

**Evaluation of Factors Causing a Delay in Management and Hospital Stay in Diabetic Foot Amputation Patients:
A Prospective Cohort Study**

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ABSTRACT

OBJECTIVE: To determine the rate of different amputation levels in diabetic foot patients and the incidence of repetitive foot surgeries and evaluate the factors causing a delay in hospital stay and amputation of patients.

METHODOLOGY: This prospective cohort study was conducted in Dr. Ruth K.M. Pfau, Civil Hospital Karachi, Pakistan. The study selected 375 participants from the daily patient inflow in the clinic between the period of October 2021 till March 2022 using a non-probability consecutive sampling technique. Those who had a delay in hospital stay and amputation were further followed up from May - October 2022. Chi-square test and Kruskal Wallis test (p-value <0.05) were used to correlate the effect of the level of lower limb amputation and the cause of delay in amputation using SPSS version 24.0.

RESULTS: Total 246(65.60%) were males and 129(34.40%) were females. Toe amputation was the most commonly seen amputation in 173(46.1%) participants. About 168(44.8%) patients had some in-hospital delay stay during their treatment. Preoperative hurdles (Uncontrolled RBS, Osteomyelitis, etc.) were the most common factor causing in-hospital delay in 92(24.5%) patients. The level of amputation performed was found to be statistically significant with factors causing a delay in hospital stay through chi-square (p=0.003*) and Kruskal Wallis test H (2) statistic= 13.3, df= 3, H (2), P=0.004*).

CONCLUSION: Diabetic foot is a frequent cause of amputation all over the globe, majorly in developing countries like Pakistan. On-time provision of treatment to these patients can decline the global amputation rate due to diabetic foot ulcers.

KEYWORDS: Lower limb amputation, Diabetic foot, Preoperative hurdles, Diabetic ulcer, Diabetes mellitus.

INTRODUCTION

The global health burden of the 21st century is Diabetes Mellitus(DM). According to Diabetes ATLAS 2019, issued by International Diabetes Federation (IDF), 463 million people worldwide between the ages of 20-79 years have diabetes, and the numbers are projected to rise to 700 million by 2045¹. Poorly controlled diabetes leads to widespread pathological changes in different organs due to microvascular and macrovascular complications of diabetes².

Diabetic Foot Syndrome is one of the most typical complications that can present early with loss of feet sensation. Progressively present with foot ulceration, osteomyelitis, and ultimately if left untreated, can lead to amputation. Different studies showed that the prevalence of diabetic foot ulcers in Pakistan ranged from 4.0% to 10.0%, and the amputation rate went dangerously high from 21.0%⁹ to 48.0%³. Globally, we lose one lower limb every 30 seconds because of diabetic foot ulceration. Around 68-90% of amputated diabetic foot patients have an increased mortality rate. About two-thirds of the patients with a history of diabetic foot ulcers present again with a foot ulcer in the next five years⁴.

Post amputation, the incidence of a new ulcer and/or contralateral amputation of the lower limb in the next 2-5 years is 50%. Limb amputation can lead to long-term physical, psychological and socioeconomic stress not only on the patient and their families but also on the hospital due to an extended stay and post-amputation rehabilitation⁵. Diabetic foot is the leading cause of hospital admissions, among other long-term complications of diabetes, and is responsible for nearly 50% of all diabetes-related hospital bed intakes. There is a 50% lifetime risk for a patient with diabetes to develop a foot ulcer⁴. A recent study from Pakistan published in 2020 has shown the mean total cost of below knee, fingers, and toe amputation to be 886.63±23.91, 263.35±19.58, and 166.68±8.47 US\$, respectively⁵. Another study from a private sector hospital in Pakistan has shown that the mean direct cost of major (transtibial or transfemoral) and minor amputations were PKR 46,182±30,742 (\$778±518) and PKR 50,494±30,488(\$851±514) respectively and \$479±319 and \$524±316 respectively in 2012 -2013³.

