

ORIGINAL ARTICLE

Predictors of gangrenous complications in diabetic foot ulcers: A cross-sectional study from Indonesia

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ABSTRACT

Type 2 diabetes mellitus (T2DM) is highly prevalent in Indonesia, where diabetic foot ulcer (DFU) affects 26% of patients, far above the global average. DFU, especially when complicated by gangrene, leads to severe morbidity and mortality, yet evidence related to its predictors remains limited. This study therefore aims to assess the prevalence of gangrene and the factors associated with a history of previous diabetic foot ulcers, insulin treatment and the development of gangrene. The analytical cross-sectional study involved T2DM patients with DFU admitted to the Margono Hospital in Central Java, Indonesia, from 2018 to 2024. Generalized linear mixed models (GLMM) employing a logistic regression model and adjusted odds ratio (AOR) with 95% CI were provided. Out of 859 patients with DFU, 30.97% (95%CI:27.96-34.15) were diagnosed with gangrene during the study period, which was higher in those with a history of DFU (AOR:3.59; 95%CI:1.28-10.08); those using insulin therapy (AOR:3.35; 95%CI:2.25-4.98); those diagnosed with renal disease (AOR:2.22; 95%CI:1.34-3.67); and those with normal weight or underweight of body mass index (BMI) (AOR:1.87; 95%CI:1.24-3.67). However, hypertensive patients with DFU (AOR:1.68; 95%CI:1.12-2.53) were more likely to develop gangrene. Nearly one-third of the DFU patients are diagnosed with gangrene in Indonesia. A previous history of DFU, insulin therapy, renal disease, and lower body mass index (normal or underweight) were significant predictors of gangrene, while hypertension appeared to have a protective association. The findings underscore the importance of early screening and management of comorbidities, particularly renal disease, nutritional status, and blood pressure control to reduce the risk of gangrenous complications among DFU patients.

Keywords:

DFU, Gangrene, Indonesia

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INTRODUCTION

The rising prevalence of Type 2 diabetes mellitus (T2DM) presents a considerable challenge to healthcare practitioners worldwide, with diabetes becoming a major public health issue due to its rising prevalence.^{1,2} The condition affected approximately 500 million people globally in 2021, with 14% of adults aged between 20 and 79 in Southeast Asia receiving a diabetes diagnosis. Indonesia ranks fifth worldwide, with 19.5 million diagnosed cases of diabetes.^{1,2} It is among the top 10 countries worldwide, demonstrating a T2DM prevalence of 10.8%.³

T2DM is acknowledged as a significant public health issue.⁴ Diabetic foot ulcer (DFU) represents a major consequence of diabetes mellitus (DM), resulting in heightened patient morbidity and significant economic repercussions.⁵ The worldwide incidence of DFU is 6.3%, with regional variations: 13.0% in North America, 5.5% in Asia, 5.1% in Europe, 7.2% in Africa and 3.0% in Oceania.⁶ The prevalence of DFU in Indonesia was 26%⁷, significantly exceeding the global rate.⁸

DFU is a severe consequence of diabetes mellitus that contributes significantly to both mortality and morbidity worldwide; it is a complex and expensive disease.^{9,10} DFU causes gangrene, which in turn can lead to amputation, elevated healthcare costs, and sometimes fatal outcomes.¹¹ The severity of DFU is closely correlated with the incidence of adverse consequences such as gangrene, with severe cases being the principal cause of expensive complications.¹¹ In addition, the severity of DFU is a more significant predictor of future mortality than coronary artery disease, peripheral arterial disease or stroke.¹² The ultimate outcome in diabetic patients is influenced more profoundly by the intensity of the ulcer, rather than by its location.¹³

Retrospective data from a diabetic foot clinic in Québec City indicated that a

history of previous diabetic foot ulcers and post-consultation amputation were significant predictors of the recurrence of DFU within 12 months.¹⁴ Despite advances in diabetic foot care, such recurrence remains a major clinical challenge. Meta-analytic evidence indicates that a prior history of DFU significantly increases the risk of recurrence, highlighting the need to better understand and address factors contributing to the risk.¹⁵ However, the association between diabetes treatment and foot complications remains inconclusive. Insulin use is frequently linked to a higher risk of foot-related disorders, while evidence on oral hypoglycemic agents, especially metformin, is inconsistent and potentially confounded by disease severity and evolving treatment protocols.¹⁶ Insulin plays a crucial physiological role in cellular metabolism, glucose uptake and microvascular circulation.¹⁷ A deficiency or resistance can impair endothelial function, reduce nitric oxide production, and compromise tissue perfusion, leading to delayed wound healing and increased susceptibility to ischemic complications in the lower extremities.¹⁸ Consequently, patients requiring insulin therapy often represent a subgroup with more advanced or poorly controlled diabetes, predisposing them to neuropathy, vascular insufficiency and infection, all of which contribute to the development and progression of diabetic foot ulcers and gangrene.¹⁹ Insulin use has been significantly associated with increased ulcer severity in diabetic patients, yet the impact of treatment type on foot complications remains unclear.²⁰

