Progression of Diabetic Foot Ulcers To Lower Limb Amputations: A Retrospective Analysis

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ABSTRACT

Objective To determine the frequency and performed risk factor analysis of progression of diabetic foot ulcer (DFU) to lower limb amputation in a tertiary care teaching hospital.

Study design Retrospective observational study.

Place & Duration of study Department of General Surgery, East Surgical Ward, Mayo Hospital / Kind Edward Medical University Lahore, from January 2024 to January 2025.

Methods Records of adult patients admitted with DFU were reviewed. Data collected included demographic variables, glycemic control (HbA1c), co-morbid condition, characteristics of the ulcer (site, size, Wagner grade), severity of infection by International Working Group on the Diabetic Foot / Infectious Diseases Society of America (IWGDF / IDSA) criteria, presence of peripheral arterial disease (PAD), ulcer duration before presentation, and outcomes. Associations with amputation were analyzed using Chi-square test. A p-value of <0.05 was taken as significant. Due to complete data separation from advanced ulcer severity, an L1-penalized logistic regression model was used for multivariable analysis.

Results A total of 134 patients were included with the mean age of 56.1±11.4 years. The study included 102 (76.1%) males. Most of the patients presented with advanced disease. (n=113-84.3%) had Wagner Grade 4–5 ulcers. Amputation was done in 101 (75.4%) patients. On univariate analysis, chronic kidney disease (CKD - p = 0.026), peripheral neuropathy (p < 0.001), PAD (p = 0.036), rural residence (p = 0.042), and Wagner grade (p = 0.016) were significantly associated with amputation. In multivariable penalized regression, Wagner grade was the only independent predictor (adjusted OR = 2.5 per grade increase).

Conclusion A high proportion of patients admitted with DFU required amputation. Majority of them presented late with advanced Wagner grade and severe infection.

Key words Diabetic foot ulcer, Lower-extremity amputation (LEA), Wagner classification, Peripheral arterial disease.

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INTRODUCTION:

Diabetes mellitus is a global health crisis, with over 537 million affected worldwide. Among its complications, diabetic foot ulcer is one of the most disabling, often progressing to infection, gangrene, and amputation.[1,2] Globally, 19 to 34% of diabetics develop DFU, with amputation rates of 19 to 50%.[3-5] In Pakistan, delayed presentation, poor glycemic control, and lack of specialized care contribute to higher amputation rates.[6]

Amputation leads to disability, reduces quality of life with increased mortality. Despite this burden, a limited local data is found in relation to frequency of DFU progression to amputation. This study was conducted to determine the frequency and risk factors of amputation in patients who presented with diabetic foot ulcer.

METHODS:

Study design, place & duration: This was a retrospective observational study conducted in the Department of General Surgery, East Surgical Ward, Mayo Hospital / King Edward Medical University Lahore, from January 2024 to January 2025.

Ethical considerations: The institutional review board approval was sought to review the records (Letter number: 616/RC/KEMU dated August 2025).

Inclusion and exclusion criteria: All patients =18 years admitted with DFU of any Wagner grade were included. Patients who presented with traumatic ulcers, amputations done due to any other reason and with incomplete records, were excluded.

Sample size estimation: This was a retrospective review of the records. Data of all the patients who presented during the study period were included.

Study protocol: In this study the ulcers were graded according to the Wagner classification; Grade-1- superficial ulcer, Grade-2 - ulcer up to tendon / joint capsule, Grade-3 - deep ulcer with osteitis / abscess formation; Grade 4 - localized gangrene of forefoot / heel, and Grade 5 - extensive gangrene of the foot. The severity of infection was classified by IDSA/IWGDF criteria into; Mild - limited to skin / subcutaneous tissue without systemic signs, Moderate – deeper / more extensive involvement without systemic inflammatory response and Severe - local infection with systemic toxicity or metabolic instability. The peripheral arterial disease was assessed on clinical grounds with presence of ischemia as demonstrated by diminished / absent pulses, cool limb, delayed capillary refill, with Doppler evidence where available.

The data were recoded into a pre designed form. The variables collected included age, gender, residence, smoking status, duration of diabetes, level of HbA1c, presence of comorbid conditions like hypertension (HTN), ischemic heart disease (IHD), chronic kidney disease (CKD), presence of neuropathy. In addition, duration, site and size (area in cm^2) of the ulcer, Wagner grade, severity of infection, presence of PAD were recorded. The outcomes were reported healed or amputation needed with its level. All patients received standard care for diabetes mellitus and management of the foot ulcers.

