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**RESEARCH ARTICLE**

# Correlation between haemoglobin, leukocytes, HbA1c, and albumin levels with diabetic foot ulcer severity: a cross-sectional study

**Nur Anna Chalimah Sadyah[1,2,3*], Heri-Nugroho HS[4], Agung Putra[5,6], Ignatius Riwanto[7]**

[1]Doctoral Study Program of Medical and Health Science, Universitas Diponegoro, Semarang, Indonesia
[2]Department of Internal Medicine, Sultan Agung Islamic Hospital, Semarang, Indonesia
[3]Department of Internal Medicine, Faculty of Medicine, Universitas Islam Sultan Agung, Semarang, Indonesia
[4]Department of Internal Medicine, Faculty of Medicine, Universitas Diponegoro, Semarang, Indonesia
[5]Stem Cell and Cancer Research, Semarang, Indonesia
[6]Department of Postgraduate Biomedical Science, Faculty of Medicine, Universitas Islam Sultan Agung, Semarang, Indonesia
[7]Department of Surgery, Faculty of Medicine, Universitas Diponegoro, Semarang, Indonesia
[*]Correspondence: Nur Anna Chalimah Sadyah; Address: Jl. Raya Kaligawe KM 4, Kota Semarang, Jawa Tengah 50275; Email address: nuranna@unissula.ac.id

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**ABSTRACT**

Diabetic foot ulcers (DFUs) represent a serious complication of diabetes mellitus, associated with significant morbidity and healthcare costs. The progression of DFUs is influenced by systemic and local factors, including haemoglobin levels, leukocyte count, glycated haemoglobin (HbA1c), and serum albumin. This study aims to explore the relationship between these clinical parameters and the severity of DFUs. We enrolled 62 patients with DFUs and classified ulcer severity as mild, moderate, or severe according to the Wagner classification system. Using Spearman's rank correlation, we found significant associations: lower hemoglobin and albumin levels correlated with more severe ulcers ($\rho$ = -0.34, $p$= 0.0065; $\rho$= -0.41, $p$ = 0.00084, respectively), while higher HbA1c and leukocyte counts were associated with increased ulcer severity ($\rho$ = 0.62, $p$ = 0.000; $\rho$= 0.40, $p$ = 0.0013, respectively). These findings suggest that hematologic and biochemical markers may serve as valuable indicators of DFU progression, potentially guiding clinical decision-making and improving patient outcomes. Further research is needed to elucidate the underlying mechanisms and evaluate targeted interventions for this high-risk population.

## 1. Introduction

Chronic diabetic foot ulcers (DFUs) are a severe complication of diabetes mellitus, contributing significantly to morbidity, mortality, and healthcare costs globally (Akkus & Sert, 2022). The management of DFUs is inherently challenging due to their progressive nature, which is primarily influenced by interactions between systemic and local factors that impair wound healing. Key biomarkers such as haemoglobin serve as indicators of anaemia and erythrocyte status, while leukocyte count reflects the body's immune response. Glycated haemoglobin (HbA1c) provides insights into long-term glycemic control, and serum albumin indicates overall protein metabolism and potential kidney dysfunctions (Casadei *et al.*, 2021).

Despite the recognised importance of these biomarkers, the specific relationship between their

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levels and the severity of DFUs—classified according to the Wagner system—has not been thoroughly studied, particularly within the Indonesian population (Shah *et al.*, 2022; Ziegler *et al.*, 2021). Emerging evidence suggests that abnormalities in these parameters are associated with delayed wound healing and worse clinical outcomes in DFU patients. For instance, recent studies have demonstrated that low haemoglobin and albumin levels are correlated with increased ulcer severity and a higher risk of amputation, whereas elevated HbA1c and leukocytosis are linked to persistent infection and poor prognosis (Jiménez-García *et al.*, 2024; Sharma *et al.*, 2024).

This underscores the necessity of systematically evaluating how routinely measured laboratory markers relate to clinical severity, mainly when classified using standardised systems like the Wagner classification, which ranges from superficial ulcers to deep tissue involvement with osteomyelitis (Matheson *et al.*, 2021; Shah *et al.*, 2022). Nonetheless, few studies have comprehensively addressed these associations within the broader clinical context of DFUs.