Pakistan is a developing country having many challenges related to the health economy. Diseases like diabetes, with only one complication (foot amputation), impact health budgets. The exact rate and projected cost nowadays would help to strategize better and improve the health-related economy, so the study will help to identify the factors for the delay in the management and the strategies to control the number of foot surgeries of diabetes in Pakistan. The long duration of an average length of stay in a hospital reflects the extra usage of hospital resources on a single patient. The current data on diabetic foot amputations and the total hospital stay of such patients is minimal.

Very few published studies have evaluated the total length of hospital stay and outcomes of patients with diabetic foot who underwent amputation. Accurate data on the factors that contribute to these needless delays in the in-hospital stay of such patients was not yet available. So, the primary objective of this study was to determine the rate of different levels of amputation in diabetic foot patients, their outcome at six months, and the number of repetitive foot surgeries and evaluate the factors causing a delay in hospital stay and amputation in our setup.

METHODOLOGY

This study was conducted at the Department of Internal medicine and Diabetic foot care clinic in Dr. Ruth K.M. Pfau, Civil Hospital, Karachi, Pakistan, after getting Approval from the institutional review board (IRB) of Dow University of Health Sciences (DUHS), Karachi (IRB no. 2021/549). The participants were selected from the daily patient inflow in the clinic between the period of October 2021 till March 2022 using a non-probability consecutive sampling technique. Those who had a delay in hospital stay and amputation were further followed up from May - October 2022 to evaluate the underlying delaying factors. The clinic is a well-equipped centre of the hospital, engaging around 100-200 diabetic foot patients daily.

Inclusion criteria for participants included: (1) Patients who recently underwent amputation due to diabetic foot complications or came for post-amputation follow-up. (2) Patients who were readmitted due to any post-amputation complication within one month after their surgery. (3) Patients older than 18 years and with a diagnosed diabetes mellitus according to American Diabetes Association guidelines.

Exclusion criteria included: (1) All those patients who underwent any amputation secondary to trauma, PVD, and malignancies. (2) Pregnant and lactating mothers. (3) Patients who got transferred to postoperative ICU for conditions other than diabetic foot immediately after their amputation. (3) Patients with any cognitive and hearing impairment.

The sample size was calculated using the Raosoft sample size calculator⁶ with an amputation rate in Pakistan of 21%³ at a 95% confidence level and 5% margin of error and was found to be 373.

$$SS=Z^2x(p)x(1-p)/c^2$$

Where,

Z= Z value =1.96 for 95% confidence interval

P = percentage

C=confidence interval

$$= (1.96)^2x(0.21)x(1-0.21)/(0.04)^2$$

$$= 373$$

Two participants were included in the middle of the study due to the loss of follow-up, and the final sample size was 375. All data was progressively updated in a separate electronic health record (EHR) base for follow-up. A self-prepared questionnaire containing 18 standard items was used to interview the participants and collect data. Two authors collected the data at separate times of the day to avoid the risk of bias. Standard values for all variables were used, which included demographic profile, duration of diabetes, history of smoking, comorbidities like Hypertension(HTN), Ischemic Heart Diseases(IHD), Chronic Kidney Disease(CKD), etc., Complete Blood Count(CBC) report, Hemoglobin A1c(HbA1c) levels, Random Blood Glucose(RBS) levels, the extent of ulcer involvement (Forefoot/ Fullfoot ulcer), level/type of amputation (Toe, foot, below the knee and above the knee), a total length of hospital stay (<2 weeks or >2 weeks) and the total number of amputations/surgeries performed.

Diabetic foot ulcer was defined, and its grading was done according to Wagner Meggitt's classification of diabetic foot (Grades 0-5)⁷.

Minor amputations were defined as amputations done at the level of forefoot, midfoot, and hindfoot⁸.

Significant amputations are performed above the ankle joint, below the knee, through the knee, above the knee, or hip disarticulation⁸.

The factors causing delay in-hospital stay were defined as:⁹

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- 1-Lack of health care facilities (trained diabetic footcare team, availability of operation date).
- 2- Preoperative hurdles and Change in patient's medical status (Uncontrolled RBS, Osteomyelitis, etc.).
- 3- Intermittent closure of elective surgeries due to COVID-19.

