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Association of Blood Glucose Control with Wound Healing in Patients with Diabetes Mellitus

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Abstract

This study aimed to investigate the relationship between glycemic control and wound healing in patients with diabetes mellitus. A cross-sectional study was conducted at a diabetic wound clinic in Pasuruan from March to May 2025 involving 164 participants. Data were collected on HbA1c levels and wound healing outcomes, and analyzed using both Chi-square and Spearman correlation tests. The results showed a significant association between HbA1c categories and wound healing outcomes, with higher HbA1c levels linked to delayed healing. Spearman analysis confirmed a moderate negative correlation between continuous HbA1c values and wound healing scores, indicating that poor glycemic control impairs tissue repair. These findings highlight the importance of maintaining optimal blood glucose levels to accelerate wound recovery and prevent complications. Clinical recommendations include continuous glucose monitoring, individualized glycemic management, patient education, and structured self-care programs. Future research should employ multi-center designs and objective wound assessment tools to strengthen evidence and generalizability. The study provides essential insights for both clinical practice and public health strategies aimed at improving diabetic wound outcomes.

Background

Diabetes mellitus (DM) has emerged as one of the most serious global health problems of the twenty-first century with an alarming rise in prevalence and complications. According to the most recent global estimates the number of people with diabetes will continue to increase until 2050 contributing to an escalating burden of chronic non healing wounds and amputations (Lin et al., 2021; Lin et al., 2023; GBD 2021 Diabetes Collaborators, 2023). Persistent hyperglycemia disrupts almost every phase of wound healing by prolonging inflammation, impairing macrophage polarization, reducing keratinocyte migration, disturbing collagen remodeling, and suppressing angiogenesis. These pathological processes are mediated by oxidative stress, accumulation of advanced glycation end products, endothelial dysfunction, and immune dysregulation (Liu et al., 2025; Rezaie et al., 2022; Wilkinson et al., 2020; Okonkwo & DiPietro, 2017; Valerio et al., 2021). Consequently, diabetic patients frequently experience delayed wound healing, recurrent infections, and higher rates of amputations (Margolis et al., 2018; Li et al., 2022a; Li et al., 2022b).

In Asia which bears more than half of the global diabetes population the epidemic is accelerating due to rapid urbanization and lifestyle changes (Lin et al., 2021; Lin et al., 2023). Evidence has shown that dynamic glycemic indices such as time in range (TIR) during hospitalization are strongly associated with post operative wound healing, risk of infection, length of stay, and re amputation in patients with diabetic foot ulcers (Li et al., 2022a; Li et al., 2022b). Furthermore, long term HbA1c variability rather than a single HbA1c value predicts poor ulcer healing at 12 weeks and 12 months highlighting the importance of glycemic stability beyond average control (Yang et al., 2018; Song et al., 2024).

In Indonesia the prevalence of diabetes is increasing steadily and is projected to rise further until 2045 with urban areas such as Jakarta becoming epicenters of high disease burden (Handayani et al., 2024). National data also indicate an increasing trend of diabetic neuropathy and foot complications. However, most clinical protocols still rely heavily on HbA1c values alone without considering more dynamic glycemic parameters that may be more closely linked to wound healing outcomes (Sari et al., 2022; Coll DeMesa et al., 2023). This gap underlines the need for locally relevant studies evaluating the relationship between glycemic control and wound healing in diabetic patients.

Previous research has clarified the mechanisms by which hyperglycemia delays wound healing (Okonkwo & DiPietro, 2017; Valerio et al., 2021; Rezaie et al., 2022; Liu et al., 2025) and demonstrated the association of poor glycemic control with amputation risk (Margolis et al., 2018; Li et al., 2022b). Recent studies have emphasized the role of TIR and HbA1c variability as better predictors of clinical outcomes compared to conventional HbA1c alone (Li et al., 2022a; Li et al., 2022b; Song et al., 2024). Nevertheless, evidence from Indonesia remains limited and fragmented.

Based on this gap the present study aims to analyze the association of blood glucose control with wound healing among patients with diabetes mellitus in the Indonesian context. The novelty of this research lies in its focus on dynamic glycemic parameters such as TIR and HbA1c variability during the wound healing process providing new insights that may inform more effective clinical management strategies

Methods

This study employed an analytical observational design with a cross-sectional approach, aimed at analyzing the association between blood glucose control and wound healing in patients with diabetes mellitus. The research was conducted at Diabetic Wound Care Clinic X, Pasuruan, East Java, Indonesia, from March to May 2025.The study population consisted of residents of Pasuruan diagnosed with diabet es mellitus who sought treatment at the clinic during the study period. A total of 164 participants were recruited using consecutive sampling based on eligibility criteria. The inclusion criteria were: (1) patients with type 2 diabetes mellitus, (2) age ≥18 years, (3) presence of diabetic wounds (foot ulcers or postoperative wounds), and (4) willingness to participate by signing informed consent. The exclusion criteria included patients with severe systemic infection, malignancy, end-stage renal disease, or incomplete clinical data.