Therefore, this study aims to investigate how levels of haemoglobin, leukocyte count, HbA1c, and albumin influence ulcer severity among patients treated at Sultan Agung Islamic Hospital in Semarang. By elucidating these relationships, the study seeks to enhance understanding of DFU management and provide evidence-based recommendations to improve patient outcomes and service quality for this high-risk population.

## 2. Materials and Methods

### 2.1. Study Design and Ethical Considerations

This cross-sectional study was conducted using retrospective data from medical records of patients with diabetic foot ulcers (DFUs) treated at Sultan Agung Islamic Hospital, a tertiary care centre in Semarang, Indonesia. Data collection spanned from January 2023 to December 2023. The study was approved by the Health Research Ethics Committee of Sultan Agung Islamic Hospital, Semarang (ethical clearance number: 123/KEPK/II/2024). All procedures conformed to the principles of the Declaration of Helsinki.

### 2.2. Population and Samples

A total of 62 patients were included through consecutive sampling, based on the availability of complete clinical and laboratory data. Patients aged ≥18 years with a confirmed diagnosis of DFU and complete laboratory records were eligible for inclusion. Exclusion criteria comprised missing clinical information and the presence of comorbid conditions that could confound wound healing assessment, such as active malignancy, chronic liver disease, or immunosuppressive conditions.

While no formal power analysis was performed owing to the retrospective design, the sample size of 62 exceeds the minimum of 30 typically recommended for correlation analyses with moderate effect sizes, supporting the validity of the results.

### 2.3. Data Collection

Demographic variables, including age and gender, were documented. Laboratory parameters collected were haemoglobin (g/dL), leukocyte count ($\times 10^9$/L), glycated haemoglobin (HbA1c, %), and serum albumin (g/dL). These parameters were measured using standard automated laboratory procedures at the hospital's clinical pathology unit, following routine protocols. Normal reference ranges were predefined as follows: haemoglobin (13–17 g/dL for men, 12–16 g/dL for women), leukocyte count (4–11 $\times 10^9$/L), HbA1c (<5.7% considered normal, 5.7–6.4% prediabetes, ≥6.5% diabetes), and serum albumin (3.5–5.0 g/dL).

### 2.4. Assessment of Ulcer Severity

Ulcer severity was classified based on the Wagner classification system, which stratifies ulcers into three stages for analysis:

- Mild: Grade 1 (superficial ulcer, no infection)
- Moderate: Grade 2 (deep ulcer involving tendons, bones, or joints)
- Severe: Grades 3–5 (deep ulcers with abscess, osteomyelitis, or gangrene)

### 2.5. Statistical Analysis

Data analysis was performed using R Studio (version 4.3.0). Descriptive statistics summarised patient characteristics: means ± standard deviations for continuous variables and frequencies with percentages for categorical variables. The relationship between clinical biomarkers and ulcer severity was evaluated using Spearman's rank correlation coefficient, suitable for the ordinal nature of ulcer classification. A significance level of $p < 0.05$ was adopted for statistical testing.

Associations between biomarkers and ulcer severity were visualised using the ggplot2 package. Scatter plots depicted each biomarker against ulcer severity, with fitted regression lines to illustrate trends. Correlation coefficients and p-values were annotated directly on the plots. Data manipulation and cleaning were conducted with the dplyr package, while figure styling and annotations were enhanced using ggpubr to ensure consistency.

## 3. Results

The present study enrolled 62 diabetic patients to evaluate the relationships between clinical characteristics—including albumin, haemoglobin, HbA1c, and leukocyte count—and the severity of diabetic foot ulcers (DFUs). The demographic and clinical characteristics of the study population are summarised in Table 1. Most participants were female, and the majority of ulcers were classified as moderate according to the Wagner classification system (61.29%). Only two patients (3.23%) had severe ulcers, which should be interpreted with caution due to the small sample size in this category.

Figure 1 displays scatter plots illustrating the relationships between clinical parameters and ulcer severity. Each plot includes a red regression line to indicate the trend, alongside Spearman's rank correlation coefficient (ρ) and the corresponding p-value. There is a significant inverse correlation (ρ = -0.41, p = 0.00084), suggesting higher albumin levels are associated with lower ulcer severity (Figure 1a). A significant negative correlation (ρ = -0.34, p = 0.0065) indicates that higher haemoglobin levels are linked to milder ulcers (Figure 1b). A strong positive correlation (ρ = 0.62, p = 9.4e-08) was observed, implying that higher HbA1c levels are associated with increased ulcer severity (Figure 1c). A moderate positive correlation (ρ = 0.40, p = 0.0013) was identified, with higher leukocyte counts correlating with more severe ulcers.