Data were analyzed using SPSS version 24.0. Cronbach's alpha test was used to check the data reliability. Mean \pm Standard Deviation (SD) was calculated for all the continuous variables. Descriptive statistics like frequencies and percentages were calculated for all the variables, and the confidence interval (CI) was calculated for different variables at 95%. The Chi-square test and Kruskal Wallis test were used to correlate the effect of the level of lower limb amputation and the cause of delay in amputation. A p-value of <0.05 was considered significant. To reduce the risk of bias, the two authors analyzed the data separately and interpreted the same results.

RESULTS

We evaluated a total of 450 patients' data for the study. Out of these, 75 participants were excluded due to incomplete reports and cause of foot amputation for reasons other than diabetic foot ulcer. Finally, 375 patients' records were selected for the study. Out of these 375 participants, 246(65.60%) were males and 129(34.40%) were females. The male-to-female ratio was around 3.8:2. Around 61 (16.27%) patients were less than 39 years of age, and 314 (83.73%) were above 40 years of age. A total of 147(39.2%) patients had a duration of diabetes between 0-9 years, 170(45.3%) patients between 10-19 years, 54(14.4%) patients between 20-29 years, and 4(1.1%) patients had a duration of 30 years or above. The mean duration of diabetes was 10-19 years. Toe amputation 173(46.1%) was found to be the most frequent type performed.

Descriptive statistics of study characteristics of participants can be seen in detail in **Table I**.

TABLE I: DESCRIPTIVE STATISTICS OF DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF STUDY PARTICIPANTS (n=375)

Characteristics	Frequency n (%)
Age	
<39 years	61(16.3%)
>40 years	314(83.7%)
Gender	
Male	246(65.6%)
Female	129(34.4%)
Total length of stay in hospital	
<2 weeks	189(50.4%)
>2 weeks	186(49.6%)
History of smoking	
Yes	139(37.1%)
No	236(62.9%)
Any Comorbidity	
Yes	273(72.8%)
No	102(27.2%)
If yes, then specify the Comorbidity	
Hypertension(HTN)	108(39.6%)
Chronic Kidney Disease(CKD)	13(3.5%)
Hepatitis B/C	18(4.8%)
Ischemic Heart Disease (IHD)	61(16.3%)
Others (Thyroid disorders, Stroke history, etc.)	12(3.2%)
CKD with HTN	19 (5.1%)
IHD with HTN	42(11.2%)
Patient's Hemoglobin (Hb) Level	
0-9 gm/dl	137(36.5%)
10-20 gm/dl	238(63.5%)
Random Blood Glucose (RBS) level	
0-99 mg/dl	12(3.2%)
100-199 mg/dl	132(35.2%)
200-299 mg/dl	139(37.1%)
300-399 mg/dl	76(20.3%)
400 mg/dl or above	16(4.3%)
Extent of involvement of ulcer at the time of amputation	
Forefoot ulcer	213(56.8%)
Full foot ulcer	162(43.2%)
Glycated hemoglobin (HbA1c) level	
<39mmol/mol (<5.7%)	32(8.5%)
39-46mmol/mol (5.7-6.4%)	251(66.9%)
≥47mmol/mol (≥6.5%)	92(24.5%)
Level of amputation performed	

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Toe amputation	173(46.1%)
Foot amputation	146(38.9%)
Below-the-knee (BKA) amputation	47(12.5%)
Above-the-knee (AKA) amputation	9(2.4%)
Number of amputations/surgeries performed	
First	281(74.9%)
Second	91(24.3%)
Three or above	3(0.8%)

Out of 375 patients, 168(44.8%) said they had some in-hospital delay stay during their treatment, while 207(55.2%) patients had no delay. Different factors that caused the delay were identified and can be seen in detail in **Table II**. Preoperative hurdles like uncontrolled RBS, infected wounds (Osteomyelitis), etc. (n=92) were found to be the most common cause that led to a delayed in-hospital stay of participants who had foot and below-the-knee (BKA) amputations specifically.