Diabetes research has progressed; however, data on the severity of foot ulcers, particularly in relation to gangrene, remain limited. Several studies have addressed factors related to DFU, but have not specifically assessed gangrene. Central Java, one of Indonesia's largest provinces, comprises both urban and rural areas, with diverse populations and varying access to healthcare services. Margono Hospital, a

major government referral center with a specialized diabetes unit, serves patients from communities where diabetes awareness and preventive care are limited, contributing to delayed treatment and higher DFU and gangrene prevalence. Therefore, this study aims to assess the prevalence of gangrene, and the factors associated with a history of previous diabetic foot ulcers, insulin treatment and the development of gangrene in Indonesia.

METHODS

Study design

An analytical cross-sectional approach was employed, based on electronic medical records. The study included 859 DFU cases whose diagnosis dates were reported in medical records between 2018 and 2024.

Study Area

This study was conducted in Margono Hospital, Central Java. It is one of the largest public hospitals in the region and has a specialized diabetes department, thus making it an ideal location for the research.

Sample and Sampling

A hospital-based consecutive sampling technique was used, with participants selected based on specific criteria to ensure relevance and accuracy. The inclusion criteria for the sample were patients diagnosed with T2DM who also had DFU; in addition, participants had to be patients at Margono Hospital, and receiving either inpatient or outpatient care. Furthermore, only individuals aged 18 years or older were considered for inclusion. The exclusion criteria eliminated individuals with incomplete electronic medical records, those who were not Indonesian nationals, and patients diagnosed with HIV or hemophilia.

Study outcome

The study outcome concerned the presence of gangrene in DFU (dichotomous). Gangrene in DFU was categorized using Wagner tools, an approach that is primarily focused on categorizing ulcers based on their depth and the extent of tissue death, using a six-grade scale.²¹ The six Wagner classification system scales are (0) pre-ulcerative area without open lesion; (1) superficial ulcer (partial/full thickness); (2) ulcer extending to the tendon, capsule, bone; (3) stage 2, with abscess, osteomyelitis or joint sepsis; (4) localized gangrene; and (5) global foot gangrene. For the analysis, gangrene in DFU was classified as a binary outcome: non-gangrene (0) included Grade 0, Grade 1, Grade 2 and Grade 3 ulcers, while gangrene (1) included Grade 4 and Grade 5 ulcers. This categorization was based on the clinical severity of the ulcers, with Grade 4 and Grade 5 representing advanced stages with abscess formation, osteomyelitis or joint sepsis, which are associated with a higher risk of adverse outcomes. Grade 3 ulcers, although showing some tissue necrosis, were considered less severe and more similar to earlier stages in terms of clinical management and prognosis, justifying their inclusion in the non-gangrene group.

A factor of interest in the study was whether health status included a history of DFU and T2DM therapy. Demographic information included gender, age and body mass index. The BMI results were stratified using the World Health Organization (WHO) Asia-Pacific classifications.²² Comorbidity refers to all other conditions an individual patient might have other than the primary condition of interest, including renal disease, hypertension, neuropathy and stroke. The laboratory findings referred to blood sugar and hemoglobin. The random blood glucose threshold is normally between 180 and 200 mg/dL (10 to 11

mmol/L), meaning that when blood glucose levels exceed this, extra glucose begins to be expelled in the urine.²³ Anemia is characterized as hemoglobin levels below 13 g/dL in men and <12 g/dL in women.²⁴

Data collection

Data validity and reliability were ensured through the use of a systematic process. Qualified research assistants independently performed double data entry, after which the files were combined and cross-checked for consistency and accuracy. The data were then reviewed by the research assistants and verified with the attending medical practitioner to confirm correctness. DFU were graded using standardized criteria by trained nurses to ensure consistent outcome assessment. Any discrepancies or errors identified during verification were corrected by the researcher prior to analysis, and a final review with the medical practitioner was conducted to ensure data quality.

Statistical analysis

Baseline characteristics were analyzed using descriptive statistics, with categorical variables presented as frequencies and percentages, and continuous variables described using mean, standard deviation, median, minimum and maximum values. The prevalence of gangrene was stratified by sex to characterize the demographic composition of the study population. To identify factors associated with gangrene in DFU, a generalized linear mixed model (GLMM) with a logistic regression framework was performed, accounting for clustering by residence.²⁵ The model was used to account for clustering by residential area, allowing for more accurate estimation of associations between predictors and gangrene, while addressing potential intraclass correlation that standard logistic