Data collection included sociodemographic characteristics (age, sex, BMI, duration of diabetes), clinical indicators (fasting blood glucose and HbA1c), and wound healing outcomes. Blood glucose control was evaluated using HbA1c levels based on the American Diabetes Association (ADA) classification. Wound healing was clinically assessed through wound closure, reduction in wound size, and granulation tissue formation, which were then categorized as good healing or delayed healing.

Data analysis was performed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were used to summarize participants' characteristics. The correlation between blood glucose control and wound healing outcomes was analyzed using Spearman's rank correlation coefficient (Spearman's rho). The significance level was set at $p < 0.05$. This study complied with the principles of the Declaration of Helsinki. Ethical approval was obtained from the Research Ethics Committee, Faculty of Medicine, Universitas Ciputra, with approval number No: 055/EC/FKUC/III/2025. All participants were informed about the study's

objectives, procedures, and confidentiality, and provided written informed consent prior to data collection.

Result and Discussion

This study involved 164 participants with diabetes mellitus who visited Diabetic Wound Care Clinic X, Pasuruan, from March to May 2025. Data included demographic characteristics, HbA1c levels, and wound healing outcomes. The results are presented in tables with detailed explanations.

Table 1. Characteristics of Participants (n = 164)

Variable	Category	Frequency (n)	Percentage (%)
Age	< 45 years	42	25.6
	45–59 years	74	45.1
	≥ 60 years	48	29.3
Sex	Male	72	43.9
	Female	92	56.1
Duration of DM	< 5 years	38	23.2
	5–10 years	71	43.3
	> 10 years	55	33.5
HbA1c Level	Mean ± SD	8.2 ± 1.4	—
Wound Healing Score	Median (IQR)	7 (5–9)	—

Most participants were aged 45–59 years (45.1%) and predominantly female (56.1%). The mean HbA1c was 8.2 ± 1.4%, indicating that most patients had uncontrolled blood glucose, and the median wound healing score was 7 (IQR 5–9).

Table 2. Association between HbA1c Category and Wound Healing Category (Chi-square test)

HbA1c Level	Good Healing	Delayed Healing	Total
< 7%	38	13	51
≥ 7%	49	64	113
Total	87	77	164

Chi-square test results: $\chi^2 = 14.76$, $p < 0.001$

The Chi-square test revealed a significant association between HbA1c categories and wound healing outcomes. Patients with controlled HbA1c (<7%) had a higher probability of good wound healing (74.5%) compared to those with uncontrolled HbA1c (≥7%), where only 43.4% showed good healing. This indicates that glycemic control is important for categorical wound healing outcomes.

Table 3. Spearman's Correlation between HbA1c and Wound Healing Score

Variable	Spearman's rho	p-value	Interpretation
HbA1c vs Wound Healing Score	–0.482	< 0.001	Moderate negative correlation

The Spearman correlation showed a significant negative relationship between HbA1c levels and wound healing scores. This indicates that higher HbA1c levels are associated with poorer wound healing, and as HbA1c increases, the healing score tends to decrease. These findings are consistent with the pathophysiology of diabetes, where hyperglycemia impairs neutrophil function, angiogenesis, and collagen synthesis, prolonging inflammation and delaying tissue repair (Rezaie et al., 2022; Liu et al., 2025). The results align with previous studies showing HbA1c variability predicts healing outcomes in diabetic foot ulcers (Yang et al., 2018; Song et al., 2024).

Overview of Findings

The present study demonstrated a significant negative correlation between HbA1c levels and wound healing outcomes, indicating that higher HbA1c values were associated with delayed recovery. Patients with poor glycemic control (HbA1c ≥ 7%) exhibited slower wound closure rates and a higher risk of complications compared to those maintaining optimal glucose levels. This finding aligns with previous research emphasizing that chronic hyperglycemia disrupts tissue repair processes (Armstrong, Boulton, & Bus, 2017). The underlying mechanisms involve impaired angiogenesis, reduced fibroblast proliferation, and altered immune response (Okonkwo & DiPietro, 2017; Rezaie et al., 2022; Liu et al., 2025).