TABLE II: DESCRIPTIVE STATISTICS OF FACTORS CAUSING DELAY IN-HOSPITAL STAY OF PATIENTS FOR DIABETIC FOOT AMPUTATION (n=168)

Factors causing delay in-hospital stay	Frequency n (%)
Lack of health care facilities (Lack of a trained diabetic foot care team, lack of operation date availability), etc.	26(6.9%)
Preoperative hurdles like uncontrolled RBS, infected wounds (Osteomyelitis), etc.	92(24.5%)
Intermittent closure of elective surgeries due to COVID-19.	50(13.3%)

Table III Shows the correlation between different types of amputations performed in participants and other variables. Participants associated comorbidities were found to be statistically significant with the type of amputation performed ($p=0.006$). The mean Patient's HbA1c levels were between 6-10% (42-86 mmol/mol) and were found to be statistically significant with the amputation rate ($p=0.003$). Around 189(50.4%) patients had a total length of hospital stay of < 2 weeks, while 186(49.6%) patients had a total length of > 2 weeks. No significant correlation was found between the duration of hospitalization and the type of amputation performed ($p=0.51$). Results also showed that 213(57%) had a Forefoot extent of ulcer, and 162(43%) had a Full-foot extent. The extent of involvement of the ulcer was found to be statistically significant to the type of amputation performed. ($p=0.000$). Patients with a toe amputation initially presented with a forefoot ulcer, and those with a foot amputation or a major amputation primarily initially with a whole foot ulcer. There was a negative correlation between the type of amputation and the number of repetitive amputations/surgeries performed ($p=0.44$). The type of amputation performed was found to be statistically significant with the different factors causing delay in-hospital stay during the patient's treatment ($p=0.003$).

TABLE III: CORRELATION OF RATE OF DIFFERENT LEVELS OF AMPUTATIONS WITH CLINICAL AND LABORATORY VARIABLES

Variables	Toe amputation (n=173)	Foot amputation (n=146)	Below-the-knee (BKA) amputation (n=47)	Above-the-knee (AKA) amputation (n=9)	X ² (df, N)= p-value
Age					(3, N=375)
<39years	31	23	5	2	= 0.63
>40years	142	123	42	7	
Gender					(3, N=375)
Male	113	95	31	7	= 0.89
Female	60	51	16	2	
Total length of stay in hospital					(3, N=375)
<2weeks	87	77	19	5	= 0.51
>2weeks	85	69	28	4	
History of smoking					(3, N=375)
Yes	61	53	23	2	= 0.26
No	112	93	24	7	
Associated Co-morbid					(18, N=273) = 0.006*
HTN	41	47	21	0	
CKD	3	6	4	0	
Hepatitis B/C	9	7	0	2	
IHD	27	25	7	3	
Others (Thyroid disorders, stroke history, etc.)	9	3	0	0	
CKD with HTN	12	5	2	0	
IHD with HTN	15	24	2	1	
Patient's Hemoglobin (Hb) Level					(3, N=375)=
0-9 gm/dl	66	52	15	3	0.87
10 or above gm/dl	107	94	32	6	
Extent of involvement of ulcer at the time of amputation.					(3, N=375) =
Forefoot ulcer	163	37	5	0	0.000*
Full-foot ulcer	10	109	42	9	
Glycated hemoglobin (HbA1c) level					(6, N=375)=
<39mmol/mol (<5.7%)	30	22	2	2	