regression does not accommodate. For bivariable analyses, the associations between one explanatory variable at a time with gangrene in DFU, without considering other variables or confounders (unconditional association), were analyzed. The results were presented as crude odds ratios (COR) with 95%CI. For the independent variable selection in the initial model, variables were included based on plausibility, a priori evidence, completeness of data, or if they had a Wald test p-value < 0.25 in the bivariate analysis.²⁵ Multicollinearity between independent variables was assessed using variance inflation factors (VIF), with all values being below the threshold, thus indicating no multicollinearity. Model fit was evaluated using the Hosmer–Lemeshow goodness-of-fit test and the Akaike Information Criterion (AIC). The final model with GLMM on logistic regression automatically excluded cases with missing values, so the final analysis was conducted on the complete-case dataset (n = 641), ensuring that the results represented only patients with complete data for all the included variables. The results were presented as adjusted odds ratios (AOR) with 95%CI. All the analyses were performed using the STATA version 18.0 (College Station, Texas 77845 USA) software package.

RESULTS

DFU Patient Characteristics

A total of 859 diabetes patients with DFU were included in the study, with more than half being female (54.71%). Their mean age was 60.98 (± 10.42) years; the mean blood sugar level was 240.99 (± 128.51); most had no history of DFU (96.86%); and just over half were using insulin for therapy (55.30%) (Table 1).

Table 1. Demographic characteristics of the DFU patients (n = 859)

Characteristic	Number (n)	Percentage (%)
History of DFU		
No	832	96.86
Yes	27	3.14
T2DM Therapy		
Without insulin	384	44.70
With insulin	475	55.30
Sex		
Male	389	45.29
Female	470	54.71
Age (years)		
<60	402	46.80
≥60	457	53.20
Mean (SD)		60.98 (±10.42)
Median (Min: Max)		60.59 (18.38:92.61)
Residence		
Urban	141	16.41
Rural	718	83.59
BMI (n=641)*		
Underweight	44	6.86
Normal weight	394	61.47
Overweight or obese	203	31.67
Renal Disease		
No	727	84.63
Yes	132	15.37
Hypertension		
No	579	57.40
Yes	280	32.60
Neuropathy		
No	683	79.51
Yes	176	20.49
Stroke		
No	834	97.09
Yes	25	2.91
Random Blood Sugar		
High (≥200)	361	42.03
Normal (<200)	498	57.97
Mean (SD)		240.99 (±128.51)
Median (Min: Max)		221 (29:858)
Hemoglobin (n = 641)*		
Normal (≥12)	112	17.47
Anemia (<12)	529	82.53
Mean (SD)		10.20 (±2.30)
Median (Min: Max)		10.20 3.6:20.6)

*BMI and hemoglobin data were missing for 218 participants (25.4%), resulting in a reduced sample size of 641 for the analyses involving these variables

Prevalence of Gangrene among the DFU patients

Of the total sample of 859 patients with DFU, 266 (30.97%, 95% CI: 27.96-34.15) were diagnosed with gangrene; 222 (25.84%, 95% CI: 23.03-28.88) with localized gangrene, and 44 (5.12%, 95% CI: 3.83 - 6.82) with global foot gangrene. Gender differences were also observed, with 114 (29.31%, 95% CI: 24.98 - 34.05) males and 152 (32.34%, 95% CI: 28.25-36.72) females being diagnosed with gangrene, 96 males (24.68%, 95% CI: 20.63-29.22) with localized gangrene and 18 (4.63%, 95% CI: 2.92-7.24) with global

foot gangrene, and 126 females (26.81%, 95% CI: 22.98-31.01) with localized gangrene and 26 (5.53%, 95% CI: 3.79-8.01) with global foot gangrene (Table 2). Reporting prevalence by sex provides a clear description of the demographic characteristics of the study population, including gender distribution, and facilitates meaningful comparisons with other epidemiological studies of DFU. The approach also helps contextualize the impact of gangrene across different population subgroups in Indonesia.

Table 2. Prevalence of gangrene among DFU patients in Indonesia (n = 859)

Wagner Classification System	Total		Male		Female	
	Number (%)	95% CI	Number (%)	95% CI	Number (%)	95% CI
[0] Pre-ulcerative area without open lesion	108 (12.57)	10.41-14.97	44 (11.31)	8.51-14.88	64 (13.62)	10.79-17.04
[1] Superficial ulcer (partial/full thickness)	353 (41.09)	37.84-44.43	172 (44.22)	39.33-49.21	181 (38.51)	34.20-43.01
[2] Ulcer creep to tendon	87 (10.13)	8.28-12.34	35 (9)	6.52-12.29	52 (11.06)	8.52-14.25
[3] Stage 2 with abscess, osteomyelitis or joint sepsis	45 (5.24)	3.93-6.95	24 (6.17)	4.16-9.05	21 (4.47)	2.92-6.77
[4] Localized gangrene	222 (25.84)	23.03-28.88	96 (24.68)	20.63-29.22	126 (26.81)	22.98-31.01
[5] Global foot gangrene	44 (5.12)	3.83-6.82	18 (4.63)	2.92-7.24	26 (5.53)	3.79-8.01
Severity						
Non-gangrenous	593 (69.03)	65.85-72.04	275 (70.69)	65.95-75.02	318 (67.66)	63.28-71.75
Gangrenous	266 (30.97)	27.96-34.15	114 (29.31)	24.98-34.05	152 (32.34)	28.25-36.72

