Journal of Medicine and Health (JMH) **e-ISSN: 2442-5257**
Vol. 8 No. 2 August 2026 **https://doi.org/10.28932/jmh.v8i2.16626**

Research Article

Risk Factors Associated with Amputation in Patients with Diabetic Foot Ulcer in Sultan Fatah Regional General Hospital

Faktor Risiko Terkait dengan Amputasi pada Pasien dengan Ulkus Kaki Diabetik di Rumah Sakit Umum Regional Sultan Fatah

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Received: July 11, 2026
Accepted: July 26, 2026

Abstract

Diabetes mellitus (DM) is a chronic metabolic disease with increasing global prevalence and high mortality rates. Diabetic foot ulcer (DFU) is a debilitating yet preventable DM complication and a leading cause of non-traumatic lower-extremity amputation, affecting quality of life. This study aimed to analyse risk factors associated with amputation in patients with DFU in Sultan Fatah Regional General Hospital. This cross-sectional analytic study used medical records of DFU patients hospitalized between January–December 2023. Variables included gender, age, body mass index (BMI), DM and DFU duration, hypertension, haemoglobin level, leucocyte count, lipid profile, glycated haemoglobin (HbA1c), estimated-glomerular filtration rate (eGFR), and amputation status. A total of 114 patients were analysed using univariate analysis, bivariate analysis (Fisher's exact test), and multivariate analysis (logistic regression). The amputation rate in this study was 8.8%. Highly significant association was shown between amputation and both DM and DFU duration ($p<0.01$), while low haemoglobin, high HbA1c, and low eGFR showed significant association ($p<0.05$). DM duration was found as an independent risk factor in this study (OR=17.58; 95% CI: 1.88–164.62; $p<0.05$). Identifying these risk factors may help guide targeted prevention efforts aimed at lowering amputation rates and preserving quality of life in this patient group.

Keywords*: amputation; diabetes mellitus; diabetic foot ulcer; risk factor*

How to Cite:
Krisnanda MA, Puspitaningtyas PE, Krisnanda MA. Risk factors associated with amputation in patients with diabetic foot ulcer in Sultan Fatah Regional General Hospital. Journal of Medicine and Health. 2026; 8(2): 159-67. DOI: https://doi.org/10.28932/jmh.v8i2.16626.

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Introduction

Diabetes mellitus (DM) is a long-term metabolic disorder marked by persistently high blood glucose levels, arising either from insufficient insulin production by the pancreas or from the body's inability to use the insulin it produces effectively.[1,2] The global prevalence and mortality of DM reached 7.17% and 3.34% respectively in 2023, making it one of the top ten leading causes of global deaths.[3,4] Diabetic foot ulcer (DFU) represents one of the most debilitating complications of DM, affecting approximately 19–34% of patients during their lifetime and constituting a leading cause of non-traumatic lower-extremity amputations globally.[5,6] Lower-extremity amputation significantly reduces quality of life, increases healthcare costs, and is associated with high mortality rates, emphasizing the importance of early identification of patients at risk.[7]

A number of studies have examined the drivers of amputation risk in DFU population. In one large meta-analysis, being male, a smoking history, previous foot ulceration, osteomyelitis, gangrene, a lower BMI, and a raised leucocyte count were each significantly linked to a greater likelihood of lower-extremity amputation.[8] In a separate meta-analysis conducted among Chinese DFU patients, a comparable set of correlates emerged, including prior ulceration, a Wagner grade above 3, diabetic peripheral vascular disease, BMI, ulcer duration, total cholesterol, triglyceride, low-density lipoprotein (LDL), high-density lipoprotein (HDL), fasting blood glucose, white blood count, HbA1c, high-sensitivity C-reactive protein (hs-CRP), and uric acid.[9] Coexisting conditions such as hypertension, coronary artery disease, peripheral arterial disease, and chronic kidney disease have likewise been linked to greater amputation risk across several reports.[10–12]

Despite advances in multidisciplinary management, the burden of DFU-related amputation persists. Therefore, this study aimed to analyse the risk factors associated with amputation in patients with DFU in Sultan Fatah Regional General Hospital. Improved understanding of these factors may support early risk identification, guide clinical decision-making, and facilitate targeted prevention strategies to reduce the incidence of amputation among DFU patients.