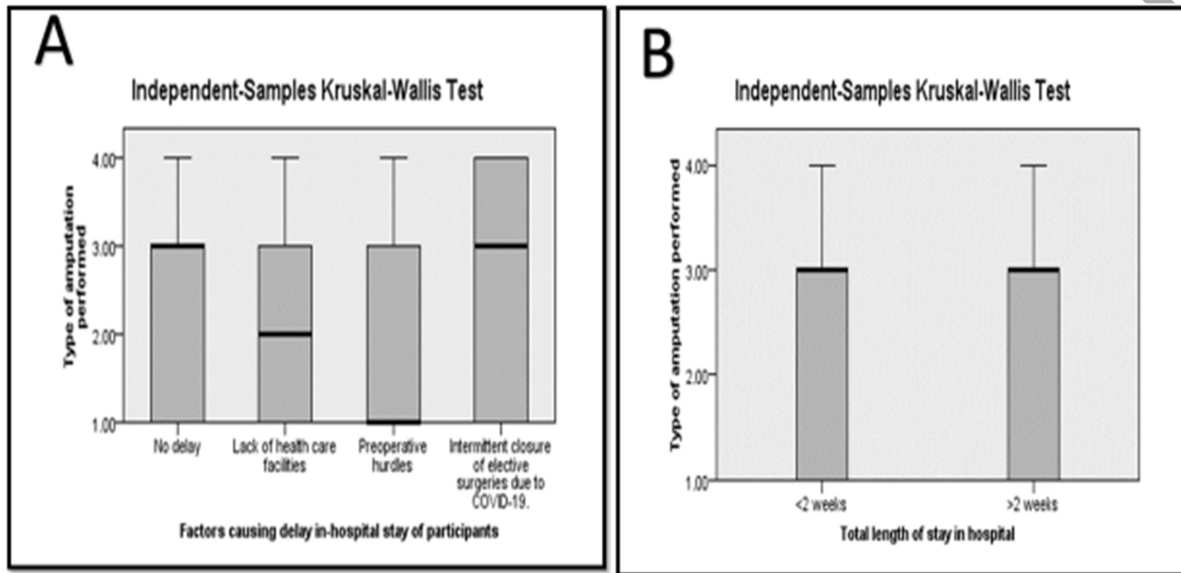
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39-46mmol/mol (5.7-6.4%)	83	85	23	5	< 0.003*
≥47mmol/mol (≥6.5%)	60	39	22	2	
Number of amputations/surgeries performed					(6, N=375) = 0.44
First	130	108	34	5	
Second	41	38	12	4	
Third or above	2	0	1	0	
Factors causing delay in-hospital stay					(9, N=375) = 0.003*
No delay.	98	84	20	4	
Lack of health care facilities.	12	11	1	2	
Preoperative hurdles.	49	31	11	1	
Intermittent closure of elective surgeries due to COVID-19.	14	20	15	2	

*Indicates statistically significant relationship at p-value <0.05

Kruskal-Wallis Test was conducted to compare the distribution of different types/levels of amputations performed and the factors causing delays in-hospital stay of participants. Statistically significant differences (H (2) statistic= 13.3, df = 3, H (2), P=0.004*) were found among the categories of participants (1.00= Toe amputation, 2.00= Foot amputation, 3.00= BKA amputation, and 4.00= AKA amputation) (see **Figure I-A**). The result also corresponds to our results of the independent Chi-square test for the same variables (see **Table III** above).

FIGURE I: KRUSKAL-WALLIS TEST BETWEEN THE TYPE OF AMPUTATION PERFORMED AND FACTORS CAUSING DELAY IN-HOSPITAL STAY OF PARTICIPANTS (FIGURE A) AND TOTAL LENGTH OF STAY IN HOSPITAL (FIGURE B). (CI= 95%)



However, no significant difference was found between the type/level of amputation performed and the total length of hospital stay of participants (1.00= Toe amputation, 2.00= Foot amputation, 3.00= BKA amputation, and 4.00= AKA amputation) with Kruskal-Wallis Test ($H(2) \text{ statistics} = 0.42, df = 1, p = 0.51$) (see **Figure I-B**). The result also corresponds to our results of the independent Chi-square test for the same variables (see **Table III** above).

DISCUSSION

The diabetic foot is the most common late complication of diabetes. It manifests a broad spectrum of symptoms and complications, initiating with loss of sensation in feet, progressive ulceration, gangrene, osteomyelitis, and most feared complication, amputation¹⁰. The feet of patients with diabetes are ignored not only by the patients themselves but also by the healthcare providers, leading to amputations and long-term hospitalization¹¹. Diabetes mellitus has become an epidemic in Pakistan as the country ranks within the top ten worldwide for having the most diabetic population; being a developing country, this high prevalence of DM, impaired glucose tolerance, and ultimately a high amputation rate and hospitalization duration commences a significant burden on the country's health care system¹².