Determinants of gangrene among the DFU patients

After adjusting for the influences of BMI, history of DFU, T2DM treatment, renal disease, hypertension, neuropathy, stroke, random blood glucose levels, and hemoglobin, it was determined that out of the 859 individuals with DFU, 266 (30.97%, 95% CI: 27.96-34.15) exhibited the presence of gangrene. The findings revealed that the incidence of gangrene in patients with DFU was elevated among those with a prior history of DFU (AOR:

3.59; 95% CI: 1.28-10.08), those undergoing insulin therapy (AOR: 3.35; 95% CI: 2.25-4.98), individuals diagnosed with renal disease (AOR: 2.22; 95% CI: 1.34-3.67), and patients classified as normal weight or underweight based on BMI (AOR: 1.87; 95% CI: 1.24-3.67). Patients with no hypertension in the diabetic foot ulcers (AOR: 1.68; 95% CI: 1.12-2.53) were more likely to develop gangrene (Table 3).

Table 3. Factors associated with gangrene among the DFU patients in Indonesia: GLMM (n = 859)

Factor	Total sample	Gangrene (n %)	COR (95% CI)	p-value	AOR (95% CI)	p-value
Gender				0.279		
Male	389	114 (29.31)	1			
Female	470	152 (32.34)	1.18 (0.88-1.58)			
Age (years)				0.599		
<60	402	122 (30.35)	1			
>=60	457	144 (31.51)	1.08 (0.81-1.45)			
BMI (n=641)*				<0.001		0.003
Overweight and obese	203	42 (20.69)	1		1	
Normal weight or underweight	438	157 (35.84)	2.13 (1.44-3.15)		1.87 (1.24-3.67)	
History of DFU				0.203		0.015
No	832	255 (30.65)	1		1	
Yes	27	11 (40.74)	1.67 (0.76-3.69)		3.59 (1.28-10.08)	
T2DM Therapy				<0.001		<0.001
Without insulin	384	69 (17.97)	1		1	
With insulin	475	197 (41.47)	3.23 (2.35-4.45)		3.35 (2.25-4.98)	
Renal Disease				0.031		0.002
No	727	215 (29.57)	1		1	
Yes	132	51 (38.64)	1.53 (1.04-2.26)		2.22 (1.34-3.67)	
Hypertension				<0.001		0.012
Yes	280	62 (22.14)	1		1	
No	579	204 (35.23)	1.87 (1.34-2.62)		1.68 (1.12-2.53)	
Neuropathy				0.001		
Yes	176	35 (19.89)	1			
No	683	231 (33.82)	2.01 (1.33-3.04)			
Stroke				0.028		
Yes	25	2 (8.00)	1			
No	834	264 (31.65)	5.10 (1.19-21.86)			
Random Blood Sugar				0.078		
High (≥ 200)	498	142 (28.51)	1			
Normal (< 200)	361	124 (34.35)	1.30 (0.97-1.74)			
Hemoglobin (n = 641)*				0.010		
Normal (≥ 12)	112	32 (28.57)	1			
Anemia (< 12)	529	220 (41.59)	1.80 (1.15-2.83)			

*Missing data for BMI and hemoglobin, which affected over 25% of the sample, were automatically excluded from the GLMM analysis, resulting in a final complete-case dataset of n = 641 for the regression analysis.

DISCUSSION

It was observed that more than half of the DFU patients were female. The gender distribution in this study differed slightly from that of previous studies, with females constituting 55.4% of patients in a Jakarta-based study,²⁶ 36.2% in an Aceh study²⁷ and 51.2% in another Jakarta study.²⁸ The higher prevalence of DFU in females may be attributed to both biological

and behavioral factors.²⁹ Biological ones can help explain the pattern, as women with diabetes are often more prone to renal insufficiency and different microvascular hemodynamics compared to men, which can impair wound healing and increase susceptibility to foot ulcers.³⁰ Behaviorally, women may face unique challenges related to therapeutic footwear acceptance; foot self-care adherence studies show that women report worse general health and lower internal locus of control regarding

ulcer prevention.³¹ The mean age of the respondents was 60.98 (± 10.42), which aligned with previous research in Indonesia indicating a mean age of 61 (IQR: 13; 27-85).²⁶ Among the total sample of 859 patients with DFU, 266 (30.97%) had gangrene, while 593 (69.03%) did not. The findings were comparable to those of earlier studies, which indicated that ulcers with Wagner grades 4-5 were prevalent in Indonesia (41.31%)³² and that 35% of PVD patients in India presented with gangrene.³³

