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Clinical Outcomes of Diabetic Foot Ulcer: A 5-year retrospective analysis at a Tertiary Referral Hospital in Ethiopia.

Principal investigator: Melaku Taye (Endocrinology Fellow)

A thesis to be submitted to the Department of Internal Medicine, College of Health Sciences, Addis Ababa University, in partial fulfillment of the subspecialty certificate in Endocrinology and Metabolism.

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ABSTRACT

Background

Diabetic foot ulcer is a common, serious, and costly complication of diabetes. It is the leading cause of non-traumatic lower extremity amputation carrying a high risk of morbidity and mortality. The clinical outcomes of diabetic foot ulcer in Ethiopia are not well studied. This study aimed to assess the outcomes of diabetic foot ulcer at tertiary care setting in Ethiopia.

Methods

A retrospective study conducted including all consecutive patients with diabetic foot ulcer admitted to a 642-bed tertiary hospital in Ethiopia from January 2018 to October 2022. Data were collected using a pretested, structured questionnaire. Then, the open data kit (ODK) completed form was exported and analyzed using SPSS version 25. Descriptive statistics were used to describe participants' characteristics. To identify determinants of lower extremity amputation, bivariable and multivariable binary logistic regression analyses were done. Statistical significance was considered at the level of significance of 5%, and adjusted odds ratio (AOR) with 95% confidence interval (CI) was used to present the estimates of the strength of the association.

Results

A total of 146 participants were included (79.5% were males, mean (±SD) age was 59.4 (±11.7) years). Glycemic goal achieved in 12.3% of patients while only 4.8% met their triple targets of blood glucose, blood pressure and lipids. Lower extremity amputation was performed in 53.4% of the patients with major amputation done for the overwhelming majority. In-patient mortality was 8.2%. Independent predictors of amputation were: long standing diabetes (duration ≥10 years: Adjusted Odds Ratio: 2.42; [95% Confidence Interval: 1.01-5.80]), longer ulcer duration before presentation (every week of delayed presentation: 1.14 [1.01-1.03]), history of previous foot ulcer (4.34 [1.55-12.13]), advanced ulcer stages with University of Texas stage C or D (2.86 [1.19-6.90]). There was statistically non-significant trend of increased risk of amputation with advancing age and insulin treatment.

Conclusion: the rate of lower extremity amputation in diabetic foot ulcer was excessively high. Long standing diabetes, ulcer duration, history of previous foot ulcer, and advanced ulcer severity were significantly associated with amputation. Prompt attention to these risk factors may reduce amputation rate among these patients. The high LEA rate in a low-income country indicates the mega-disparity in preventive and limb saving interventions reflecting the global health inequity that needs addressing.

Key words: diabetic foot ulcer, lower extremity amputation, retrospective review, Ethiopia.

1. INTRODUCTION

1.1. Background

Diabetes foot ulcers (DFUs) can be defined as a full-thickness wound (i.e, involving the subcutaneous tissue) below the ankle, or as a lesion of the foot penetrating through the dermis, in people with diabetes mellitus (1). They are complex, chronic wounds, which have a major long-term impact on the morbidity, mortality and quality of patients' lives (2).

DFU is one of the most common and disabling complication of diabetes mellitus that increases morbidity, mortality, and healthcare expenditures globally. Diabetic foot ulcers complicate the disease in more than 15% of people living with diabetes during their lifetimes with at least one limb being lost due to DFU somewhere in the world every 30 seconds. It is the leading cause of lower-extremity amputation and hospitalization. It has been demonstrated that lower extremity amputation is an independent strong predictor of mortality in diabetes. Treatment seems ineffective in preventing death as mortality rate at 5 years post diabetes-related amputation has been described as high as 74%, worse than most cancers (2–6).

In Africa, diabetic foot disease is a growing problem. The prevalence of DFU is reported to be between 4.5% and 18.7%. It has a high rate of in-hospital mortality (7). Several institution-based studies in Ethiopia also showed a high prevalence of DFUs ranging from 12.98-19.31% (8–10).

Diabetic foot ulcer can result in infection, gangrene, amputation, long-term disability, and even death. The outcomes are influenced by many factors, such as the severity and duration of the ulcer, the presence of infection or ischemia, the availability and accessibility of health care services, and the adherence to treatment guidelines (11–14).

DFUs can have a significant impact on patients' quality of life. Thus, DFU outcome assessment should also include consideration of the patients' subjective feelings. Assessment of the health-related QoL of patients is becoming steadily more important and should be an integral part of clinical evaluations of the prognosis of DFU and its complications (15–19).

DFU is also linked to significant financial outlays. The costs associated with the treatment of DFUs, including hospitalization, surgeries, medications, and ongoing care, are significant for both healthcare systems and individuals. The direct costs of DFU include medical expenses for

diagnosis, treatment, hospitalization, surgery, rehabilitation, and prosthetics. The indirect costs include productivity loss, disability, and social welfare (20–25).

In Ethiopia, due to the high incidence of diabetes and the limited resources available for prevention and control, diabetic foot ulcers (DFU) pose a serious health risk. Studies showed that DFUs significantly increase morbidity, disability, and healthcare expenses in Ethiopia (8–10,26).

This study was designed to obtain retrospective data on clinical outcomes of DFU and the individual and diabetes-specific factors influencing the clinical outcomes at tertiary care setting in Ethiopia.

1.2. Statement of the problem

DFU is a common, complex and costly complication of diabetes. It often results in amputations and increased healthcare costs. It is estimated that 19–34% of patients with diabetes are likely to be affected with a diabetic foot ulcer in their lifetimes, and the International Diabetes Federation reports that 9.1–26.1 million people will develop DFUs annually. This number is rising with increased longevity and medical complexity of people with diabetes (27,28).

Diabetic foot ulcers are more common in resource limited developing countries. The overall occurrence of DFUs in developed countries is 5% compared to higher magnitude in developing countries including 19.1% in Nigeria, 12.98% in Ethiopia. This indicates low-income country with limited resources has highest rates of DFU that worsen the outcomes of the diabetes (10,29).

Rate of lower extremity amputation (LEA) is the most important outcome of DFU studies globally. The LEA rates were quite different in the different countries with significantly higher rate in developing countries than developed nations. Between 2001 and 2010, the LEA rate of the hospitalized patients with DFU in the United States was approximately 16.5% (34.8% for major and 61.2% for minor amputations) (30). A study in China indicated that the overall LEA rate among the DFU patients was about 19.03%, with major and minor amputation rates of 2.14% and 16.88%, respectively (31). In Africa, about 15% of the DFU patients underwent major amputation (32). The prevalence rate of LEAs was 30.4% in Ethiopia and in Nigeria (33,34). This reflects the systematic yet modifiable healthcare disparity in preventive and limb saving interventions adversely impacting socioeconomically disadvantaged people in low-income countries.

Studies on DFU in Ethiopia mainly focused on incidence or preventive foot care behaviors. This study tried to assess the major clinical outcomes at Tikur Anbessa Specialized Hospital (TASH).

1.3. Significance of the study

This study is significant for several reasons. First, it will present up-to-date and thorough information on the clinical outcome of DFU at TASH, one of Ethiopia's biggest hospitals providing the only specialized ulcer clinic service. It will inform the improvement of practice and diabetes care standards contributing to addressing the burden of DFU at TASH and other comparable settings.

Additionally, it will help people with diabetes who have DFU or are at risk for developing it, as well as their families, caregivers, policymakers, researchers, and other interested parties in diabetic foot care.

