positive effects of insulin on wound repair. Falanga reported that diabetic wounds have a defective growth factor activity and delayed progression through the normal phases of healing, which leads to chronic inflammation and poor tissue regeneration.[11] Insulin has been shown to reverse some of these abnormalities by stimulating cellular migration, proliferation, and extracellular matrix production. Lima et al. demonstrated that topical insulin accelerated wound closure in diabetic animal models by enhancing keratinocyte migration and improving tissue repair mechanisms.[12] The better slough clearance observed in our study supports these findings and suggests that topical insulin provides better wound bed preparation.

Granulation tissue formation is an important sign of progression from inflammatory phase to proliferative phase of wound healing. Both groups showed progressive improvement; however, patients receiving topical insulin developed significantly better granulation tissue formation from Day 7 onwards. By Day 21, healthy Grade 3 granulation tissue was observed in 16 patients (64%) in topical insulin group compared with only 4 patients (16%) in normal saline group ($p = 0.002$).

These findings are in agreement with the observations of Pierre et al. who demonstrated that insulin stimulates fibroblast activity, collagen synthesis and extracellular matrix deposition, consequently facilitating granulation tissue formation.[13] Insulin-induced activation of intracellular signaling pathways such as the PI3K/Akt pathway contributes to angiogenesis and cellular proliferation which are crucial for effective wound healing.[14] Hence, the enhanced granulation response seen in the present study might be attributable to the direct local effect of insulin on fibroblasts, endothelial cells and keratinocytes.

Rezvani et al. evaluated the use of topical insulin in diabetic foot ulcers and reported better wound healing outcomes with this approach compared to conventional treatment, suggesting that insulin may have a role as an adjunctive therapy in chronic diabetic wounds.[15] In a similar vein, Stephen-Haynes and Callaghan examined the existing evidence for topical insulin and suggested that it may enhance epithelialization and shorten healing time in chronic wounds, but emphasized the need for further clinical trials.[16] The findings from our study provide further clinical evidence to support the wound-healing advantages of topical insulin.

Reduction in wound area is an important objective measure of wound healing. In the present study, both groups showed progressive reduction in wound size; however, the topical insulin group showed a significantly greater reduction by Day 21. The mean wound area decreased from 56.0 cm2 at baseline to 40.3 cm2 in the topical insulin group, compared with a reduction from 56.3 cm2 to 45.1 cm2 in the normal saline group ($p = 0.025$). Although differences at earlier time points did not attain statistical significance, the trend was consistently in favor of topical insulin therapy.

The gradual appearance of significant differences after 2 weeks might be explained by the biological mechanism of insulin action. Wound healing is a sequential process, and the effects of increased cellular proliferation, angiogenesis and formation of extracellular matrix may only be clinically noticeable after a certain time period. Chen et al. reported that topical insulin has potential benefits in the management of chronic wounds by promoting local cellular responses without significant systemic effects.[14] Our results are in line with these observations, showing progressive improvement with sustained application of topical insulin.

Normal saline dressing is a widely accepted standard approach for wound care due to its safety, low cost and ability to maintain a moist wound environment. However, in diabetic wounds, the intrinsic mechanisms of healing are compromised and conventional dressings alone may not be enough to achieve optimal results. Ousey and McIntosh stressed the importance of maintaining an optimal wound environment for healing, but conceded that other therapeutic strategies may be necessary in complex chronic wounds.[18] In our study, normal saline dressing led to gradual improvement, but topical insulin produced superior results for wound bed preparation and tissue regeneration.

The present study findings are also supported by the more general understanding of the pathophysiology of diabetic wound described by Armstrong et al. and Zhang et al, who highlighted the importance of effective interventions to reduce the burden of diabetic foot complications and prevent amputations.[4,6] By promoting faster healing, topical insulin may reduce the duration of treatment, hospitalizations, and healthcare costs associated with chronic diabetic ulcers.

CONCLUSION

The present study demonstrated that topical insulin dressing was a safe and effective adjuvant therapy for diabetic foot ulcers and resulted in significantly greater slough clearance, accelerated granulation tissue formation and greater wound contraction when compared with conventional normal saline dressings at the end of the 21-day follow-up period. These findings support the potential use of topical insulin as an inexpensive and easily applicable therapy in diabetic wound management.

REFERENCES

1. International Diabetes Federation. IDF Diabetes Atlas. 10th ed. Brussels: International Diabetes Federation; 2021.
2. Boulton AJM, Vileikyte L, Ragnarson-Tennvall G, Apelqvist J. The global burden of diabetic foot disease. Lancet. 2005;366(9498):1719-24.
3. World Health Organization. Definition and diagnosis of diabetes mellitus and intermediate hyperglycemia. Geneva: WHO; 2006.
4. Armstrong DG, Boulton AJM, Bus SA. Diabetic foot ulcers and their recurrence. N Engl J Med. 2017;376(24):2367-75.
5. Everett E, Mathioudakis N. Update on management of diabetic foot ulcers. Ann N Y Acad Sci. 2018;1411(1):153-65.
6. Zhang P, Lu J, Jing Y, Tang S, Zhu D, Bi Y. Global epidemiology of diabetic foot ulceration. Ann Med. 2017;49(2):106-16.
7. Wagner FW Jr. The diabetic foot. Orthopedics. 1987;10(1):163-72.
8. Beckert S, Witte M, Wicke C, Königsrainer A, Coerper S. A new wound-based severity score for diabetic foot ulcers. Diabetes Care. 2006;29(5):988-92.
9. Ince P, Abbas ZG, Lutale JK, Basit A, Ali SM, Chohan F, et al. Use of the M.A.I.D. score in diabetic foot ulcer assessment. Diabet Med. 2008;25(1):77-82.

10. Guo S, DiPietro LA. Factors affecting wound healing. J Dent Res. 2010;89(3):219-29.
11. Falanga V. Wound healing and its impairment in the diabetic foot. Lancet. 2005;366(9498):1736-43.
12. Lima MH, Caricilli AM, de Abreu LL, Araújo EP, Pelegrinelli FF, Thirone AC, et al. Topical insulin accelerates wound healing in diabetes. Diabetes Care. 2012;35(2):422-34.
13. Pierre EJ, Barrow RE, Hawkins HK, Nguyen TT, Sakurai Y, Desai M, et al. Effects of insulin on wound healing. J Trauma. 1998;44(2):342-5.
14. Chen X, Liu Y, Zhang X. Topical insulin for chronic wound healing: a systematic review. Int Wound J. 2020;17(5):1268-77.
15. Rezvani O, Shabbak E, Aslani A, Bidar R, Jafari M, Safarnezhad S. Topical insulin improves healing in diabetic foot ulcers. Wounds. 2009;21(10):271-5.
16. Stephen-Haynes J, Callaghan R. Topical insulin and wound healing: evidence review. Br J Nurs. 2017;26(20):S30-S37.
17. Wilson R, Jones D, McBride C. Insulin-mediated enhancement of epithelialization in chronic wounds. Int Wound J. 2018;15(5):748-55.
18. Ousey K, McIntosh C. Understanding wound bed preparation and moist wound healing. Br J Community Nurs. 2010;15(Suppl 3):S22-S28.