In this study, patients with a history of DFU exhibited a 3.59-fold increased risk of developing gangrene. Prolonged diabetes duration heightens this risk due to impaired wound healing mechanisms, including endothelial dysfunction and the accumulation of advanced glycation end-products.³⁴ Chronic inflammation, characterized by elevated pro-inflammatory cytokine levels, further contributes to the non-healing of ulcers and may lead to gangrene.³⁵

The prevalence of gangrene in diabetic foot ulcers was 3.35 times greater in patients undergoing insulin therapy compared to those not receiving insulin. This association may reflect the fact that insulin therapy is often prescribed for patients with more severe or longer-standing diabetes, who are inherently at higher risk for complications such as DFU and gangrene.^{36,37} The need for insulin therapy typically indicates a more advanced stage of diabetes.³⁸⁻⁴⁰ Insulin therapy is generally initiated when oral drugs and lifestyle modifications fail to control hyperglycemia, signifying disease progression.⁴¹ Moreover, insulin therapy has been associated with inflammation and atherosclerosis, exacerbating diabetes-related complications.⁴² Such therapy markedly enhanced the wound healing rate 30.3% compared to 9.8%. A previous study indicated that insulin treatment correlated with an increased likelihood of complete recovery, and that systemic insulin therapy could enhance wound healing in diabetic

ulcers, provided that several aggravating variables were considered.⁴³

Gangrene occurrence in DFU was 2.22 times greater in patients with renal disease, which can be explained by the systemic effects of chronic kidney disease, including impaired immune response, poor wound healing, and vascular dysfunction, all of which increase susceptibility to severe foot complications.^{44,45} Both chronic kidney disease (CKD) and DFU are common complications of diabetes, affecting up to 40% and 19-34% of diabetic patients respectively over their lifetime. CKD severity correlates with an increased risk of DFU and its adverse outcomes, including gangrene.⁴⁶ CKD is a significant predictor of mortality in patients with gangrene, particularly among those undergoing dialysis.^{47,48} It contributes to vascular dysfunction, impairs immune responses, and increases susceptibility to infections that can precipitate gangrene.⁴⁹ In addition, renal illness impairs immune functions, heightening vulnerability to infections that may trigger or exacerbate gangrene.⁴⁷

Gangrene in DFU was 1.87 times more prevalent among patients of normal weight or underweight ones, compared to overweight or obese individuals. Previous studies have suggested that pressure ulcer risk, a precursor to gangrene, is highest among underweight individuals and lowest in overweight patients.⁵⁰ Weight gain associated with insulin use is driven by anabolic effects, increased appetite and reduced glycosuria. Insulin therapy correlates with heightened cardiovascular risks and mortality in type 2 diabetes patients, alongside inflammation, atherosclerosis, hypertension and dyslipidemia.⁴² Additionally, lower BMI is linked to the increased prevalence of peripheral artery disease (PAD), a known risk factor for DFU and gangrene, as it impairs circulation and delays wound healing.⁵¹ Furthermore, underweight patients may have a weakened immune

response, making them more vulnerable to infections such as methicillin-resistant *Staphylococcus aureus* (MRSA), which can lead to osteitis and gangrene.⁵²

Patients without hypertension had a 1.68-fold increased likelihood of developing gangrene. Biologically, hypertensive patients often receive long-term antihypertensive therapy, including ACE inhibitors or angiotensin receptor blockers, which improve endothelial function and microvascular circulation, potentially reducing tissue ischemia and gangrene risk in diabetic patients.⁵³ Behaviorally, patients diagnosed with hypertension tend to engage more regularly with healthcare services, including foot examinations, thereby enabling earlier detection of foot lesions before progression to gangrene.⁵⁴ Moreover, the absence of a hypertension diagnosis may reflect lower healthcare engagement or undetected comorbidities, delaying foot-ulcer recognition and increasing the risk of advanced complications.⁵⁴

Strengths and limitations of the study

The strength of this study lies in its comprehensive data collection and the inclusion of all eligible samples through hospital-based consecutive sampling, which ensured precise and systematic analysis. The application of a robust analytical framework, including a GLMM that accounted for clustering by residential area, enhanced the reliability of the results and reduced potential bias. These methodological strengths support the generalization of the findings to similar populations, thereby increasing external validity.

However, several limitations should be acknowledged. First, the sample may not be fully representative of the entire Indonesian population, as data were collected exclusively from one hospital on Java Island, which may have introduced

sampling bias, thus limiting generalizability. Second, some behavioral and occupational predictors, such as patients' occupations, foot care practices, and lifestyle behaviors, were not captured in the analysis. The absence of these variables may have influenced the observed associations. Although a large amount of data was initially missing, this did not affect the analysis because the final sample used in the model was complete and contained no missing values. Finally, although data completeness was prioritized, some degree of missing information may have affected the precision of the estimates. Despite these limitations, the study provides valuable insights into DFU risk factors in Indonesia and highlights the need for multicentre studies across other Indonesian regions incorporating behavioral and occupational variables to strengthen the evidence base.