Statistical analysis: Data were analyzed using Python-based statistical tools. Categorical variables were presented as frequency and percentage. Ulcer area (continuous) was summarized as mean ± standard deviation (SD) and median (interquartile range, IQR). Associations between clinical variables and amputation were assessed using the Chi-square test. A p-value <0.05 was considered statistically significant. Univariate odds ratios (ORs) with 95% confidence intervals (CIs) were calculated for relevant predictors (IHD, CKD, peripheral neuropathy, PAD, sex, residence). Wagner grade was dichotomized (Grade 4–5 vs. Grade 1–3) due to complete separation, resulting in an infinite OR.

Due to extreme imbalance in ulcer severity and complete separation in outcomes, an L1-penalized logistic regression model was used to identify independent predictors of amputation. Variables included in the model were age, sex, residence, HTN, IHD, CKD, peripheral neuropathy, PAD, and Wagner grade. Adjusted odds ratios (AORs) were derived from penalized coefficients.

RESULTS:

A total of 134 DFU patients were treated during the study period. Majority (n=102 – 76.1%) of the patients were male. Amputation was done in 101 (75.4%) cases which included 69 males and all the females (n=32) who were managed in the facility. Out of the total, 81 (60.4%) were from urban areas and 47 (35.1%) were smokers. Co-morbid conditions documented included hypertension (n=53 – 39.6%), IHD (N=51 – 38.1%), and CKD (n=40 – 29.9%). Peripheral neuropathy was reported in 38 (28.4%) and PAD in 40 ((9.9%) patients. Duration of ulcer in majority (n=91 – 76.9%) of the patients was less than one month while in 23 (17.2%) it was present for more than three months. The size of the ulcer was documented 104 (77.6%) patients only. The mean size was 10 cm^2 and median 7 cm^2 (IQR - 3-14). Details are given in table I.

Out of the total amputations (n=101), Major amputations (below and above knee joints) were performed in 50 (BK=26, AK=24) patients. Minor amputations (toe level and transmetatarsal level) were performed in 50 (32 and 18 respectively) patients. In one patient level of the amputation was

Table I: Baseline Characteristics of Patients with DFU (n = 134)

Variable	Category	Number (n)	Percentage (%)
Age distribution	<50 years	56	41.8
	50–59 years	36	26.9
	60–69 years	18	13.4
	>70 years	24	17.9
HbA1c%	<7%	5	3.7
	7–9%	4	3.0
	>9%	9	6.7
	Not documented	116	86.6
Duration of diabetes	<5 years	18	13.4
	5–10 years	12	9.0
	>10 years	19	14.2
	Not documented	85	63.4
Ulcer site	Toe	45	33.6
	Forefoot	23	17.2
	Midfoot	25	18.7
	Hindfoot	15	11.2
	Heel	13	9.7
	Not documented	13	9.7
Wagner grade	Grade 1	4	3.0
	Grade 2	5	3.7
	Grade 3	11	8.2
	Grade 4–5	113	84.3
Infection severity	Mild	25	18.7
	Moderate	57	42.5
	Severe	31	23.1
	Not documented	21	15.7

Table II: Association of Clinical Variables with Amputation

Variable	p-value
Age group	0.467
Residence	0.042* (Rural)
Smoking	0.063
Duration of diabetes	0.138
HbA1c category	0.329
Hypertension	0.105
Ischemic heart disease (IHD)	0.002*
Chronic kidney disease (CKD)	0.026*
Peripheral neuropathy	0.0002*
Wagner grade	0.015*
Infection severity	0.540
Peripheral arterial disease (PAD)	0.036*
Ulcer duration	0.099
Gender	0.00021 (Males)
Ulcer site	0.195
Ulcer size (area)	Non-significant

Significant *

Table III. Univariate Odds Ratios for Predictors of Amputation

Variable	OR	95% CI	Interpretation
Ischemic heart disease (IHD)	0.29	0.13 – 0.65	Appears protective among patients without IHD who had more severe ulcers.
Chronic kidney disease (CKD)	0.48	0.21 – 1.11	Not statistically significant (trend).
Peripheral neuropathy	0.36	0.15 – 0.82	Significant
Peripheral arterial disease (PAD)	0.41	0.18 – 0.94	Significant
Male sex	0.03	0.00 – 0.55	Artifact
Rural residence	0.44	0.20 – 0.98	Significant
Wagner Grade 4–5 vs Grade 1–3	? (infinite)	Not estimable	Strongest univariate predictor.