2. LITERATURE REVIEW

2.1. Definition and overview of diabetic foot ulcer

Diabetic foot ulcer (DFU) is defined as a full-thickness wound below the ankle in a person with diabetes, regardless of duration. DFU can lead to infection, amputation, and death, and has a significant impact on the quality of life and health care costs of patients and society. Diabetes that has been uncontrolled for a long time can frequently result in diabetic foot ulcers, which are extremely morbid. Studies reported the lifetime risk of foot ulcer is 19-34%, and this number is rising with increased longevity and medical complexity of people with diabetes (28,35).

The foot does not ulcerate spontaneously. DFUs develop as a consequence of a combination of factors. Neurological, vascular, and biomechanical factors contribute to diabetic foot ulceration. In addition to these triads, impaired wound healing has been established as a key means of DFU progression (28,36).

Diabetic foot infections are common infections in patients with diabetes, frequently leading to severe complications and unfavourable outcomes. Treating diabetic foot infections is not easy as the blood flow is compromised and the antibiotics usually cannot reach the diseased area. If not treated promptly and appropriately, diabetic foot infections pose potentially disastrous progression to deeper tissue infections and septic gangrene which requires amputation (37,38).

2.2. Classification of DFUs

Classifying ulcers based on the degree of tissue loss, ischemia, and infection can help identify risk of limb-threatening disease. Numerous classification systems have been created to describe the severity, prognosis, and treatment choices of DFU in clinical practice.

Wagner's grading

This system evaluates the depth of the ulcer and the occurrence of osteomyelitis or gangrene. It was widely used for its simplicity, but its shortcomings include its lack of specificity, reliability, and does not take vascular status into account (39).

Wagner classification system

Grade	Ulcer depth
0	Pre-ulcerative area without open lesion/ Skin intact but bony deformities lead to "foot at risk
1	Superficial ulcer (partial/full thickness)
2	Deeper, full thickness extension/ Ulcer creep to tendon, capsule, bone
3	Deep/Stage 2 with abscess, osteomyelitis, or joint sepsis
4	Localized gangrene
5	Global foot/ Extensive gangrene

University of Texas (UT) grading and staging

The University of Texas (UT) suggested categorization system that evaluates ulcer depth horizontally and infection and ischemia states vertically, taking into account several common clinical signals and symptoms of DFU. This approach classifies DFU by depth (ranging from 0 to 3), then stages them according to whether or not they are infected or have ischemia (from A to D). The system's capacity to forecast outcomes and inclusion of more important parameters are its strengths, but its limitation includes complexity (39,40).

University of Texas classification system

	Grade 0	Grade 1	Grade 2	Grade 3

Stages	Pre- or post-ulcerative site	Superficial wound not involving tendon, capsule, or bone	Wound penetrating to tendon or capsule	Ulcer penetrating to bone of joint
Lesions without infection or ischemia (A)				
Infected/non-ischemic lesions (B)				
Ischemic noninfected lesions (C)				
Ischemic infected lesions (D)				

S(AD)SAD system

Developed primarily for clinical audits, the size (area, depth), sepsis, arteriopathy, and denervation [S(AD)SAD] method was first suggested in 1999. The method was initially validated in 2004, and afterwards other criteria that the UT system did not have were added in order to better clarify the classification of ulcers for future research. It consists of five components that are rated in grades 0–3 according to severity: size (area, depth), infection (sepsis), ischemia (arteriopathy), and neuropathy (denervation) (41).

Size (area, depth), sepsis, arteriopathy, denervation system

Grade	Size				
	Area	Depth	Sepsis	Arteriopathy	Denervation
0	Skin intact	Skin intact	None	Pedal pulses present	Pin pricks intact
1	< 1 cm^2	Superficial (skin and subcutaneous tissue)	Surface	Pedal pulses reduced or one missing	Pin pricks reduced

2	1-3 cm^2	Tendon, periosteum, joint capsule	Cellulitis	Absence of both pedal pulses	Pin pricks absent
3	> 3 cm^2	Bone or joint space	Osteomyelitis	Gangrene	Charcot

SINBAD system

The site, ischemia, neuropathy, bacterial infection, area, and depth (SINBAD) system was proposed as a simplified and improved version of the S(AD)SAD system to lessen the difficulties in clinical use brought on by the inclusion of more complicating criteria while maintaining the descriptions of ulcer characteristics to the greatest extent possible. The SINBAD system still has five components (area, depth, infection, ischemia, and neuropathy), and assigns a point value of 0 or 1 to each component to produce an evaluation scale with scores ranging from 0 to 6 to describe the severity of the condition. Except for normal clinical examinations, the improved system's simplicity and robustness allow for the collection of the required data without the use of specialized equipment (42).

Site, ischemia, neuropathy, bacterial infection, area, depth system

Category	Definition	Score
Site	Forefoot	0
	Midfoot and hindfoot	1
Ischemia	Pedal blood flow intact: At least one palpable pulse	0
	Clinical evidence of reduced pedal flow	1
Neuropathy	Protective sensation intact	0
	Protective sensation lost	1
Bacterial infection	None	0
	Present	1
Area	Ulcer < 1 cm^2	0
	Ulcer ≥ 1 cm^2	1
Depth	Ulcer confined to skin and subcutaneous tissue	0
	Ulcer reaching muscle, tendon or deeper	1

Total possible score		6

Wound, Ischemia, and foot Infection (WIfI) system

The dichotomy for ischemia in the existing systems does not have an adequate severity grading and cannot satisfy clinical criteria due to the increasing occurrence of neuroischemic ulcers. The Society for Vascular Surgery Lower Extremity Guidelines Committee introduced the Wound, Ischemia, and Foot Infection (WIfI) approach in 2014, which addressed the three major risk factors that may result in lower limb amputation: WIfI. The wound is scored on the basis of size, depth, severity, and predicted difficulty in attaining wound healing; ischemia is graded according to the ABI; and foot infection is graded according to the scope and depth of the wound. The three variables are given scores ranging from 0 to 3 (43).

Wound, Ischemia, and foot Infection system

Grade	Wound	Ischemia			Foot infection system
	Clinical features	ABI (mmHg)	ASP (mmHg)	Toe pressure, $TcPO_2$ (mmHg)	Clinical manifestations
0	No ulcer no gangrene	≥ 0.80	> 100	≥ 60	No symptoms or signs of infection. Infection present, as defined by the presence of at least two of the following items: (1) Local swelling or induration; (2) Erythema 0.5 cm-2 cm around the ulcer; (3) Local tenderness or pain; (4) Local warmth; and (5) Purulent discharge (thick, opaque to white, or sanguineous secretion)

1	Small, shallow ulcer(s) on the distal leg or foot; no exposed bone, unless limited to the distal phalanx	0.6-0.79	70-100	40-59	Local infection involving only the skin and the subcutaneous tissue exclude other causes of an inflammatory response of the skin (*e.g.*, trauma, gout, acute Charcot neuro-osteoarthropathy, fracture, thrombosis, and venous stasis)
2	Deeper ulcer with exposed bone, joint, or tendon generally not involving the heel; shallow heel ulcer without calcaneal involvement, gangrenous changes limited to digits	0.4-0.59	50-70	30-39	Local infection with erythema > 2 cm, or involving structures deeper than skin and subcutaneous tissues (*e.g.*, abscess, osteomyelitis, septic arthritis, and fasciitis), and no systemic inflammatory response signs
3	Extensive, deep ulcers involving forefoot and/or midfoot; deep, full-thickness heel ulcers with or without calcaneal involvement, extensive gangrene	≥ 0.39	< 50	< 30	Local infection with signs of SIRS, as manifested by two or more of the following: (1) Temperature > 38 °C or < 36 °C; (2) Heart rate > 90 beats/min; (3) Respiratory rate > 20 breaths/min or $PaCO_2$ < 32 mmHg; and (4) White blood cell count

	involving the forefoot and/or midfoot; full-thickness heel necrosis with calcaneal involvement				> 12000 or < 4000 cu/mm or 10% immature bands

ABI: Ankle-brachial index; ASP: Ankle systolic pressure; TcPO2: Transcutaneous oxygen pressure; SIRS: Systemic inflammatory response.