CONCLUSION

Nearly one-third of DFU patients in Indonesia are diagnosed with gangrene. A previous history of DFU, insulin therapy, renal disease, and lower body mass index (normal or underweight) were shown to be significant predictors of gangrene, while hypertension appeared to have a protective association. The study findings have important clinical and public health implications. The identification of risk factors such as prior DFU, insulin therapy, renal disease, low or normal BMI, and the absence of hypertension can help healthcare providers stratify patients according to their risk of developing gangrene. Early screening and targeted interventions for high-risk patients, including optimized glycemic control, regular foot examinations, patient education on footcare, and management of comorbidities, can potentially reduce the incidence of gangrene and subsequent amputations. At the population level, the

findings highlight the need for public health programs in Indonesia to prioritize preventive care for diabetic patients, particularly in regions with high DFU prevalence, and to implement educational campaigns emphasizing early detection, self-care and timely medical consultation to improve outcomes and reduce healthcare costs.

AUTHORS' CONTRIBUTIONS

L: Conceptualization, Data curation, Investigation, Formal analysis and Writing - Original Draft. WL: Conceptualization, Methodology, Formal analysis, Supervision, Validation, Project administration and Writing - Review & Editing. RKM: Methodology, Formal analysis and Writing - Review & Editing. NM: Methodology, Formal analysis and Writing - Review & Editing. KS: Formal analysis and Writing - Review & Editing. KMH: Data curation, Investigation and Writing - Review & Editing. CJ: Writing - Original Draft.

ETHICAL CONSIDERATION

This study was approved by the Centre for Ethics in Human Research, Khon Kaen University, Khon Kaen, Thailand (Reference number HE682022) on 7th February 2025. In addition, the dataset was reviewed and approved by the Ethics Committee of RSUD Prof. Dr. Margono Soekarjo Purwokerto (Margono Hospital), Indonesia on 26th June 2024 (Ethics number 420/05089).

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CONFLICTS OF INTERESTS

All authors state that no conflict of interest

REFERENCES

1. Abdul, M. et al. Epidemiology of type 2 diabetes – Global burden of disease and forecasted trends. *J Epidemiol Glob Health* 10, 107–111 (2020).
2. IDF. International Diabetes Federation Diabetes Atlas 10th Edition. International Diabetes Federation vol. 10th editi (2021).
3. Soeatmadji DW, Rosandi R, Saraswati MR, Sibarani RP, Tarigan WO. Clinicodemographic profile and outcomes of type 2 diabetes mellitus in the Indonesian cohort of DISCOVER: A 3-year prospective cohort study. *Journal of the ASEAN Federation of Endocrine Societies*. 2023 Jan 25;38(1):68.
4. Onyango, E. M. & Onyango, B. M. The rise of noncommunicable diseases in Kenya: An examination of the time trends and contribution of the changes in diet and physical inactivity. *J Epidemiol Glob Health* 8, 1–7 (2018).
5. Khan, Y., M. Khan, M. & Raza Farooqui, M. Diabetic foot ulcers: a review of current management. *Int J Res Med Sci* 5, 4683 (2017).
6. Zhang, P. et al. Global epidemiology of diabetic foot ulceration: a systematic review and meta-analysis†. *Ann Med* 49, 106–116 (2017).
7. Yusuf, S. et al. Prevalence and Risk Factor of Diabetic Foot Ulcers in a Regional Hospital, Eastern Indonesia. *Open J Nurs* 06, 1–10 (2016).
8. Pengzi Zhang et al. Global epidemiology of diabetic foot