Methods

This retrospective observational study used a cross-sectional design, drawing on electronic medical record (EMR) data from DFU patients managed at Sultan Fatah Regional General Hospital from January to December 2023. Ethical clearance for the study was granted by the Research Ethics Committee of Universitas Ngudi Waluyo (approval no. 208/KEP/EC/UNW/2026, issued 30 March 2026). A total sampling approach was applied,

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whereby every adult patient (older than 18) admitted with DM and DFU to Sultan Fatah Regional General Hospital within the study period was enrolled. Exclusion criteria included all patients with >30% incomplete data on the EMRs.[13] The collected EMR data included patients' amputation status as the dependent variable, and gender, age, BMI, DM and DFU duration, hypertension, haemoglobin level, leucocyte count, lipid profile, HbA1c, and eGFR as the independent variables, chosen because earlier literature, reviewed in the Introduction, has linked each of them to amputation risk in DFU patients. Based on amputation status, patients were divided into amputation and non-amputation groups, and each independent variable was subsequently categorised into two groups as follows. Amputation group was defined as those who had any surgery of the foot, whether it was major or minor amputation, while non-amputation group was defined as those who had any debridement, other surgery, and/or other conservative managements for their DFU.[14,15] Gender was divided into male and female groups, while age was divided into ≥60 years old and <60 years old groups.[13] BMI was calculated by dividing patients' weight in kilograms by their height in metres squared. We divided BMI into normal and abnormal groups using the Asia-Pacific classification.[16] DM duration was divided into >10 years and ≤10 years groups, while DFU duration was divided into >30 days and ≤30 days groups.[17] Hypertension was defined as patients who were on antihypertensive medication, had history of hypertension, or had systolic/diastolic blood pressure ≥140/90 mmHg on admission.[18] Haemoglobin level of <13 g/dL in males or <12 g/dL in females was considered low, while leucocyte count of >11,000 cells/mm^3 was considered high.[19] Lipid profile was divided into two groups for each lipid type, whether it was normal or abnormal (high or low) based on management guideline of dyslipidaemia in Indonesia by The Indonesian Society of Endocrinology.[20,21] Total cholesterol of ≥200 mg/dL, triglyceride of ≥150 mg/dL, and LDL of ≥100 mg/dL were considered high, while HDL of <40 mg/dL was considered low.[20,21] HbA1c was divided into ≥6.5% and <6.5% groups.[13,22] eGFR was calculated with the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) 2021 equation using the MDCalc website, then considered <60 mL/min/1.73m^2 as low eGFR group.[12,23–26] Data were processed and analysed using IBM SPSS version 23 (IBM Corp., Armonk, NY, USA). Univariate analysis was used to describe the distribution of each variable, and bivariate analysis was performed using Fisher's exact test, given the categorical nature of the data and the presence of expected cell counts below five in more than 20% of cells, at a significance level of $\alpha = 0.05$. Variables found to be significantly associated with amputation in the bivariate analysis ($p<0.05$) were subsequently entered into a multivariate logistic regression analysis to identify independent risk factors, applying the same significance threshold.

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Results

Among 147 DFU patients admitted to Sultan Fatah Regional General Hospital during January–December 2023, 33 were excluded, leaving 114 eligible patients (43 male [37.7%]; 71 female [62.3%]). Ten of these patients (8.8%) underwent amputation, while the remaining 104 (91.2%) did not. Table 1 summarises the demographic, clinical, and laboratory profile of both groups.

Table 1 summarises the bivariate analysis of the risk factors using Fisher's Exact Test. Among the risk factors, DM duration, DFU duration, haemoglobin level, HbA1c, and eGFR were found to be significant (p-value <0.05). These significant risk factors would then proceed to multivariate analysis using the Logistic Regression Test, which are described in Table 2. In the multivariate analysis, the only significant risk factor was DM duration (adjusted OR 17.58; 95% CI 1.88, 164.62; p-value <0.05).