The perfusion, extent, depth, infection, and sensation (PEDIS) classification

The PEDIS Classification was developed by the International Working Group of the Diabetic Foot (IWGDF) in 2003 for clinical research purposes. It classifies DFUs according to five variables which are considered to be the most relevant pathogenesis of the development of DFU. While the PEDIS classification system is more objective and exact to assess DFU to predict the clinical outcome in research setting, applicability for routine clinical setting is limited (44,45).

Grade	Perfusion	Extent	Depth	Infection	Sensation	Score
1	No PAD	Skin intact	Skin intact	None	No loss	0
2	PAD, no CLI	< 1 cm^2	Superficial	Surface	Loss	1
3	CLI	1-1 cm^2	Fascia, muscle, tendon	Abscess, fasciitis, septic arthritis		2

4		>3 cm^2	Bone or joint	SIRS		3

King’s College of classification of diabetic foot ulcers

The King’s College Classification is a simple staging system. It is based on the types of clinical presentation of the diabetic foot-ulcer, cellulitis, gangrene and amputation. The advantage of this system is that it is simple to use and is useful for planning the appropriate treatment for each stage. Its disadvantage is that it has not been well-validated (46,47).

Stage	Description
Stage 1	Normal foot
Stage 2	High risk foot
Stage 3	Ulcerated foot
Stage 4	Cellulitic foot
Stage 5	Necrotic foot
Stage 6	Major amputation

In summary, classification of DFUs serves to improve communication amongst care providers and stratifies severity. Until now, more than 10 different systems have been developed to classify diabetic foot ulcers for daily clinical practice. However, no system has found universal acceptance and different centres of excellence use different classification systems. This indicates the complexity of DFUs and makes of comparison of studies very difficult.

2.3. Management principles of DFU

The nature and severity of the ulcer, as well as the patient's preferences and goals, determine the DFU therapy modality. The major goals of treatment are to facilitate recovery, guard against infection, maintain limb functionality, and lessen recurrence. Surgical debridement, reducing pressure from weight bearing, treating lower extremity ischemia and foot infection, and early referral for multidisciplinary care are first-line therapies for diabetic foot ulcers (48).

Wound care: The modality of wound care depends on the characteristics of the ulcer, resources available, expertise and patient preference. In order to promote healing, ward off infection, and lessen discomfort, various dressings, agents, or therapies are applied to the ulcer site. The two types of wound treatment are conventional (using materials like gauze, hydrocolloid, hydrogel, foam, alginate, and silver) and advanced (such as growth factors, skin substitutes, negative pressure wound therapy, hyperbaric oxygen therapy, electrical stimulation, and ultrasound) (49). The use of autologous minimally manipulated homologous adipose tissue (AMHAT) has also shown promising results in the treatment of DFUs. Several studies reported significant reductions in wound size and high rates of complete epithelialization following the application of AMHAT (50–52).

Infection control: infection can slow recovery, exacerbate tissue damage, and raise the possibility of death or amputation. Identification and treatment of the causing bacteria, removal of necrotic or diseased tissue, administration of topical or systemic antibiotics, and observation of the wound for indications of improvement or deterioration are all components of infection control. Based on the findings of the culture and sensitivity tests, the severity of the infection, the patient's allergies and comorbid conditions, and the local antimicrobial resistance patterns, antibiotics should be chosen (49).

Offloading: Offloading is the use of various tools or methods to reduce or eliminate friction or pressure at the ulcer site. By enhancing blood flow, oxygen supply, and tissue regeneration at the wound bed, offloading can improve healing. Total contact casts, removable cast walkers, half-shoes, felted foam, crutches, wheelchairs, and bed rest are examples of offloading devices. The ulcer's location, size, depth, infection state, patient compliance, and availability all factor into the selection of an offloading device (48,49).

Glycemic control: Due to the fact that hyperglycemia can hinder wound healing, increase inflammation, and make a person more susceptible to infection, maintaining normal blood glucose levels is crucial for controlling and avoiding DFU. Pharmacological interventions (such as insulin or oral hypoglycemic medications), dietary changes, physical activity, self-monitoring, and education can all help to regulate blood sugar levels (53,54).

Preventive education plays a significant role in DFU management. It entails educating patients on how to examine and take care of their feet, including regular foot washing, moisturizing if they have dry feet, nail care, and avoiding walking bare feet or wearing slippers with thin soles. Self-monitoring of the temperature of the skin on the feet may also be used to look for inflammation. The goal of a comprehensive intervention that also addresses clinicians may include patient education. The major goals of preventive education are to promote self-care behaviors and treatment compliance, increase patient and healthcare provider communication and collaboration, and increase understanding of the risk factors and complications of DFU. According to reports, preventing DFU is easy, doable, and highly effective when combined with patient education and intense nursing care (35,55).

The following table summarizes some of the main features of these treatment components:

Component	Objective	Examples	Factors affecting choice
Glycemic control	Prevent and manage DFU	Pharmacological agents, dietary modification, exercise, self-monitoring, education	Blood glucose levels, patient compliance, side effects

Offloading	Reduce or eliminate pressure or friction on ulcer site	Total contact casts, removable cast walkers, half-shoes, felted foam, crutches, wheelchairs, bed rest	Ulcer location, size, depth, infection status, patient compliance, availability
Infection control	Identify and treat causative microorganisms	Debridement, topical or systemic antibiotics	Culture and sensitivity results, severity of infection, patient allergies and comorbidities, local antimicrobial resistance patterns
Wound care	Facilitate healing, prevent infection, reduce pain	Conventional or advanced dressings, agents or therapies	Ulcer characteristics,

2.4. Common Outcomes of diabetic foot ulcer

Foot ulcers are a common, serious, and costly complication of diabetes.

2.4.1. Healing rate of DFU

The healing rate of DFU is defined as the percentage of ulcers that completely epithelialize or close within a specified amount of time. Depending on the study design, demographic, setting, intervention, and outcome measurement, the healing rate of DFU varies greatly. However, most studies show that DFUs heal less quickly than other kinds of chronic wounds (56).

A prospective observational 12-month follow up of the multinational Concordance in Diabetic Foot Ulcer Infection [CODIFI] study that included 400 participants to evaluate the incidence of wound healing, ulcer recurrence, lower extremity amputation, lower extremity revascularization and death demonstrated that the ulcer had healed in 45.5% individuals. It showed the adverse prognostic effect of limb ischemia, longer ulcer duration and the presence of multiple ulcers (57).

In the EURODIALE Study, a prospective cohort study of 1,088 diabetic foot ulcer patients across 14 centres in Europe, 23% of the patients had not healed after a year of follow-up. Older age, male

sex, heart failure, inability to stand or walk without help, end-stage renal disease, larger ulcer size, peripheral neuropathy and PAD were predictors of non-healing (58).

A retrospective study of 232 patients hospitalized with diabetic foot ulcer in Thailand from 2009-2013 showed that 82.1% of the admissions achieved complete healing (including minor amputations) at 12 months. Ulcer of the heel was predictive of non-healing (13).

A prospective observational study at a tertiary hospital in Ethiopia including 115 patients with diabetic foot ulcer found out that 69.57% of patients achieved healing. Higher Wagner grading, and inappropriate antibiotic use were predictive of non-healing ulcer (33).

2.4.2. Recurrence of DFU

Recurrence refers to the development of a new ulcer at the same or different site after a previous ulcer has healed. DFU has a high recurrence rate that rises over time. It is a serious outcome that affects the prognosis and quality of life of patients with diabetes (35).