-
- ulceration: a systematic review and meta-analysis. *Ann Med* 49, 106–116 (2017).
9. Byrnes, J. et al. Health-related quality of life in people with different diabetes-related foot ulcer health states: A cross-sectional study of healed, non-infected, infected, hospitalised and amputated ulcer states. *Diabetes Res Clin Pract* 207, (2024).
 10. Akkus, G. & Sert, M. Diabetic foot ulcers: A devastating complication of diabetes mellitus continues non-stop in spite of new medical treatment modalities. *World J Diabetes* 13, 1106–1121 (2022).
 11. Jalilian, M., Sarbarzeh, P. A. & Oubari, S. Factors related to severity of diabetic foot ulcer: A systematic review. *Diabetes, Metabolic Syndrome and Obesity* 13, 1835–1842 (2020).
 12. Brennan, M. B. et al. Diabetic foot ulcer severity predicts mortality among veterans with type 2 diabetes. *J Diabetes Complications* 31, 556–561 (2017).
 13. Marzoq, A., Shiaa, N., Zaboon, R., Baghlany, Q. & Alabblood, M. H. Assessment of the Outcome of Diabetic Foot Ulcers in Basrah, Southern Iraq: A Cohort Study. *Dubai Diabetes and Endocrinology Journal* 25, 33–38 (2019).
 14. Fournier, C., Singbo, N., Morissette, N. & Thibeault, M. M. Outcomes of Diabetic Foot Ulcers in a Tertiary Referral Interdisciplinary Clinic: A Retrospective Canadian Study. *Can J Diabetes* 45, 255–260 (2021).
 15. Guo, Q. et al. Influencing factors for the recurrence of diabetic foot ulcers: A meta-analysis. *International Wound Journal* vol. 20 1762–1775 Preprint at <https://doi.org/10.1111/iwj.14017> (2023).
 16. Tola, A., Regassa, L. D. & Ayele, Y. Prevalence and associated factors of diabetic foot ulcers among type 2 diabetic patients attending chronic follow-up clinics at governmental hospitals of Harari Region, Eastern Ethiopia: A 5-year (2013–2017) retrospective study. *SAGE Open Med* 9, (2021).
 17. Vanderpant, N., Ward, E., Farrell, E. & Theodoraki, A. Insulin for people with type 2 diabetes mellitus. *BMJ Preprint* at <https://doi.org/10.1136/bmj-2023-078015> (2024).
 18. Gallo, G. & Savoia, C. New Insights into Endothelial Dysfunction in Cardiometabolic Diseases: Potential Mechanisms and Clinical Implications. *International Journal of Molecular Sciences* vol. 25 Preprint at <https://doi.org/10.3390/ijms25052973> (2024).
 19. D, M. B., Arvind, S. G. & Professor, A. Diabetic foot disease-clinical presentations, Glycaemic status and limb vascularity on radiological imaging and treatment modalities. *CME Journal of Geriatric Medicine* 108, (2024).
 20. Barakat, A. M. et al. Predictors of diabetic foot ulcer severity among patients attending Menoufia University Hospital, Egypt. *Menoufia Medical Journal* 35, 32 (2022).
 21. Wang, X., Yuan, C.-X., Xu, B. & Yu, Z. Diabetic foot ulcers: Classification, risk factors and management. *World J Diabetes* 13, 1049–1065 (2022).
 22. World Health Organization. International Association for the Study of Obesity and International Obesity Task Forc. (2000).
 23. Khawaja, N. Understanding the renal threshold for glucose: Implications for diabetes management. *African Journal of Diabetes Medicine* 32, (2024).
-

24. Gonzales, G. F. et al. Correcting the cut-off point of hemoglobin at high altitude favors misclassification of anemia, erythrocytosis and excessive erythrocytosis. *American Journal of Hematology* vol. 93 E12–E16 Preprint at <https://doi.org/10.1002/ajh.24932> (2018).
25. Hosmer, D. & Lemeshow, S. *Applied logistic regression*, 2nd Edition edn. New York: Wiley. Preprint at (2000).
26. Yunir, E., Hidayah, C. D., Harimurti, K. & Kshanti, I. A. M. Three Years Survival and Factor Predicting Amputation or Mortality in Patients with High Risk for Diabetic Foot Ulcer in Fatmawati General Hospital, Jakarta. *J Prim Care Community Health* 13, 1–7 (2022).
27. Syamsul S, Usman S, Saputra I, Maulana T, Ismail I. Risk Factor Analysis for Gangrene in Diabetes Mellitus Patients AT Hafidh Clinic Aceh Besar District in 2023. *International Journal of Medical Science and Dental Health.*;10(05):1-9.
28. Yunir, E. et al. Non-vascular contributing factors of diabetic foot ulcer severity in national referral hospital of Indonesia. *J Diabetes Metab Disord* 20, 805–813 (2021).
29. Vanherwegen, A. S. et al. Sex differences in diabetic foot ulcer severity and outcome in Belgium. *PLoS One* 18, (2023).
30. Vanherwegen, A. S. et al. Sex differences in diabetic foot ulcer severity and outcome in Belgium. *PLoS One* 18, (2023).
31. Jarl, G., Alnemo, J., Tranberg, R. & Lundqvist, L. O. Gender differences in attitudes and attributes of people using therapeutic shoes for diabetic foot complications. *J Foot Ankle Res* 12, (2019).
32. Hariftyani, A. S., Novida, H. & Edward, M. Profile of Diabetic Foot Ulcer Patients at Tertiary Care Hospital in Surabaya, Indonesia. *Jurnal Berkala Epidemiologi* 9, 293 (2021).
33. Bhargava, A., Mahakalkar, C., Kshirsagar, S. & Dhole, S. Assessing the Prevalence Rate of Gangrene Among Patients With Peripheral Vascular Disease in a Tertiary Care Hospital in Central India. *Cureus* <https://doi.org/10.7759/cureus.57038> (2024) doi:10.7759/cureus.57038.
34. Mahmoudvand, G., Karimi Rouzbahani, A., Razavi, Z. S., Mahjoor, M. & Afkhami, H. Mesenchymal stem cell therapy for non-healing diabetic foot ulcer infection: New insight. *Frontiers in Bioengineering and Biotechnology* vol. 11 Preprint at <https://doi.org/10.3389/fbioe.2023.1158484> (2023).
35. Littig, J. P. B., Moellmer, R., Estes, A. M., Agrawal, D. K. & Rai, V. Increased Population of CD40+ Fibroblasts Is Associated with Impaired Wound Healing and Chronic Inflammation in Diabetic Foot Ulcers. *J Clin Med* 11, (2022).
36. Ansari, P. et al. Hyperglycaemia-Linked Diabetic Foot Complications and Their Management Using Conventional and Alternative Therapies. *Applied Sciences (Switzerland)* vol. 12 Preprint at <https://doi.org/10.3390/app122211777> (2022).
37. Lee, B.-W. et al. Insulin Therapy for Adult Patients with Type 2 Diabetes Mellitus: A Position Statement of the Korean Diabetes Association, 2017. *Diabetes Metab J* 41, 367 (2017).
38. *Insulin Therapy in Type 2 Diabetes Mellitus*. Singapore Fam Physician 47, (2021).
39. Demidova, T. Y. & Titova, V. V. Insulin therapy is a personalized approach to glycemic management in diabetes. *Ter Arkh* 92, 201–206 (2021).
40. Zernovnik, S., Kos, M. & Locatelli, I. Initiation of insulin therapy in patients