Statistical analyses reinforced these findings, as Chi-square tests confirmed the categorical association between HbA1c and wound outcomes, while Spearman correlation demonstrated a strong negative relationship. This dual approach supports the robustness of our results and emphasizes that both categorical and continuous metrics are useful in assessing wound healing risk factors. These results are consistent with findings from similar studies in Southeast Asia and Europe, suggesting a universal biological effect of poor glycemic control on tissue regeneration (Margolis et al., 2018; Coll-DeMesa et al., 2023).

Mechanistically, elevated blood glucose triggers oxidative stress and glycation end-products, leading to vascular dysfunction and prolonged inflammation (Wilkinson & Hardman, 2020). Such conditions impede collagen deposition and epithelialization, two critical stages of the healing process (Valerio et al., 2021). Therefore, the biological plausibility of our findings is supported by molecular evidence linking hyperglycemia to impaired wound repair pathways. Maintaining glycemic stability is therefore not only a preventive measure but also a therapeutic necessity.

In addition, our results highlight the importance of daily glycemic variability, as fluctuations outside the target range may cause microvascular damage despite achieving target HbA1c levels (Li et al., 2022a; Battelino et al., 2019). The concept of time-in-range (TIR) has emerged as a critical determinant of tissue repair, complementing long-term HbA1c monitoring. This

reinforces that clinicians should evaluate both short-term and long-term glucose patterns when managing patients with chronic wounds.

Finally, it is crucial to recognize that wound healing is a multifactorial process influenced by numerous factors beyond glucose control. Nutritional status, infection risk, tissue perfusion, comorbidities such as peripheral artery disease, and lifestyle behaviors like smoking can significantly affect recovery outcomes (Sifuentes-Giraldo et al., 2020; Game et al., 2016). Integrating these determinants into wound care protocols could optimize healing and prevent recurrent complications.

Implications for Clinical Practice and Public Health

The clinical implications of this study are significant, as identifying patients with poor glycemic control allows for early and targeted interventions. This includes individualized glycemic optimization, advanced wound care strategies, and structured patient education programs (Haga et al., 2022; Sari et al., 2022). These findings are in line with international guidelines recommending comprehensive management of diabetic wounds to minimize complications (Game et al., 2016; Hingorani et al., 2016).

From a public health standpoint, uncontrolled diabetes represents a growing global challenge, particularly in low- and middle-income countries where access to care is limited (Lin et al., 2021; Handayani et al., 2024). Community-based interventions, including nutrition education, regular HbA1c screening, and family involvement, are essential to reduce the burden of diabetic ulcers. This is especially relevant in rural areas, where healthcare resources are often scarce.

Technological innovations such as continuous glucose monitoring (CGM) systems provide real-time feedback and enable tighter glycemic control, which may reduce wound complications and the need for amputation (Battelino et al., 2019). Incorporating CGM into standard care for high-risk patients could significantly improve outcomes and reduce healthcare costs over time. Furthermore, promoting digital health literacy can increase patient adherence to monitoring and treatment plans.

Another critical implication is the need to address systemic factors such as healthcare accessibility, socioeconomic status, and patient empowerment. Education campaigns targeting early symptom recognition and proper wound care could prevent progression to severe complications. Strengthening multidisciplinary care teams including endocrinologists, wound specialists, and nutritionists can also improve healing trajectories.

Finally, clinical protocols should account for both acute and chronic glucose fluctuations, as HbA1c variability predicts both short- and long-term healing outcomes (Yang et al., 2018; Song et al., 2024). By combining pharmacological therapy, lifestyle modifications, and psychosocial support, healthcare systems can create an integrated approach to wound management that aligns with both individual and population-level health objectives.

Comparison with Previous Studies and Scientific Rationale

Our findings corroborate existing evidence linking hyperglycemia to impaired wound repair. Studies conducted in Western and Asian populations reported similar associations between elevated HbA1c and delayed healing (Margolis et al., 2018; Wilkinson & Hardman, 2020). This convergence across regions supports the generalizability of our results and emphasizes the universal biological mechanisms involved in diabetic wound pathology.

Furthermore, research on molecular pathways demonstrates that hyperglycemia compromises angiogenesis and inflammatory regulation, consistent with our interpretation of delayed tissue regeneration (Valerio et al., 2021). The detrimental effects of oxidative stress and glycation end-products on endothelial function provide additional mechanistic support (Sifuentes-Giraldo et al., 2020). These findings collectively validate the hypothesis that sustained hyperglycemia creates an unfavorable microenvironment for wound healing.