The incidence of recurrence of DFU is high and varies depending on the duration and frequency of follow-up. A review of 19 studies evaluating the recurrence of ulcers, approximately 40% of patients with DFUs experience a recurrence within 1 year, nearly 60% within 3 years, and 65% within 5 years after DFUs healed (better known as remission) (28). Another review estimated that the cumulative incidence of recurrence was 8.5% at 6 months, 26.1% at 1 year, 41.1% at 2 years, and 59.8% at 3 years (59).

According to a systematic review and meta-analysis by a pooled estimate for recurrence rate including 49 studies globally showed high recurrence rates of diabetic foot ulcers (22.1% per person-year) with rates varying widely in different regions. Recurrence rate was 24.9% per py in Europe, 17.8% per py in North America, 16.9% per py in Africa and 17.0% per py in Asia , Turkey had the highest recurrence rate of 44.4% per py and Bangladesh had the lowest of 4.3% per py (60).

Risk factors for the recurrence of DFUs included male gender, smoking, longer duration of diabetes, and duration of previous DFUs. Plantar ulcers, diabetic peripheral neuropathy and peripheral artery disease also conferred higher risk for DFU recurrence (61). Plantar location, bone infection, poor diabetes control and elevated CRP define those at high risk for recurrence in the prospective follow-up analysis of the Eurodiale study (62).

The consequences of recurrence of DFU are severe and costly. Recurrence can lead to chronic wounds, infections, amputations, disability, depression, reduced quality of life, increased health care utilization, and mortality(59,61) .

2.4.3. Amputation of DFU

Amputation of DFU is the removal of part or all of a limb affected by DFU that cannot be healed or salvaged by other means. Amputation can be caused by a variety of disorders, such as gangrene, severe infection, and non-healing wounds. DFU has a high amputation rate that varies depending on the kind and degree of amputation. DM-related lower limb amputations are divided into major and minor amputations according to the plane of amputation. Major amputation refers to an amputation above the ankle when alleviation of the severe disease state through vascular remodeling, drug control, or minor amputation is not possible. Minor amputation refers to an open or closed local amputation with limited tissue excision, normally at the level of the ankle or below. Loss of a limb leads to enormous morbidity and many patients are not able to afford a prosthesis. Most remain disabled for life and lead a poor quality of life (63).

A prospective observational study carried out at the All-India Institute of Medical Sciences including 81 patients with DFUs demonstrated that 30% of patients had minor amputations and 21% underwent major amputations in six months. PEDIS score, poor glycemia, and presence of PAD were predictive of risk of amputations (64).

Several studies in China showed that the annual incidence and 7-year average incidence of amputation for DFU patients were 5.1 and 9.9% respectively. Major amputation was associated with previous amputation history, smoking, CAD, Wagner 5, ABI <0.4 and HbA1c (65,66).

Diabetes-related LEA rates have significantly declined in many Western countries (67,68). This is however not the case in many parts of Africa where DFU-related LEA rates are still very high (32,69).

2.4.4. Osteomyelitis and Infection of DFU

DFUs significantly increase the risk of foot infections including osteomyelitis. Infection can be caused by a variety of factors, such as poor wound care, immunosuppression, or multidrug-resistant organisms. Foot infection is a well recognized risk factor for major amputation in diabetic patients (70).

The osteomyelitis is one of the most common expression of diabetic foot infection, being present approximately in present in 10%-15% of moderate and in 50% of severe infectious process. Any bone in the foot can be affected by osteomyelitis of DFU, although the forefoot is the most frequently affected and has a better prognosis than the midfoot and hindfoot (71).

2.4.5. Hospital stays

Diabetic foot ulcers can require hospitalization for infections, ischemia, amputations or other reasons. The mean length of inpatient stay for ulcer-only, minor amputation, and major amputation was 13.3, 20.5, and 59.6 days, respectively (11,72).

According to the study in Korea, the degree of inflammatory reaction (ESR), recent blood glucose control (HbA1c), BMI, and significant vascular disease (CVA or CAD) at the time of hospital admission all had an impact on how long patients were in the hospital (73).

2.4.6. Mortality rate of DFU

A systematic review and meta-analysis of observational studies including 34 studies and 16 countries found that the overall mortality of DFU was high, with nearly 50% mortality within 5 years. Cardiovascular disease and infection were the two leading causes of death. The predictors of mortality were older age, CKD, PAD, presence of CVD and amputation (74).

A multi center study in Nigeria demonstrated high intra-hospital mortality (21.5%) among patients with DFU, with the majority of death occurring among those with advanced ulcers, bacteraemia, cardiac failure, and renal impairment (75).

The mortality outcome of a diabetic foot ulcer can be influenced by various factors. Older age, renal impairment and the presence of bacteremia were strongly predictive of mortality (76).

There is scarcity of data on hard outcomes of DFU in Ethiopia. In one study, the overall mortality rate was 21% and sepsis was the most identified cause (26).

2.5. Cost of Diabetic Foot Ulcer

Direct expenditures are expenses such as prescription drugs, bandages, antibiotics, surgery, hospitalization, rehabilitation, and other costs directly associated with the diagnosis, treatment, and prevention of DFU. The costs associated with the effects and repercussions of DFU on an individual and society, such as impairment, diminished productivity, presenteeism and absenteeism, caregiver burden, reduced quality of life, etc., are referred to as indirect costs. The

cost of DFU can vary according on the ulcer's size, length, degree of infection, propensity to heal, and frequency of recurrence. The cost of DFUs may vary with the interventions used to treat foot ulcers and management approaches (77).

A study from Canada estimated that the annual direct cost of DFU was $547 million (Canadian dollars) in 2011–2012. The average cost per patient with DFU was $21,371 for those who healed within 1 year and $53,694 for those who did not healor died within 1 year. The cost of DFU was comparable to that of stroke ($21,514) and higher than that of breast cancer ($13,026) (25).

A review os cost of DFU in Europe showed that the direct cost of gangrene in 2003 ranged from $ 3,352 to $ 8,818. Amputations cost an average of $ 15,046 in 2001 and $ 38,621 in 2005. Amputations' direct costs ranged from $13,842 in 2001 to $83,728 from 2005 to 2009. Amputation's indirect costs were more consistent, ranging from $1,043 to $1,442 (24). While in 2001, the US healthcare system recorded a US$10.9 billion expenditure towards diabetic foot care management and treatment (78). The total medical cost for the management of diabetic foot disease in the United States (US) ranges from US$9 to US$13 billion in addition to the cost for management of DM alone. Mean cost per patient-year was US $3368 (ulcer-only), US $10468 (minor amputation), and US $30131 (major amputation) (11).

The cost of treating a DFU in a lower-middle income Nigeria can range from US$113 to US$1,544. Antibiotics and analgesics were the main items purchased with the majority of this expense. Late-stage presentation, dressing, and surgical care were to blame for the higher procurement-related costs (79).

While all the above studies outline the financial impact of DFU, there are limited data available on cost analysis of DFU in low income countries including Ethiopia.