Table IV: Penalized Multivariable Logistic Regression for Predictors of Amputation

Variable	Adjusted OR (penalized)	Interpretation
Age (per year)	0.99	NS
Male sex	0.16	NS after penalization (unstable)
Rural residence	1.00	NS
Hypertension	0.66	NS
Ischemic heart disease	1.00	NS
Chronic kidney disease	0.79	NS
Peripheral neuropathy	0.86	NS
Peripheral arterial disease	1.00	NS
Wagner grade (per grade)	2.53	Independent predictor

Note: Penalized L1 logistic regression was used; odds ratios are shrunk toward the null to address overfitting and separation. (NS: Not significant)

not recorded. Association of different variables with amputation is shown in table II. In table III univariate odds ratios as predictor for amputation and in table IV the multivariable logistic regression findings are reported.

DISCUSSION:

The observed amputation frequency of 75.4% among admitted DFU patients is substantially higher than pooled international estimates. A 2024 meta-analysis of patients with diabetic foot ulcers reported an overall lower-extremity amputation (LEA) rate of 31% (95% CI 25–38%).[7] Our study also found advanced stages of disease at presentation as evidenced by the high prevalence of Wagner Grade 4–5 ulcers (84%) and gangrene at admission. Global surveillance further suggests that diabetes-related LEA remains common and unevenly distributed, with persistently high rates in low- and middle-income countries (LMICs).[8,9]

Hospital based studies from Pakistan also report lower amputation rate than current study ranging from 21% to 48% depending on case-mix and setting,[10,11] and single-center reports from tertiary hospitals typically cite amputation in one-quarter to one-third of DFU admissions.[10] The markedly higher rate of amputation in our study may be due to other factors like patients with advanced disease are frequently referred to the public sector tertiary care hospital; a referral bias. In addition, delayed health-seeking behavior on part of patients and high prevalence of PAD being additional factors. The distribution of levels of amputations in index study are in conformity the pattern described in studies from Pakistani other tertiary settings with major amputations common performed in patients who presented late.[11]

An important observation in our study was relationship of gender with the frequency of amputation. All women in this study needed amputation. However, the international literature documents disparities in diabetes-related limb loss by socioeconomic status and access to care, sex-specific differentials are heterogeneous across

settings. This needs further exploratory studies to find the exact cause and thus targeted interventions may be planned.[12]

High HbA1c level, hypertension, duration of diabetes mellitus, smoking status, ulcer site, and size were not statistically associated with amputation in our dataset. This may reflect uniformly poor glycemic control and late stage of the disease with comorbid conditions at presentation that diminish the relative influence of these variables.[13,14] Among comorbid conditions the chronic kidney disease and peripheral neuropathy were the independent predictors of the amputation. Concomitant kidney disease contributes to impaired wound healing and immune dysfunction, while neuropathy predisposes to unrecognized trauma and persistent ulceration. These associations are well-established.[15,16]

Wagner grade showed the strongest association with amputation in our study consistent with evidence that tissue depth, bone involvement, and extent of gangrene strongly predict limb loss.[17,18] Similarly, infection severity was significantly associated with amputation, aligning with IDSA/IWGDF guidelines, that emphasize that moderate to severe infection and osteomyelitis markedly increase amputation risk.[19].

The IWGDF recommendations of early identification, prompt infection control, vascular assessment and revascularization when indicated, and multidisciplinary foot care pathways are associated with reductions in major amputations globally and should be prioritized in the clinical practices in Pakistan as well.[9] Strengths of this study include a relatively large cohort, comprehensive variable assessment, and the use of penalized regression to address data separation. The reconstruction of Wagner grading further ensured standardized comparison with international datasets. Future studies are indicated to find out the outcome of implementation of service-improvement bundle (screening, fast-track referral, PAD work-up / revascularization, standardized infection protocols) with repeated audits of amputation rates to decrease the rate of amputation across genders.

Limitations of the study: This was a single-center retrospective design with potential referral bias, incomplete documentation, and reliance on clinical rather than objective vascular assessment methods such as ABI or Doppler. The retrospective nature limits control over variable quality and completeness.

CONCLUSION:

Most patients in this study presented with advanced diabetic foot ulcers, with Wagner Grade 4–5 accounting for the overwhelming majority and driving the exceptionally high amputation rate. Although several comorbid conditions showed associations with limb loss in univariate analysis, ulcer severity remained the only independent predictor in multivariable modelling.

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