Most patients were female, and the distribution of ulcer severity revealed that the majority had moderate ulcers, with only a small number exhibiting severe disease. These findings underscore significant associations between clinical biomarkers and ulcer severity. The correlation analysis demonstrated that lower albumin and haemoglobin levels are associated with more severe ulcers, highlighting their potential roles as protective factors. Conversely, elevated HbA1c and leukocyte counts correlate strongly with increased ulcer severity, suggesting these parameters may serve as risk factors for disease progression. These results support the concept that systemic inflammation, poor glycemic control, anaemia, and hypoalbuminemia contribute to worse clinical outcomes in DFU patients. Significantly, these biomarkers could aid in risk stratification and targeted management in clinical practice.

**Table 1.** Study population characteristics

| Variable | Value |
|---|---|
| Age (years) | 53.50 (range: 30 – 81) |
| Gender | |
| • Male | 30 (48.39%) |
| • Female | 32 (51.61%) |
| Hemoglobin (g/dL) | 10.7 ± 1.81 |
| Leukocyte Count ($x10^3/\mu L$) | 19.30 ± 9.12 |
| HbA1c (%) | 8.23 ± 3.01 |
| Albumin (g/dL) | 4.01 ± 1.65 |
| Ulcer Severity | |
| • Mild | 22 (35.48%) |
| • Moderate | 38 (61.29%) |
| • Severe | 2 (3.23%) |

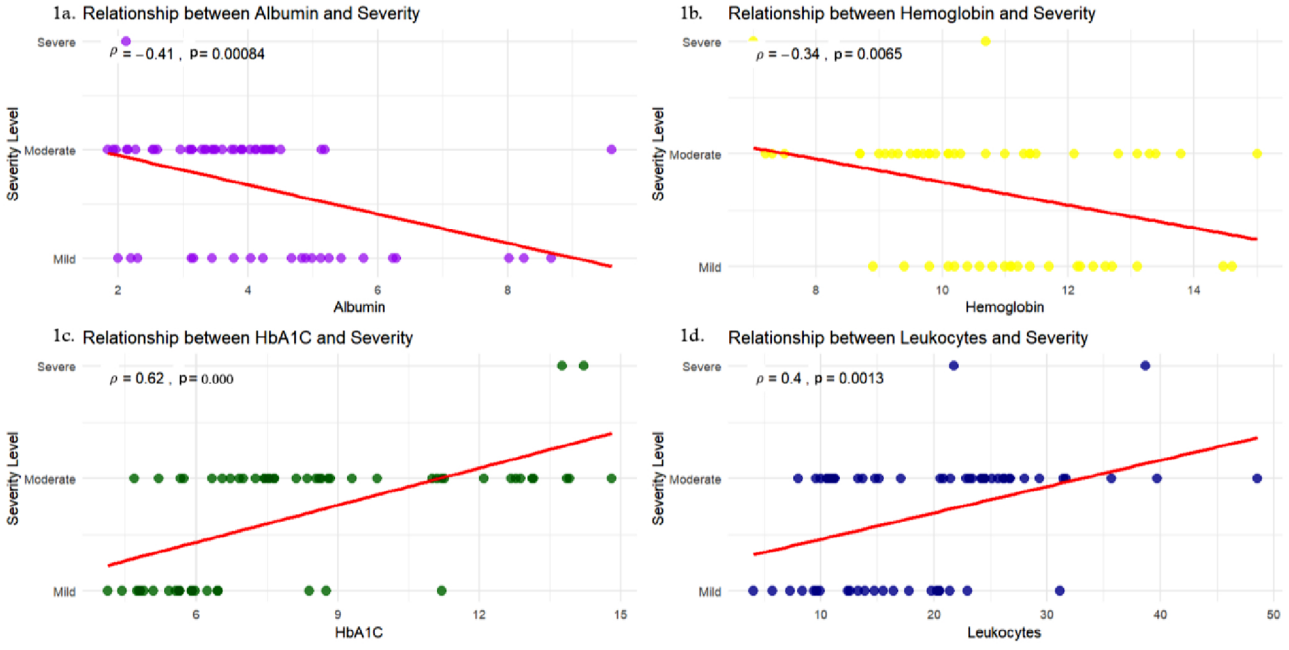


**Figure 1.** Analysis of the relationship between clinical parameters and severity: (a) albumin and severity, (b) haemoglobin and severity, (c) hba1c and severity, and (d) leukocyte count and severity

## 4. Disscussion

This study offers clinically relevant insights into the relationships between key laboratory parameters and the severity of diabetic foot ulcers (DFU). The findings emphasise the multifactorial nature of DFU progression and highlight the importance of incorporating systemic markers into risk stratification and management strategies.