2.6. Conceptual Fram

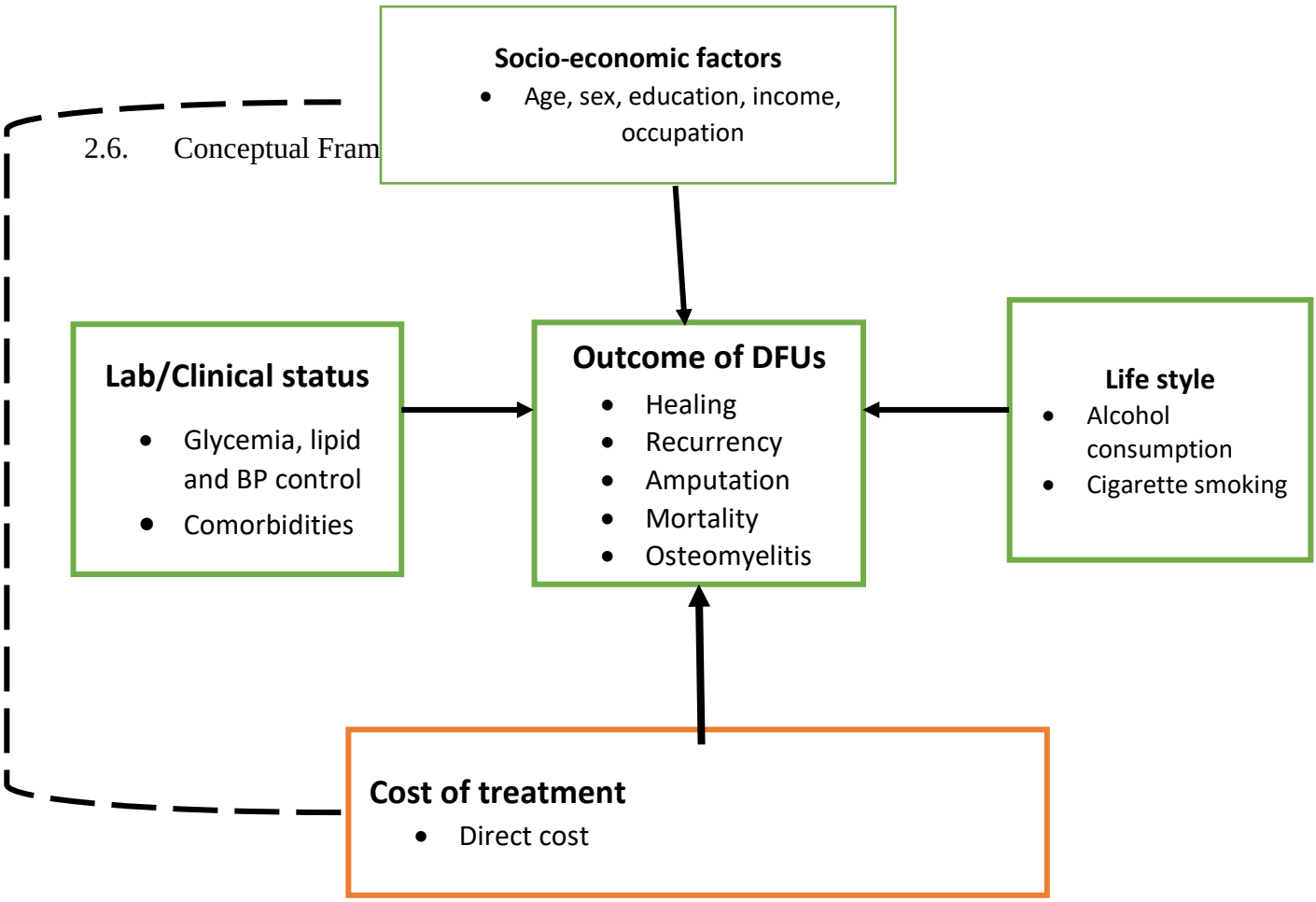

Figure 1. Conceptual framework Source

3. OBJECTIVES OF THE STUDY

3.1. General objective

- To determine the clinical outcomes of diabetic foot ulcer among people hospitalized with DFU at TASH, Addis Ababa, Ethiopia, 2018-2022.

3.2. Specific objectives

- To identify the incidence of clinical outcomes of DFU mainly lower extremity amputation among people hospitalized with DFU at TASH, Addis Ababa, Ethiopia, 2018-2022.
- To identify factors associated with lower extremity amputation among people hospitalized with DFU at TASH, Addis Ababa, Ethiopia, 2018-2022.

4. METHODS

4.1. Study setting

The study was conducted at Tikur Anbessa Specialized Hospital, located in Addis Ababa, the capital city of Ethiopia. This hospital is the largest tertiary care hospitals in the country, providing a specialized diabetes foot care. The study covered a period of five years, from January 2018 to October 2022 since the introduction of electronic medical recording.

4.2. Study Design

A hospital-based retrospective review of medical records of patients admitted with DFU and tracing their outcomes upto one year after the index ulcer requiring hospitalization.

4.3. Source and study population

The source population were all patients with diabetes diagnosed with DFU following at Tikur Anbessa Specialized Hospital during the study period. The study population were those patients with DFU who were hospitalized for DFU care.

4.4. Eligibility criteria

Inclusion criteria included: patients with a clinical diagnosis of DFU who have complete medical records available for the study period. Patients were excluded due to incomplete medical records or had ulcer above the ankle.

4.5. Sample Size Determination

All consecutive patients hospitalized for DFU care, either to medical or surgical ward, between January 2018 and October 2022 were enrolled.

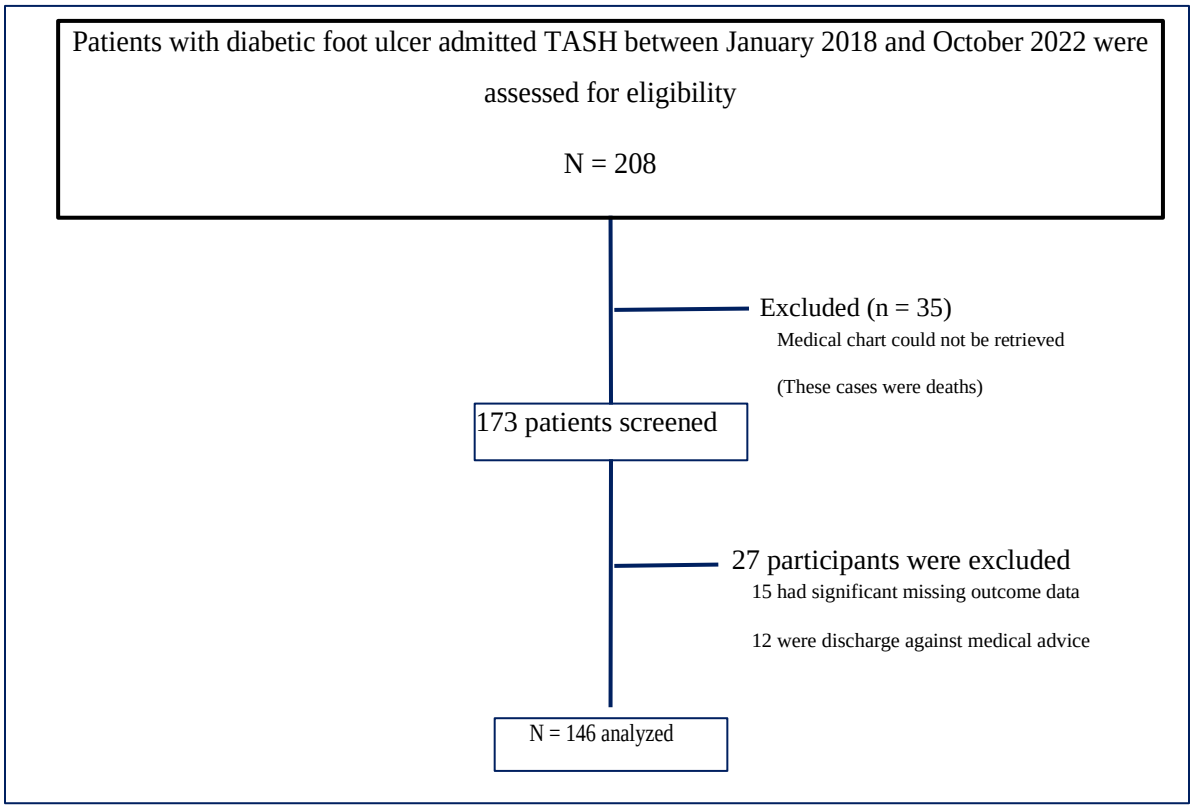

Figure 2. This flowchart shows the strategy to identify patients hospitalized with DFU for the study

4.6. Study variables

4.6.1. Outcome variables

- Primary outcome:
  - Lower extremity amputation status (minor, major amputations)
- Secondary outcome:
  - Ulcer remission
  - In-hospital Mortality
  - Infection rate including osteomyelitis

4.6.2. Explanatory variables

- Sociodemographic variables: age, sex, educational status, marital status, occupation, household income and residence.