Table 1 Analysis of the Risk Factors in Amputation and Non-Amputation Groups

Risk Factor		Amputation		Non-Amputation		Total		*p*-value
		n	%	n	%	n	%	
Gender	Male	4	9.3	39	90.7	43	37.7	1.00
	Female	6	8.5	65	91.5	71	62.3	
Age (years old)	≥60	2	5.4	35	94.6	37	32.5	0.49
	<60	8	10.4	69	89.6	77	67.5	
BMI	Abnormal	8	10.8	66	89.2	74	64.9	0.49
	Normal	2	5.0	38	95.0	40	35.1	
DM Duration (years)	>10	9	23.7	29	76.3	38	33.3	<0.01*
	≤10	1	1.3	75	98.7	76	66.7	
DFU Duration (days)	>30	8	25.8	23	74.2	31	27.2	<0.01*
	≤30	2	2.4	81	97.6	83	72.8	
Hypertension	Hypertension	4	12.1	29	87.9	33	28.9	0.47
	Non-Hypertension	6	7.4	75	92.6	81	71.1	
Haemoglobin Level	Low	9	14.1	55	85.9	64	56.1	0.04*
	Normal	1	2.0	49	98.0	50	43.9	
Leucocyte Count	High	7	9.1	70	90.9	77	67.5	1.00
	Normal	3	8.1	34	91.9	37	32.5	
Total Cholesterol	High	2	16.7	10	83.3	12	30.0	0.57
	Normal	2	7.1	26	92.9	28	70.0	
Triglyceride	High	1	5.6	17	94.4	18	45.0	0.61
	Normal	3	13.6	19	86.4	22	55.0	
LDL	High	2	8.3	22	91.7	24	60.0	1.00
	Normal	2	12.5	14	87.5	16	40.0	
HDL	Low	3	11.5	23	88.5	26	65.0	1.00
	Normal	1	7.1	13	92.9	14	35.0	
HbA1c	High	9	14.3	54	85.7	63	58.3	0.04*
	Normal	1	2.2	44	97.8	45	41.7	
eGFR	Low	7	18.9	30	81.1	37	36.6	0.03*
	Normal	3	4.7	61	95.3	64	63.4	

*Statistical significance at *p*-value <0.05

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Table 2 Logistic Regression Analysis of the Significant Risk Factors

Risk Factor	Unadjusted			Adjusted		
	β	OR (95% CI)	*p*-value	β	OR (95% CI)	*p*-value
DM Duration	2.79	16.32 (1.70–156.33)	0.015	2.87	17.58 (1.88–164.62)	0.012*
DFU Duration	1.76	5.79 (0.84–39.82)	0.074	1.60	4.93 (0.81–30.14)	0.084
Haemoglobin	1.62	5.08 (0.41–62.62)	0.205	-	-	
HbA1c	2.01	7.45 (0.46–121.94)	0.159	2.21	9.09 (0.95–87.45)	0.056
eGFR	-0.40	0.67 (0.07–6.43)	0.729	-	-	

Abbreviations: β, Regression coefficient; OR, Odds Ratio; CI, Confidence interval
*Statistical significance at *p*-value <0.05

Discussion

This study set out to compare the demographic, clinical, haematological, and biochemical profiles of DFU patients who underwent amputation against those who did not. The observed amputation rate of 8.8% was comparable to the 9.9% reported by Lu et al.[12] Bivariate analysis identified DM duration, DFU duration, haemoglobin level, HbA1c, and eGFR as significantly associated with amputation.

DM duration emerged as the first of our significant risk factors, a finding that echoes the retrospective study by Yang et al.[17] Additionally, this study reported that prolonged DM duration was determined as the independent risk factor and associated with a 17-times higher risk for amputation in DFU patients. A longer duration of DM allows both vascular and non-vascular diabetic complications, notably peripheral neuropathy and peripheral arterial disease, to accumulate over time; these represent core mechanisms behind impaired healing and worsening ulcers, which in turn raise amputation risk.[5,6,17,27] Chronic inflammation and immune dysfunction associated with DM further heighten susceptibility to infection.[27] Amputation risk rises further when DFU is complicated by infection, particularly in cases involving osteomyelitis or gangrene.[8]

DFU duration was our second significant risk factor, in line with earlier reports linking a longer ulcer duration to an independently higher amputation risk, likely because such ulcers tend to be more advanced or poorly controlled by the time patients present.[9,17] A longer DFU duration often signals delayed healing and may point to underlying complications, including peripheral neuropathy, peripheral arterial disease, persistent infection, and suboptimal glycaemic control.[5,27] In the absence of effective, sustained management, DFU can continue to progress, worsening clinical outcomes and raising the risk of amputation.[8] DFU severity is commonly graded using the Wagner classification, with ulcer depth, osteomyelitis, and necrosis or gangrene worsening as Wagner grade increases.[12] Several studies have reported Wagner grade itself as a significant predictor of amputation in DFU patients.[9,10,14,18]

Consistent with the findings of Lu et al., low haemoglobin was our third significant risk factor for amputation.[12] Low haemoglobin diminishes the blood's oxygen-carrying capacity,