Haemoglobin levels were significantly associated with DFU severity. Anaemia, prevalent in patients with diabetes, exacerbates peripheral ischemia and reflects underlying systemic conditions such as chronic kidney disease and cardiovascular disease (Shabhay *et al.*, 2021). These systemic changes impair wound healing and promote infection, contributing to DFU progression.. Huang *et al.* (20219) stipulated that it is probably prudent to treat anaemia as early as possible in the timeline of diabetes, when it may help prevent the development of ulcers.

Poor glycemic control, reflected by elevated HbA1c, was also associated with increased DFU severity. Chronic hyperglycemia disrupts key physiological processes necessary for wound healing, including immune response, collagen synthesis, and angiogenesis (Casadei *et al.*, 2021). Furthermore, it amplifies oxidative stress and inflammation, worsening ulcer progression. Effective glycemic management through patient education, lifestyle modification, and pharmacologic therapy remains a cornerstone of DFU care (Nano *et al.*, 2020). HbA1c not only assesses metabolic control but is also linked to long-term outcomes, such as limb amputation and mortality (Pemayun & Naibaho, 2017).

The positive correlation between leukocyte count and ulcer severity supports the pivotal role of infection and systemic inflammation in DFU pathogenesis. Elevated leukocyte levels suggest active infection, which is a critical factor in the development of severe complications in large-area ulcers (Tong *et al.*, 2020). Infections trigger excessive tissue inflammation and necrosis, hindering healing. Prompt identification and management of infection through appropriate anti-infective therapy are vital to prevent further deterioration (Jiménez-García *et al.*, 2024).

Low serum albumin levels were inversely associated with ulcer severity, reflecting poor nutritional status and systemic inflammation—both of which impair wound healing (Bezerra *et al.*, 2020). Hypoalbuminemia has been linked to prolonged hospital stay, increased amputation risk, and higher mortality rates (Shabhay *et al.*, 2021). Addressing nutritional deficits through targeted interventions, including protein supplementation, is an essential aspect of comprehensive DFU management (Kateel *et al.*, 2018; Sharma *et al.*, 2024).

The integration of these four parameters—haemoglobin, HbA1c, leukocyte count, and albumin—provides a holistic view of the systemic and local factors influencing DFU severity. Together, they can guide clinicians in risk stratification and individualised management. For example, patients with high leukocyte counts may benefit from intensified infection control measures, while those with low albumin might require nutritional support, potentially improving clinical outcomes (Leal de Araújo *et al.*, 2024). This approach aligns with the perspectives of Albright and Fleischer, who advocate for considering systemic markers as part of routine DFU care (Albright & Fleischer, 2021).

Furthermore, these findings reinforce the importance of a multidisciplinary approach to DFU management (Nano *et al.*, 2020). Advances in predictive analytics and machine learning may enable the development of personalised care pathways by identifying high-risk patients and tailoring interventions accordingly (Yu *et al.*, 2024). Previous studies underscore the prognostic value of these markers; for instance, Ammar *et al.* (2021) demonstrated that anaemia and leukocytosis are associated with a higher risk of limb amputation in DFU patients. Hypoalbuminemia may also interfere with the interpretation of HbA1c, highlighting the need for integrated metabolic and nutritional assessments (Feng *et al.*, 2021).

Emerging therapies, such as autologous leukocyte–platelet–fibrin patches, show promise in enhancing healing and reducing amputations by modulating inflammation and coagulation (Mendivil *et al.*, 2023). Interventions targeting chronic systemic inflammation, coagulation abnormalities, anaemia, and glycemic control may improve prognosis in DFU patients. Such integrative management approaches are supported by the development of predictive models, for example, Peng & Min (2023) created nomograms based on haemoglobin and albumin to assess DFU risk, facilitating early intervention and optimised resource allocation

It is important to acknowledge that this study is cross-sectional in design, which restricts the ability to infer causality between the clinical parameters and ulcer severity. While significant associations were identified, these should not be interpreted as predictive or definitive of disease progression. Additionally, the relatively small sample size may limit the generalizability of the findings to broader populations. Future longitudinal studies are necessary to validate these results and to explore the underlying causative mechanisms more comprehensively.