- Life style factors: cigarette smoking, alcohol use
- Clinical and laboratory measures
- Comorbidities
- Types of treatments
- Local ulcer characteristics
- DFU-specific interventions

4.7. Data collection method and tools

ODK version 1.25.2 software was used to collect the data along with the KoboToolbox server to store the collected data. Four trained data collectors were involved in data collection.

Data was collected from patient medical records using a structured data extraction form. The form included sections for sociodemographic information, comorbidities, clinical and laboratory measures, treatment modalities, ulcer characteristics and outcomes.

4.8. Data Quality and management

Data quality was ensured by training data collectors, pre-testing the data extraction form, and conducting regular supervision and spot-checks during the data collection process. The collected data were checked for completeness and consistency on each day of data collection. Few missing data were imputed after checking the missing values process is random (MCAR test, $P = 0.591$).

4.9. Data processing and analysis

Data was analyzed using statistical software (SPSS version 25). Descriptive statistics was calculated to summarize key variables of participants' characteristics. Descriptive statistics included mean with SD and median with IQR for continuous variables, while frequency and percentage tables were used for categorical data.

Bivariable binary logistic regression analyses was done to assess the unadjusted association between potential predictors. Factors significantly associated with the outcome at $p<0.2$ was included in a multivariable regression model to determine the independent predictors of LEA using the Hosmer and Lemeshow test for goodness of fit. Statistical significance was considered at the level of significance of 5%, and adjusted odds ratio (AOR) with 95% confidence interval (CI) was used to present the estimates of the strength of the association.

4.11 Operational definitions

Amputation refers to the surgical removal of a limb or part of a limb due to the ulcer. It can be minor (removal of a toe or part of the foot) or major (removal of the entire foot or leg).

Ulcer remission refers to the complete closure of the ulcer without the need for further dressing.

4.12 Ethical approval

The study was conducted in accordance with ethical guidelines for medical research. Ethical approval was obtained from the research ethics committee of the department of Internal Medicine, Addis Ababa University approved the study. The data of the participants were anonymized.

5. RESULTS

5.1 Demographic characteristics

A total of 146 participants were included in this study. The mean (±SD) age of the participants was 59.4 (±11.7) years. One hundred sixteen participants (79.5%) were males. The majority of the respondents (75.3%), were urban residents. About two third of the patients (64.4%) paid out of pocket for the service. The details are shown in table 1.

Table 1 Demographic and socio-economic characteristics of people hospitalized with diabetic foot ulcer at TASH, Addis Ababa, Ethiopia, 2018-2022.

Variable (n = 146)	Number	Percent (%)
Sex		
Male	116	79.5
Female	30	20.5
Residence		
Urban	110	75.3
Rural	36	24.7
Current marital status		
Never married	6	4.1
Married	124	84.9
Divorced/separated	4	2.7
Widowed	12	8.2
Education level		
No formal education	32	21.9
Primary education	33	22.6
Secondary education	61	41.8
Higher education	20	13.7
Occupation		
Government employee	26	17.8
Private employee	55	37.7
House wife	17	11.6
Farmer	17	11.6
Retired	16	10.9
Others	15	10.4
Average monthly income (wealth quantile)		
Lowest	34	23.3
Second	27	18.5
Middle	26	17.8
Fourth	28	19.2
Highest	31	21.2

Mode of payment		
Out of pocket	94	64.4
Community-based health insurance	52	35.6

5.2 Clinical characteristics of the participants

The median duration of diabetes was 13.6 years with IQR (8, 17). A large share (n = 104, 71.2%) of the participants were diagnosed with diabetes more than 10 years prior while 5 patients (3.4%) were newly diagnosed diabetes. Eighty-eight (60.3%) of them had diagnosed hypertension. Thirteen (8.9%) patients had history of current or previous cigarette smoking. One hundred (68.5%) patients had established cardiovascular disease (ischemic heart disease, ischemic stroke and/or peripheral arterial disease). Chronic kidney disease affected 25.3% of the patients. Only four (2.7%) patients had type 1 diabetes.

A majority (n = 99, 67.8%) of patients were taking insulin, 83 (56.8%) were on metformin, 22 (15.1%) were using sulfonylurea and only a small proportion, 13 (8.9%), were prescribed SGLT2 inhibitors. Statins and aspirin were used in 119 (81.5%) and 105 (71.9%), respectively. Only 18 (12.3%) patients achieved the glycemic goal (HbA1c ≤7%). About half of them met their LDL-C ≤70 mg/dl (48.6%) and BP <130/80 mmHg (52.1%) targets. Only 4.8% achieve the triple targets. Table 2 summarizes the cardiometabolic factors.

Table 2. Clinical characteristics of people hospitalized with diabetic foot ulcer at TASH, Addis Ababa, Ethiopia, 2018-2022.

Variable (n = 146)	Findings
Age (years)	59.4 (±11.7)
Diabetes duration (years)	13.6 (8, 17)
Insulin treatment	99 (67.8)
Mean SBP (mmHg)	130 (119, 140)
Mean DBP (mmHg)	80 (70, 85)
Mean FBS (mg/dl)	158 (130, 181)
Hemoglobin A1c (%)	8.4 (7.8, 9.5)
Total cholesterol (mg/dl)	136 (116, 160)
LDL-C (mg/dl)	74 (60, 95)
HDL-C (mg/dl)	40 (30, 45)
Triglycerides (mg/dl)	120 (89, 162)
Ischemic heart disease	33 (22.6)
History of stroke	15 (10.3)
PAD	91 (62.3)
Peripheral neuropathy	109 (74.6)
CKD	37 (25.3)
Urine dipstick proteinuria, persistent	59 (40.4)
Retinopathy, any	19 (13)
Erectile dysfunction (males)	27 (18.5)

Data are means (±SD), median (Q1, Q3) or n (%).

5.3 Characteristics and outcomes of foot ulcers

The median duration of foot ulcer before admission was 30 (15, 42) days. Thirty-six (24.7%) had prior history of foot ulcer. The type of foot ulcer documented was neuro-ischemic (58.2%), ischemic (25.3%) and neuropathic (16.5%). The majority of ulcers (86.3%) had high Wagner grades (i.e Wagner grade ≥3). The University of Texas classification revealed that UT stages C

and D comprised 60.3% of the admissions. Almost all foot ulcers were invariably infected except 7 patients (4.7%). Osteomyelitis was reported in 13.7% of the patients based on foot x-ray evidence.

Lower extremity amputation (LEA) was performed in 53.4% of the patients with major amputation done for the overwhelming majority. The median length of hospitalization was 15 (10, 21) days. During hospitalization, 12 (8.2%) patients died.

Table 3. Diabetic foot ulcer characteristics and outcomes among people hospitalized at TASH, Addis Ababa, Ethiopia, 2018-2022.