Our study showed that toe amputation was the most frequent type in patients with long-term diabetes. Many previous studies have also supported our results. Jain AK et al.¹³ in their retrospective study on a total of 37 patients, also showed toe amputation to be the most frequent type in 24(64.9%) patients, trans metatarsal amputation (TMA) in 6(16.2%) patients, below the knee amputation(BKA) and above the knee amputation(AKA) in 5(13.5%) and 1(2.5%) patients respectively. Another study in Germany by Spoden, M et al.¹⁴ evaluated different levels of amputation from 2005 to 2015. Decreases were induced by higher amputation levels, whereas the amputation levels of toe/foot ray after standardization still showed a relative increase of + 12.8%.

Our results showed that increased HbA1c levels were a significant risk factor for amputation in patients. Pemayun, T. G et al.¹⁵ also showed the same results as our study that high HbA1c levels of >8% (64 mmol/mol) (p=0.002) are seen in the majority of patients undergoing lower extremity amputation due to diabetic foot ulcer.

Our data showed that around half of the patients (n=186) had greater than two weeks of hospitalization. This prolonged duration of hospitalization of such a considerable number of patients with diabetes turns out to be a substantial economic burden on the healthcare budget. Labeeq M et al.¹⁶, in their retrospective study, showed that the total cost of major amputations in a tertiary care hospital in Faisalabad, Pakistan was PKR 3,384,360 (\$27568.91), and for 22 minor amputations, was PKR 1,032,372 (\$8409.67). IN HIS STUDY, Kerr M et al.¹⁷ deduced that the cost of diabetic foot ulcer and amputation treatment in England utilizes 0.8-0.9% annual budget of the National Health Service (NHS). Their study also evaluated that the length of stay for patients with diabetes with ulcers was 8.04 days, much longer than for non-ulcer patients with diabetes. This concerning our country, which already has a fragile healthcare system, can be devastating as healthcare facilities have to be provided to these patients for much longer. Monge L et al.¹⁸ in their cohort study of 250,000 patients with diabetes, found that the 5-year incidence of hospitalization in patients of diabetes was 324 × 100,000 with major amputations and 343 × 100,000 with minor amputations. Concerning our country, which already has a fragile healthcare system, it can be very devastating as healthcare facilities have to be provided to these patients for a much longer duration.

In our study, we found that some patients who presented to the diabetic foot clinic already had a previous amputation and needed a repetitive amputation. In their research, Liu R et al.¹⁹ also found high incidence rates for both ipsilateral and contralateral repetitive amputation. At one year, the repetitive amputation rate for all contralateral and ipsilateral amputations was 19%, and at five years, it was found to be 37.1%. Murdoch DP et al.²⁰ showed that many patients who underwent a more significant toe or first-ray amputation required a repetitive amputation in the

first year following the initial procedure. The results also showed 60% of all patients had a second amputation, 21% had a third, and 7% underwent a fourth.

We also found a strong impact of the extent of ulcer involvement on the need for repetitive surgery/amputation. Malay DS et al.²¹ in his study also showed a similar result of a 63.87% failure rate to heal after 20 weeks of a previous lower extremity amputation (LEA) in patients who had an ulcer on the toe and metatarsal (forefoot) and a 67.11% failure rate to heal in those who had an ulcer from tarsal to hind foot (Full-foot).