## 5. Conclusions

This study highlights significant associations between specific clinical parameters and the severity of diabetic foot ulcers (DFUs). The key findings indicate that lower levels of haemoglobin and albumin, as well as higher HbA1c and leukocyte counts, are significantly correlated with increased severity of DFUs. These parameters may serve as critical indicators of risk among diabetic patients, underscoring the necessity of routinely monitoring them to identify those at heightened risk for developing severe DFUs. This proactive approach could lead to improved patient outcomes through timely intervention. Although causality cannot be definitively established due to the cross-sectional design of the study, the results support the potential utility of these clinical markers in early risk stratification. Future research should aim to develop predictive models incorporating these markers, which could facilitate prompt interventions and ultimately enhance the management of DFUs.

### Conflict of interest

All authors have no conflict of interest in this article.

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### References

Akkus, G., & Sert, M. (2022). Diabetic foot ulcers: A devastating complication of diabetes mellitus continues non-stop in spite of new medical treatment modalities. *World Journal of Diabetes,* 13(12): 1106–1121. https://doi.org/10.4239/wjd.v13.i12.1106

Albright, R. H., & Fleischer, A. E. (2021). Association of select preventative services and hospitalization in people with diabetes. *Journal of Diabetes and Its Complications,* 35(5): 1-5. https://doi.org/10.1016/j.jdiacomp.2021.107903

Ammar, A. S., Khalid, R., Malik, U., Zeb, M., Abbas, H. M., & Khattak, S. B. (2021). Predictors of lower limb amputations in patients with diabetic foot ulcers presenting to a tertiary care hospital of Pakistan. *The Journal of the Pakistan Medical Association,* 71(9): 2163–2166. https://doi.org/10.47391/JPMA.06-932

Bezerra, C. B., de Lima Saintrain, M. V., Lima, A. O. P., Nobre, M. A., E Silva Pesenti Sandrin, R. L., Braga, D. R. A., & Doucet, J. (2020). Clinical and epidemiological differences in diabetes: A cross-sectional study of the Brazilian population compared with the French GERODIAB cohort. *Diabetes Research and Clinical Practice,* 159(107945): 1-7. https://doi.org/10.1016/j.diabres.2019.107945

Casadei, G., Filippini, M., & Brognara, L. (2021). Glycated Hemoglobin (HbA1c) as a biomarker for diabetic foot peripheral neuropathy. *Diseases,* 9(1): 1-18. https://doi.org/10.3390/diseases9010016

Feng, X., Yang, Y., Zhuang, S., Fang, Y., Dai, Y., Fu, Y., Hu, Q., Yuan, Q., Tang, H., & Tang, L. (2021). Influence of serum albumin on HbA1c and HbA1c-defined glycemic status: A retrospective study. *Frontiers in Medicine,* 8(May), 1–10. https://doi.org/10.3389/fmed.2021.583093

Huang, Z.-H., Li, S.-Q., Kou, Y., Huang, L., Yu, T., & Hu, A. (2019). Risk factors for the recurrence of diabetic foot ulcers among diabetic patients: A meta-analysis. *International Wound Journal,* 16(6): 1373–1382. https://doi.org/10.1111/iwj.13200

Jiménez-García, J. F., Jiménez-Abad, J. F., López, L. A., & García-Fernández, F. P. (2024). Diabetic foot ulcers: evaluating the role of the specialist advanced practice nurse in complex chronic wounds. *British Journal of Nursing,* 33(15): S4–S15. https://doi.org/10.12968/bjon.2024.0006

Kateel, R., Augustine, A. J., Prabhu, S., Ullal, S., Pai, M., & Adhikari, P. (2018). Clinical and microbiological profile of diabetic foot ulcer

patients in a tertiary care hospital. *Diabetes & Metabolic Syndrome,* 12(1): 27–30. https://doi.org/10.1016/j.dsx.2017.08.008