Variables (n = 146)	Number (percent)
Types of foot ulcer	
Neuro-ischemic	85 (58.2%)
Ischemic	37 (25.3%)
Neuropathic	24 (16.5%)
Wagner grade	
Grade 1	2 (1.4%)
Grade 2	18 (12.3%)
Grade 3	67 (45.9%)
Grade 4	28 (19.2%)
Grade 5	31 (21.2%)
University of Texas stage	
Stage A	6 (4.1%)
Stage B	52 (35.6%)
Stage C	22 (15.1%)
Stage D	66 (45.2%)
DFU-specific treatment received	
Surgical revascularization	30 (20.5%)
Surgical debridement	74 (50.7%)
Lower extremity amputation	78 (53.4%)
Major amputation	66 (45.2%)
Minor amputation	12 (8.2%)
In-hospital mortality	12 (8.2%)
Ulcer remission (within one year of index ulcer)	38 (26.0%)

5.4 Risk factors for lower extremity amputation (LEA)

In this study, based on the p-value of the bivariable analysis, seven variables were identified as candidates for the multivariable analysis to assess the determinants of lower extremity amputation. These were age, duration of diabetes, glucose lowering therapy, duration of ulcer before hospitalization, history of previous ulcer, the ulcer's Wagner grade and University of Texas stage. Duration of diabetes, duration of ulcer before hospitalization, history of previous ulcer, and University of Texas stage were found to be an independent determinants of lower extremity

amputation among people hospitalized with DFU after adjusting for demographics, comorbidities, metabolic profile and ulcer characteristics. The findings are presented in table 4.

Long standing diabetes (duration ≥10 years) had significant association with amputation (AOR: 2.42; 95% CI: 1.01-5.80). Similarly, longer duration of ulcer before presentation was significantly associated with increased odds of amputation (AOR: 1.02; 95% CI: 1.01-1.03). A history of previous foot ulcer also conferred a four times higher risk of LAE (AOR: 4.34; 95% CI: 1.55-12.13). Besides, advanced ulcer stages (University of Texas stage C or D) were significantly associated with increased risk of amputation (AOR: 2.86, 95% CI: 1.19-6.90) but Wagner grades did not show a significant association to outcome.

There was statistically non-significant trend of increased risk of amputation with advancing age whereby getting older by a decade increased risk of LAE by 10% (AOR 1.10; 95% CI: 0.97-1.05). Relative to those taking oral glucose lowering therapy alone, patients taking insulin had a 2.8 fold higher unadjusted risk of undergoing amputation but this association did not remain statistically significant after adjustment (AOR: 2.41; 95% CI: 0.96-5.99).

There was trend towards fewer amputation in patients who had surgical revascularization (COR: 0.27, 95% CI: 0.109-0.689) compared with patients who did not have revascularization but this protective association in preventing amputation was lost after adjusting for the clinic-demographic factors.

The LEA rate did not differ significantly in relation to gender or other demographic factors, comorbidities (hypertension, PAD, other ASCVD, CKD, microvascular complications), metabolic profile (glycemic, BP or lipid control) or type of ulcer.

Table 4. Bivariable and multivariable binary logistic regression analysis results of factors associated with lower extremity amputation among people hospitalized with DFU at TASH, Addis Ababa, Ethiopia, 2018-2022.

Variable (n = 146)	Lower extremity amputation		COR (95% CI)	AOR (95% CI)
	No (n = 68)	Yes (n = 78)		
Age (years)	57.97 (±11.72)	60.67 (±11.64)	1.02 (0.99-1.05)	1.01 (0.97-1.05)
Duration of diabetes				
<10 years	27 (39.7%)	15 (19.2%)	1	1
≥10 years	41 (60.3%)	63 (80.8%)	2.76 (1.32-5.82)	2.42 (1.01-5.80)*
Glucose lowering treatment				
Oral therapy only	30 (44.1%)	17 (21.8%)	1	1
Insulin treatment (alone or with oral therapy)	38 (55.9%)	61 (78.2%)	2.83 (1.37-5.81)	2.41 (0.96-5.99)
Duration of ulcer before admission (days)	25.5 (14, 30)	30 (15, 60)	1.02 (1.01-1.03)	1.02 (1.01-1.03)*
Previous history of foot ulcer	6 (8.8%)	30 (38.5%)	6.46 (2.48-16.76)	4.34 (1.55-12.13)*

Wagner grade				
Grades <3	16 (25%)	4 (5.1%)	1	1
Grades ≥3	52 (75%)	74 (94.9%)	6.16 (1.96-19.40)	2.82 (0.71-11.21)
University of Texas stages				
Stage A-B	40 (58.8%)	18 (23.1%)	1	1
Stage C-D	28 (41.2%)	60 (76.9%)	4.76 (2.33-9.73)	2.86 (1.19-6.90)*

Data are mean (±SD), median (Q1, Q3) or n (%). * Statistically significant at P-value ≤0.05

6. DISCUSSION

Lower extremity amputation is one of the most important outcomes of DFU. In this study, LEA was performed in 53.4% of the patients with major amputation done for the overwhelming majority. Hospital-based data reported an amputation rate as low as 1.2% in Australia (80), 4.2% in Thailand (13), 5.1-9.9% in China (65,66), and as high as 27% in Singapore (81). In low-income countries, however, the incidence of LEA is very high with rate of 35.4-52.2% in Nigeria (34,69) and 30.4% in Ethiopian studies (33). The differences in amputation rates among studies are the result of global variations in the reported amputation rate due to differences in population and design of the studies, and the differences in severity. Additionally, inequality in access to optimized health care also contributes to the observed disparity (82).

In this study, four clinical factors showed an independent significant association with LEA rate: Long standing diabetes (duration ≥10 years), longer duration of ulcer before presentation, history of previous foot ulcer and advanced ulcer stages (university of Texas stage C or D).

The duration of diabetes showed a significant association with LEA. The majority of the patients (71.2%) had diabetes for longer than 10 years in this study, 80.8% of whom underwent LEA. Other studies showed similar findings that longer diabetes duration >10-15 years increases the risk for LEA (80,83). Similarly, patients who underwent LEA had significantly longer pre-hospitalization duration of ulcer with each week of delayed presentation increasing the risk of LEA by 14%. This finding is in agreement with few studies examining this variable (69,84). It is possible that late presentation to hospital due to delayed referral or fear of amputation might end up with complicated unsalvageable wound.

In this study, the previous history of foot ulcer was found to be an independent risk factor for amputation. There was an increase by four times in patients with a history of foot ulcer compared with first time ulcer. This was consistent with a large study in Turkiye (84) and Korea (85). Moreover, higher ulcer stage by the University of Texas classification (stage C or D), regardless of grade, was associated with increased risk of LEA. Advanced ulcer stages, the presence of infection and/or ischemia, significantly increased the risk of LEA by nearly three fold in this study. Several studies showed similar findings that amputation prevalence increased with an increasing wound stage with better association than wound grade (86–89).

Several studies including the large EURODIALE study and systematic reviews demonstrated that peripheral arterial disease was an independent risk factor associated with prevalent foot

complications in patients with diabetes and an independent factor related to amputation (58,84,90). In this study, however, PAD did not have such an evident influence on the outcome. The small sample size of this study might limit the statistical power to detect differences on the influence of PAD on LEA.

Demographic variables including age, gender, educational status, and household income were not associated with LEA rate. This observation was also seen in a large cohort of 2831 patients with diabetic foot ulcer where such demographic variables did not significantly predict amputation (90). A recent systemic review seven articles reporting on 3481 patients also confirmed an absence of any valid association between demographic factors and amputation (89).

The high LEA rate in a low-income country as depicted is this study indicates the mega-disparity in preventive and limb saving interventions. This reflects the systematic yet modifiable global health inequity adversely impacting socioeconomically disadvantaged people in low-income countries. While LEA poses a tremendous burden for any individual, it is more devastating for people from low-income countries. This calls for the need to address the disparities that exist in diabetic foot ulcer care.

7. STRENGTH AND LIMITATIONS OF THE STUDY

The use of relevant commands in ODK to obtain quality data, relatively long follow up period after index ulcer and comprehensive assessment of ulcer outcomes are among the strengths of this study.