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limiting oxygen delivery to peripheral tissues and thereby slowing wound repair. Because sufficient tissue oxygenation underpins key reparative processes, including angiogenesis, cellular proliferation, and immune defence, patients with low haemoglobin tend to experience slower resolution of DFU.[8,17,28,29] In those with coexisting peripheral arterial disease, low haemoglobin may further worsen tissue ischaemia, raising the likelihood of delayed healing, necrosis, and eventual amputation.[8,17,27]

HbA1c was our fourth significant risk factor for amputation among DFU patients in our study, similar to the results of previous studies.[9,12] A high HbA1c reflects sustained hyperglycaemia and poor glycaemic control, both of which impair wound healing through several overlapping pathways, including microvascular injury, immune dysregulation, heightened infection susceptibility, and endothelial dysfunction. Together, these changes slow DFU healing and worsen clinical outcomes, ultimately raising amputation risk.[5,12,30] Poor glycaemic control also frequently coexists with peripheral arterial disease, peripheral neuropathy, and chronic kidney disease, further compounding overall amputation risk. Chronic hyperglycaemia additionally heightens oxidative stress and inflammatory activity, which together accelerate tissue injury and hinder healing.[5,27,30]

The final significant risk factor identified in our study was eGFR, reflecting chronic kidney disease (CKD), a finding that mirrors earlier work.[10,23] CKD is commonly viewed as an overall indicator of vascular health among people with DM.[10,27,31] Low eGFR and CKD can disturb lipid metabolism, blood pressure regulation, and other metabolic parameters, compounding vascular risk.[10] Wound healing may also be compromised by low eGFR and CKD through several interrelated pathways, including uraemia-related immune impairment, persistent inflammation, endothelial dysfunction, and anaemia, each of which undermines tissue repair and infection resistance, ultimately elevating amputation risk.[5,27,31]

There were other risk factor variables that were not significant in our study, but were significant in other studies, such as gender, age, BMI, hypertension, leucocyte count, and lipid profile. Findings on the link between gender and amputation vary across the literature; possible explanations include differences in lower-limb activity, pain sensitivity, and treatment adherence, though these factors do not always track consistently with gender across different populations.[8,11] Age may be associated with amputation through delayed wound healing and treatment compliance.[13] A link between BMI and amputation could stem partly from behavioural factors, such as disease awareness, treatment adherence, and coping strategies, and partly from physiological factors, such as altered peripheral vascular perfusion and impaired healing tied to abnormal fat distribution and nutritional status.[8,9,11,13] Hypertension may contribute to amputation

risk by disrupting metabolic regulation, thereby promoting inflammation and vascular damage.[11] Elevated leucocyte count may suggest ongoing infection, which may lead to impaired wound healing, osteomyelitis, and gangrene, thus increasing the risk of amputation.[8,11] A link between lipid profile and amputation could reflect not just their value as markers of nutritional status and ulcer severity, but also their contribution to atherosclerotic plaque formation and vascular disease.[32,33] These discrepancies across studies in which variables reach significance may stem from confounding, differing sample sizes, population genetic backgrounds, and unequal access to healthcare.

This study has several limitations, including its retrospective design, small sample size, incomplete data for some variables, and single-centre setting. Additionally, participants' mean haemoglobin level was 11.2 ± 2.6 g/dL, and peripheral blood indices indicated that anaemia in this cohort was mainly microcytic, a pattern most compatible with iron-deficiency anaemia or anaemia of chronic disease. Because the study relied solely on parameters already recorded in the EMRs, no additional testing (e.g., serum ferritin, iron studies, or inflammatory markers) was carried out to pinpoint the underlying cause. As the underlying cause of anaemia could not be pinned down, its overall effect on HbA1c accuracy remains uncertain: iron-deficiency anaemia can spuriously raise HbA1c readings, whereas anaemia of chronic disease can spuriously lower them through mechanisms tied to shortened red-cell survival,[22,34] a caveat worth bearing in mind when interpreting this study's HbA1c-related results. Other risk factors reported as significant in previous studies, such as smoking, Wagner grade, DFU history, DFU location, and other laboratory results, could not be analysed due to insufficient data. Further prospective studies with larger populations and additional variables are warranted.

Conclusion

This study identified several significant risk factors for amputation among DFU patients, including DM duration, DFU duration, low haemoglobin, high HbA1c, and low eGFR. Notably, prolonged DM duration was associated with a 17-times higher risk for amputation among DFU patients. Early detection and management of these risk factors may help prevent amputation and enhance the quality of life for DFU patients.

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