Leal de Araújo, A., Negreiros, F. D. da S., Florêncio, R. S., Garces, T. D. S., Cestari, V. R. F., Mattos, S. M., Marques, S. J. S., Albuquerque, F. E. F., Araújo, W. C. O., Poveda, V. de B., & Moreira, T. M. M. (2024). Preventive interventions for diabetic foot ulcer adopted in different healthcare settings: A scoping review protocol. *PloS One*, 19(10): 1-10. https://doi.org/10.1371/journal.pone.0306486

Matheson, E. M., Bragg, S. W., & Blackwelder, R. S. (2021). Diabetes-related foot infections: Diagnosis and treatment. *American Family Physician,* 104(4), 386–394. https://www.aafp.org/pubs/afp/issues/2021/1000/p386.html

Mendivil, J. M., Henderson, L. C., Olivas, O. S., Deanda, M. A., & Johnson, M. L. (2023). Retrospective data analysis of the use of an autologous multilayered leukocyte, platelet, and fibrin patch for diabetic foot ulcers treatment in daily clinical practice. *Advances in Skin & Wound Care,* 36(11): 579–585. https://doi.org/10.1097/ASW.0000000000000054

Nano, J., Carinci, F., Okunade, O., Whittaker, S., Walbaum, M., Barnard-Kelly, K., Barthelmes, D., Benson, T., Calderon-Margalit, R., Dennaoui, J., Fraser, S., Haig, R., Hernández-Jimenéz, S., Levitt, N., Mbanya, J. C., Naqvi, S., Peters, A. L., Peyrot, M., Prabhaharan, M., … Massi-Benedetti, M. (2020). A standard set of person-centred outcomes for diabetes mellitus: results of an international and unified approach. *Diabetic Medicine : A Journal of the British Diabetic Association,* 37(12): 2009–2018. https://doi.org/10.1111/dme.14286

Pemayun, T. G. D., & Naibaho, R. M. (2017). Clinical profile and outcome of diabetic foot ulcer, a view from a tertiary care hospital in Semarang, Indonesia. *Diabetic Foot & Ankle,* 8(1): 1-8. https://doi.org/10.1080/2000625X.2017.1312974

Peng, B., & Min, R. (2023). Development of predictive nomograms for clinical use to quantify the risk of diabetic foot in patients with type 2 diabetes mellitus. *Frontiers in Endocrinology,* 14 (1186992): 01-08. https://doi.org/10.3389/fendo.2023.1186992

Shabhay, A., Horumpende, P., Shabhay, Z., Mganga, A., Van Baal, J., Msuya, D., Chilonga, K., & Chugulu, S. (2021). Clinical profiles of diabetic foot ulcer patients undergoing major limb amputation at a tertiary care centre in North-eastern Tanzania. *BMC Surgery,* 21(34): 1-7. https://doi.org/10.1186/s12893-021-01051-3

Shah, P., Inturi, R., Anne, D., Jadhav, D., Viswambharan, V., Khadilkar, R., Dnyanmote, A., & Shahi, S. (2022). Wagner's classification as a tool for treating diabetic foot ulcers: Our observations at a Suburban Teaching Hospital. *Cureus,* 14(1): 1-11. https://doi.org/10.7759/cureus.21501

Sharma, A., Srivastava, V., Shankar, R., Yadav, A. K., Ansari, M. A., & Gupta, S. K. (2024). Epidemiological profile of chronic wounds in an Indian Population: A community-based cross-sectional observational study. *Cureus,* 16(9): 1-19. https://doi.org/10.7759/cureus.68684

Tong, T., Yang, C., Tian, W., Liu, Z., Liu, B., Cheng, J., Cheng, Q., & Zhou, B. (2020). Phenotypes and outcomes in middle-aged patients with diabetic foot ulcers: A retrospective cohort study. *Journal of Foot and Ankle Research,* 13(1): 1-8. https://doi.org/10.1186/s13047-020-00386-z

Yu, X., Wu, Z., & Zhang, N. (2024). Machine learning-driven discovery of novel therapeutic targets in diabetic foot ulcers. *Molecular Medicine*, 30(1): 1-15. https://doi.org/10.1186/s10020-024-00955-z

Ziegler, D., Papanas, N., Schnell, O., Nguyen, B. D. T., Nguyen, K. T., Kulkantrakorn, K., & Deerochanawong, C. (2021). Current concepts in the management of diabetic polyneuropathy. *Journal of Diabetes Investigation,* 12(4): 464–475. https://doi.org/10.1111/jdi.13401