Our study results showed that Preoperative hurdles like uncontrolled RBS, infected wounds, osteomyelitis, etc., were the most frequent cause of delay. A meta-analysis conducted in 2019 by Martínez JL et al.²² showed that osteomyelitis in a diabetic foot ulcer could lead to uncertainty between choosing medical or surgical treatment. Both methods of treatment are effective but have complications like the choice of appropriate antibiotic according to the causative organisms, increasing antibiotic resistance in medical management and increased cost, risk of operative Comorbidity, and unstable foot in surgical management, rendering it difficult for the physician to decide. Another study by Aragón-Sánchez J.²³ emphasized using a combination of conservative surgeries and antibiotics for osteomyelitis associated with complicated diabetic foot ulcers. Lack of health care facilities (Lack of a trained diabetic foot care team, Lack of availability of date for the operation, etc.) at the time of their amputation was also a significant cause of delay in the hospital stay in our results. A study held in Karachi, Pakistan, by Riaz M et al.²⁴ also showed that there was a baseline decline in the number of amputations in diabetic patients from 27.5% to 3.92% before and after the patients were cared for by a trained multidisciplinary foot care team (MDFCT) respectively. Another study conducted in Larkana, Pakistan, by Jokhio AL et al.²⁵ discussed the reasons for the cancellation of elective surgical procedures and found that 58% of cancellations were due to patient-related factors (uncontrolled diabetes, hypertension, anemia, etc.), 20% due to administrative faults, 18% due to surgeons and the rest were due to shortage of anesthetist. Lastly, we discussed the Impact of COVID-19 on delay in amputation and treatment of diabetic foot patients due to intermittent closure of elective surgeries. Our result was supported by recent literature. Ayyaz M et al.²⁶, in their audit study in 2020, showed that the total number of monthly elective surgeries in a tertiary care hospital declined from 1607 to 536 (66.62%).

There were certain limitations in our study. First, we selected the patient only from a single tertiary care hospital. However, it is one of the city's largest tertiary care hospitals, enrolling diabetic foot patients from broad socioeconomic backgrounds. Secondly, information on patients' lifestyles and adherence to their diabetes medications was not gathered, which may have been another risk factor for repeated amputations and in-hospital delays. Lastly, the step-down of patients from the clinic for rehabilitation and partial loss of follow-up due to COVID-19 restrictions made it difficult to assess the total duration of hospital stay accurately.

CONCLUSION

Our study showed that toe amputation is the most frequent amputation done in our setup. Factors that lead to an increased risk of amputations were associated with co-morbid conditions, the extent of involvement of ulcer at the time of amputation, and high HbA1c levels. Preoperative hurdles and changes in patient's medical status (Uncontrolled RBS, Osteomyelitis, etc.) were found to be the most common cause of delay and waiting for amputation/surgery in diabetic foot patients. In contrast, lack of healthcare facilities and intermittent closure of elective surgeries due to COVID-19 were found to be less common causes. The result of our study will be helpful in future randomized control trials and prospective cohort studies developing in the same area of study. We suggest that new modified guidelines and management protocols should be inducted to reduce the frequency of amputation/surgery and delay in-hospital stay in patients with a diabetic foot ulcers in tertiary care setups. On-time provision of treatment to these patients can decline the global amputation rate due to diabetic foot ulcers.

ACKNOWLEDGEMENT

We want to thank the diabetic foot care clinic staff in Dr. Ruth K.M Pfau, Civil Hospital, Karachi, for their coordination in the data collection process.

Ethical Permission: Dow University of Health Sciences (DUHS), Karachi IRB letter No. IRB-2193/DUHS/Approval/2021/549, dated: 24-09-2021.

Conflict of Interest: The authors have no conflict of interest to declare.

Financial Disclosure / Grant Approval: No funding agency was used for this research.

Data Sharing Statement: The data supporting this study's findings are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

AUTHOR CONTRIBUTIONS

Tahir SA: Concept, design, and Critical revision of the manuscript for important intellectual content

Bhatti S: Concept, design, and Critical revision of the manuscript for important intellectual content

Zill-e-Huma: Concept, design, Ethical Approval of the study, Analysis or interpretation of data

Khan MA: Acquisition of data, Analysis or interpretation of data, Writing and drafting of the manuscript

Rehman A: Acquisition of data, Writing, and drafting of the manuscript

Tahir S: Writing and drafting of the manuscript, Critical revision of the manuscript for important intellectual content

Abbasi A: Concept, design, and Critical revision of the manuscript for important intellectual content

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