The limitation of this study is that it is a single center study with a retrospective design affecting the generalizability of the results. Besides, the long-term outcome beyond one year was not included. In addition, the missing data of patients who died significantly underestimated the mortality outcome.

8. CONCLUSION

Over half of patients underwent lower extremity amputation reflecting the persistent substantial global health inequality in diabetes related LEA rate. The independent predictors of lower limb amputations include: Long standing diabetes, longer duration of ulcer, history of previous foot ulcer and advanced severity of ulcer stages. Patients who underwent LEA were older and more likely to be treated with insulin. However, the rate did not differ significantly with the presence of PAD. These patients identified as being at increased risk of LEA should be targeted for aggressive risk factor management to reduce limb loss.

9. RECOMMENDATIONS

Based on the findings of this study, the following recommendations are forwarded to the respective bodies.

Patients with diabetes

- Patients with diabetes especially those with longer duration of diabetes and previous history of foot ulcer are recommended to adhere to optimal foot care as an ulcer carries high risk of limb loss. They should also seek medical care early as delayed presentation risks amputation.

Clinicians

- All clinicians treating patients with DFU should identify individuals with high risk for amputation especially those with long standing diabetes, long ulcer duration, recurrent ulcers, and severe ulcers and optimize preventive care to save limbs.

Healthcare leaders and policy makers

- Devising strategy to reduce morbidity and mortality of lower extremity amputation by implementing multidisciplinary diabetes care.

Researchers

- Larger prospective studies recommended to identify potentially treatable patient-, clinician- and healthcare system-related factors predisposing to high-risk foot ulcers and the associated amputation.

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ANNEXES

Annex 1: Declaration

I, the undersigned, declare that this postgraduate thesis is an original work. All sources of material used for this thesis has been duly acknowledged.

Postgraduate candidate: Melaku Taye (MD, fellow)

Signature _____

Submission date _____

This thesis has been submitted with my approval as advisor.

Advisor: Dr Ahmed Reja (MD, Endocrinologist)

Signature _____

Date _____

Annex 2: Questionnaire

MRN_____interviewer name_____

Ser. No	Questions	Response and coding	
Section 1: demographic and socioeconomic data			
101	How old are you?	_____yrs	*
102	Sex	1. Male 2. Female	*
103	Where is your residence?	1. Urban 2. Rural	
104	What is your current marital status?	1. Single 2. Married 3. Divorced 4. Widowed	*
105	Which of the following best describes your main work status over the past 12 months?	1. Government employee 2. Self-employed 3. House wife 4. Farmer 5. Others (specify)…….	*
106	What is your level of education (highest grade completed)?	1. No formal education 2. Primary school 3. Secondary school 4. Higher education	*
107	What is your average household monthly income?	_____(Birr)	*
108	How much do you think you expend to the household in a month?	_____(Birr)	

109	How much do you think you expend for household food expenditure in a month?	_____(Birr)	
110	How much do you think you expend for household subsistence expenditure in a month?	_____(Birr)	
111	What are your sources of income?	1. salaries and wages; 2. income from a business; 3. remittances; 4. grants; 5. pensions; 6. income from farming; 7. income generated through rental income and interest. 8. Others _____	
112	Total household size	_____	
113	Mode of payment	1. Out of Pocket 2. Community insurance 3. Private insurance	*
Section 2: life style factors and comorbidities			
201	How long have you been diagnosed with diabetes?	_____ years	*
202	Type of diabetes	1. Type 1 2. Type 2	

202	Have you been diagnosed with hypertension?	1. Yes 2. No	*
203	Have you been diagnosed with ischemic heart Disease?	1. Yes 2. No	*
204	Did you have previous TIA or stroke?	1. Yes 2. No	*
205	Do you have peripheral arterial disease?	1. Yes 2. No	*
206	Do you have peripheral neuropathy	1. Yes 2. No	*
207	Document any other diabetes complications (e.g. microvascular or macrovascular complications)	Specify ----------	
208	Cigarette smoking	1. Yes____ 2. No___	
209	Alcohol intake	1. Yes____ 2. No___	
Section 3: clinical parameters			
301	Average BP	_____m mHg	*
302	Weight	---------- -- kg	
303	Height	_____ cm	
Section 4: lab tests			
401	HgA1c	_____ __%	*
402	Average FBS	_____ mg/dl	*
403	Total cholesterol		*

404	LDL-C		*
405	HDL-C		*
406	Triglycerides		*
407	Serum creatinine		*
408	Albuminuria	1. None 2. +1 3. +2 4. +3	*
Section 5: Current medications		Specify drug, daily dose	
501	antidiabetics		*
502	Antihypertensives		*
503	Lipid lowering agents		*
504	ASA		*
505	Others		*
Section 6: characterstics and outcome DFU*			
601	Prior history of foot ulcer (Recurrent)	1 No 2. Yes	
602	Duration of foot ulcer before admission	_____ days	
603	Location of ulcer	1. Toes 2. Plantar metatarsal head 3. Heel 4. Ankle 5. Other _____	
604	Types of ulcers;	0. Neuropathic, 1. Ischemic, 2. Neuroischemic	Date of DFU diagnosis ___/___/___
604	Presence of infection	1. Yes	

		2. No	
605	Grade of ulcer (Wagner)		
606	Stage of ulcer (Texas)		
607	Osteomyelitis	1 No 2. Yes	
608	Healed	1 No 2. Yes	Date healing diagnosed ____/_____/_____
609	Amputation	1 No 2. Yes	Date amputation done ____/_____/_____
610	If yes,	1 Minor amputation 2 Major amputation	
611	Mortality	1 No 2. Yes	Date of death ____/_____/_____
612	Hospital admissions	Data of admission _____ Date of discharge _____	
611	Length of hospital stay	_____ days	
612	DFU-specific treatment received	1 debridement, 2 antibiotics, 3 wound care/dressing, 4 revascularization 5 amputation	
613	Discharge against medical advice	1 No 2. Yes	

Section 7: direct medical cost of treatment during hospitalization * This is a series of questions related to how much money, your household spent during this hospitalization for this patient.			
701	Cost of registration and diagnostic tests (including blood tests, urine tests, wound cultures, imaging etc.)		
702	Cost of hospitalization (including admission fee, bed fee, nursing fee, etc.)		
703	Cost of procedures (including, amputation, debridement, surgery, skin grafting, etc.)		
704	Cost of medication (including antibiotics, analgesics, antidiabetics, etc.)_		
705	Cost of dressing materials (including gauze, bandages, ointments, etc.):		

Annex 3: Abbreviations and acronyms

ABI	Ankle Brachial Index
BMI	Body Mass Index
CAD	Coronary Artery Disease
CKD	Chronic Kidney Disease
CRP	C Reactive Protein
CVA	Cerebrovascular Accident
CVD	Cardiovascular Disease
DFU	Diabetic Foot Ulcers
DM	Diabetes Mellitus
ESR	Erythrocyte Sedimentation Rate
ETB	Ethiopian Birr
HbA1c	Hemoglobin A1c
LEA	Lower Extremity Amputation
ODK	Open Data Kit
PaCO2	Partial Pressure of Carbon Dioxide in Arterial Blood
PAD	Peripheral Arterial Disease
PEDIS	Perfusion, Extent, Depth, Infection and Sensation
QoL	Quality of Life
SAD	Sepsis, Arteriopaty, Denervation
SINBAD	Site, Ischemia, Neuropathy, Bacterial Infection, Area, and Depth
SIRS	Systemic Inflammatory Response Syndrome
SPSS	Statistical Package for the Social Sciences
TASH	Tikur Anbessa Specialized Hospital
TcPO2	Transcutaneous Oxygen Pressure
US	United States

USD	United States Dollar
UT	University of Texas
WIfI	Wound, Ischemia, and Foot Infection