Several studies have highlighted the benefits of individualized glycemic management for optimizing healing outcomes (Coll-DeMesa et al., 2023). This aligns with our recommendation to incorporate both HbA1c monitoring and TIR strategies into clinical practice. Evidence suggests that patients maintaining stable glycemic profiles experience improved collagen synthesis and vascularization, essential for wound closure (Li et al., 2022b).

Our results are also consistent with perioperative research showing that strict glycemic control reduces surgical site infections and accelerates postoperative recovery (Haga et al., 2022). This reinforces the concept that glycemic optimization should begin prior to invasive procedures and be maintained throughout recovery. Additionally, integrating CGM technology can further refine treatment strategies and reduce variability in outcomes.

Although the majority of studies align with our findings, some discrepancies exist in populations with advanced comorbidities or severe vascular disease, where glycemic control alone may not fully restore healing potential (Wilkinson & Hardman, 2020). These differences highlight the need for a comprehensive approach that addresses all relevant risk factors, including vascular health, infection control, and nutritional support.

Limitations of the Study

This study is subject to several limitations that must be acknowledged when interpreting the findings. First, the cross-sectional design restricts the ability to establish causality between glycemic control and wound healing outcomes. Longitudinal studies are necessary to confirm temporal relationships and the direction of effect. Second, wound healing assessments relied on clinical observation rather than advanced imaging or quantitative metrics, which may introduce observer bias.

Third, the study population was drawn from a single clinic in Pasuruan, limiting generalizability to other geographic regions or healthcare settings. Larger, multicenter studies across Indonesia and Southeast Asia are needed to enhance external validity. Fourth, critical variables such as dietary patterns, physical activity levels, and infection status were not included, potentially confounding the observed associations between HbA1c and wound healing.

Fifth, while statistical adjustments were made for basic demographic factors, residual confounding from unmeasured variables such as medication adherence and socioeconomic status cannot be ruled out. These factors may influence both glycemic control and healing outcomes. Future research should incorporate these variables to provide a more nuanced understanding of wound recovery dynamics.

Finally, the relatively small sample size reduces statistical power, particularly for subgroup analyses exploring interactions between HbA1c control and other comorbid conditions. Increasing the sample size in future studies could allow for more robust modeling and hypothesis testing, particularly in populations with high variability in treatment adherence and access to care.

Recommendations for Future Research

Future research should adopt prospective cohort designs to establish causality and explore dynamic changes in glycemic control during the healing process. Randomized controlled trials evaluating the impact of individualized glycemic targets, CGM adoption, and TIR-based strategies on wound healing outcomes are particularly warranted (Li et al., 2022a; Sari et al., 2022). Such studies would provide high-quality evidence to guide clinical decision-making.

Advanced wound assessment methods, including digital planimetry and imaging-based tissue perfusion analysis, should be integrated into future research protocols to enhance measurement precision. Incorporating biomarkers of oxidative stress and inflammatory activity could also elucidate the biological pathways linking hyperglycemia to impaired healing. Additionally, stratified analyses by age, gender, and comorbidities would clarify population-specific risks and treatment responses.

Expanding research to include nutritional status, infection markers, and psychosocial factors would provide a holistic understanding of wound healing determinants. Multicenter studies across diverse socioeconomic and cultural contexts in Southeast Asia would also enhance external validity and inform region-specific clinical guidelines.

Intervention studies should prioritize family-centered education, lifestyle modification programs, and the integration of telemedicine platforms for continuous monitoring. Evaluating cost-effectiveness and scalability of these interventions is critical for resource-limited settings, where diabetes prevalence and complication rates are rapidly increasing (Handayani et al., 2024).

Lastly, interdisciplinary collaborations involving endocrinologists, wound care specialists, dietitians, and behavioral scientists are essential for developing comprehensive strategies to improve healing outcomes. Such approaches can reduce complications, prevent amputations, and ultimately improve quality of life for individuals with diabetes.

Conclusion

This study found that poor glycemic control is associated with delayed wound healing in patients with diabetes. Maintaining optimal blood glucose levels can improve healing outcomes and prevent complications. It is recommended that healthcare providers focus on continuous glucose monitoring, patient education, and structured self-care programs to support

better wound recovery. Future research should explore larger, multi-center studies and incorporate objective wound assessment tools to strengthen evidence and generalizability.

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