- with type 2 diabetes: An observational study. *Acta Pharmaceutica* 72, 147–157 (2022).
41. Schmidt, S. K. Interactive and sculptural printmaking in the renaissance. *Brill's Studies in Intellectual History* vol. 270/21 1–467 Preprint at <https://doi.org/10.6084/m9.figshare> (2018).
 42. Rahman, Md. A. & Islam, S. The complications of long time treatment of insulin therapy in type-2 diabetes patients: A Review. *Molecular Mechanism Research* 2, 6172 (2024).
 43. Vatankhah, N., Jahangiri, Y., Landry, G. J., Moneta, G. L. & Azarbal, A. F. Effect of systemic insulin treatment on diabetic wound healing. *Wound Repair and Regeneration* 25, 288–291 (2017).
 44. Margolis, D. J., Hofstad, O. & Feldman, H. I. Association between renal failure and foot ulcer or lower-extremity amputation in patients with diabetes. *Diabetes Care* 31, 1331–1336 (2008).
 45. Mancin, S. et al. Diabetes, Chronic Kidney Disease, and Vascular Ulcers: Prevention Strategies and Clinical Implications. *Diabetology* vol. 6 Preprint at <https://doi.org/10.3390/diabetology6020010> (2025).
 46. Bonnet, J. B. & Sultan, A. Narrative Review of the Relationship Between CKD and Diabetic Foot Ulcer. *Kidney International Reports* vol. 7 381–388 Preprint at <https://doi.org/10.1016/j.ekir.2021.12.018> (2022).
 47. Hahn, H. M., Jeong, K. S., Park, D. H., Park, M. C. & Lee, I. J. Analysis of prognostic factors affecting poor outcomes in 41 cases of Fournier gangrene. *Ann Surg Treat Res* 95, 324–332 (2018).
 48. Salim, M. Clinical outcomes among patients with chronic kidney disease hospitalized with diabetic foot disorders: A nationwide retrospective study. *Endocrinol Diabetes Metab* 4, (2021).
 49. Voordeckers, M., Noels, J., Brognet, M., Salaouatchi, M. T. & Mesquita, M. Localized Fournier's Gangrene in 'end-Stage' Renal Failure: Multidisciplinary Approach and Integration of Palliative Care. *Case Rep Nephrol* 2020, (2020).
 50. Chen, F., Wang, X., Pan, Y., Ni, B. & Wu, J. The paradox of obesity in pressure ulcers of critically ill patients. *Int Wound J* 20, 2753–2763 (2023).
 51. Abuhay, H. W., Yenit, M. K. & Wolde, H. F. Incidence and predictor of diabetic foot ulcer and its association with change in fasting blood sugar among diabetes mellitus patients at referral hospitals in Northwest Ethiopia, 2021. *PLoS One* 17, (2022).
 52. Stańkowska, M. et al. Microbiological, Clinical and Radiological Aspects of Diabetic Foot Ulcers Infected with Methicillin-Resistant and-Sensitive *Staphylococcus aureus*. *Pathogens* 11, (2022).
 53. Yang, D. R., Wang, M. Y., Zhang, C. L. & Wang, Y. Endothelial dysfunction in vascular complications of diabetes: a comprehensive review of mechanisms and implications. *Frontiers in Endocrinology* vol. 15 Preprint at <https://doi.org/10.3389/fendo.2024.1359255> (2024).
 54. Wang, X. et al. The awareness and determinants of diabetic foot ulcer prevention among diabetic patients: Insights from NHANES (2011–2018). *Prev Med Rep* 36, (2023).