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Original Research Article

A Study of the Risk Factors for Lower Limb Amputation in Diabetic Foot: A Single Centre Experience

Rajeshkumar Mahey[1], Sudatta Waghmare[2], Arjav H Nanavati[3], Tejas P Narkhede[4]*, Abhi H Kothari[5], Praveen Kumar[6]

[1]Associate Professor, Department of General Surgery, Topiwala National Medical College and B Y L Nair Hospital, Mumbai, India

[2]Assistant Professor, Department of General Surgery, Topiwala National Medical College and BYL Nair Hospital, Mumbai, India

[3]PG Resident, Department of General Surgery, Topiwala National Medical College and B Y L Nair Hospital, Mumbai, India

[4]PG Resident, Department of General Surgery, Topiwala National Medical College and B Y L Nair Hospital, Mumbai, India

[5]PG Resident, Department of General Surgery, Topiwala National Medical College and B Y L Nair Hospital, Mumbai, India

[6]PG Resident, Department of General surgery, Topiwala National Medical College and B Y L Nair Hospital, Mumbai, India

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Corresponding author: Dr. Tejas P Narkhede

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Abstract:

Introduction- Diabetes is a global health crisis, which results in major economic consequences for patients, their families and society. More than 415 million people are diagnosed with diabetes worldwide. This number is rapidly increasing and is expected to reach 640 million by 2040. About 15% of diabetics develop a foot ulcer and 12-24% of them require amputation, making diabetes a predominant aetiology for non-traumatic lower extremity amputations.

Methodology- In this study, 75 cases of patients with diabetic foot, who were admitted and treated were considered with due consent. It is a prospective observational study conducted at a tertiary care centre for 1 year.

Discussion- In our study, 40 out of 75 patients underwent amputation. The mean age group of our study was between the 5th and 7th decade with a male preponderance. Several factors were studied to find the statistical significance leading to amputations. Important risk factors for amputation in patients of diabetic foot identified as per our study were chronicity of diabetes mellitus, poor glycaemic control, foot deformity, higher Wagner's grade (IV, V) and presence of infection, neuropathy and vasculopathy.

Conclusion- Patients of diabetic foot ulcer presenting with one or more of the above risk factors should undergo a thorough evaluation, vigilant surveillance, strict glycaemic control with aggressive treatment and adequate patient counselling to prevent them from undergoing an amputation. To avoid amputation, a multidisciplinary approach is of prime importance in effectively managing patients with diabetic foot ulcer

Keywords- Lower Limb Amputation, Diabetic foot ulcer, neuropathy, vasculopathy

Introduction

Diabetes is a global health crisis. More than 415 million people are diagnosed with diabetes worldwide. This number is rapidly increasing and is expected to reach 640 million by 2040 (Ogurtsova et al.). Diabetes is the most common cause of foot ulcers, infection, and ischemia, causing hospitalisation (Gemechu et al.). This increases the burden not only on the individual but also on families and society. About 15% of diabetics develop a foot ulcer and 12-24% of them require amputation, making diabetes a predominant aetiology for non-traumatic lower extremity amputations (Pscherer et al.; Pemayun et al.; Shahi et al.)

Previous studies have reported a high mortality rate in diabetic patients with amputation. Amputation rates are 15-20 times higher in the case of diabetics (Nouvong and Armstrong). Mortality rate varies depending on the number of risk factors. Despite the presence of well-defined risk factors for diabetic foot ulcer development, there are limited data available for factors that predict amputation in a diabetic foot. [1-5]

We conducted this study to analyse the risk factors leading to lower limb amputation in the diabetic foot. The knowledge of these risk factors for amputation can help us formulate a strategy for the prevention of amputation in newly diagnosed patients with a diabetic foot ulcer. [6]

Methods and Materials

It is a prospective observational study consisting of 75 diabetic foot patients, conducted at the tertiary care centre. Patients who were admitted for lesions of the lower limbs such as cellulitis, ulcer, or gangrene with diabetes were considered for the study. Patients, who had secondary ulcers like syphilitic or malignant ulcers, pregnant females and patients less than 18 years of age or on cytotoxic/chemotherapeutic drugs were excluded from the study.

The wound was examined with respect to size, location, presence of oedema and pus and local temperature. Peripheral vascularity was assessed by ultrasonography doppler and ankle-brachial index. Peripheral neural examination for neuropathy was done by testing vibrations with a tuning fork and superficial touch sensation using Von Frey monofilament. Assessment of blood sugar levels was done using fasting and post-prandial sugar levels. A liver function test, renal function test, urine sugar and urine ketones were done. A local part X-ray was carried out to rule out osteomyelitis/Charcot's foot. Wound swab was cultured for sensitivity from patients with ulcer, abscess, and gangrene. The patients were observed till their discharge/amputation. After discharge, patients were called for a regular weekly check-up, for up to 1 month wherein their glycaemic control and wound healing status was charted.

Statistical Analysis

All the collected data were entered in Microsoft Excel sheet 2007. The data were transferred and analysed using SPSS ver. 21. Continuous variables were expressed as mean (standard deviation) and categorical variables as a percentage of several cases. The logistic regression method was used to determine independent predictors of poor outcomes. Various risk factors were initially assessed with univariate analysis, and statistically significant variables ($p< 0.05$) in the univariate analysis were included in multivariate analysis with forward conditional elimination of data. Continuous variables were entered into the model as continuous variables and categorised as categorical ones. Data was presented with 95% confidence intervals (CIs). A two-tailed P-value<0.05 was considered significant. Therapeutic efficacy was for healed wounds or wounds

having healthy granulation tissue. A correlation between various wound parameters, patient factors, their management and the incidences of amputations was calculated.

The presentation of the categorical variables was done in the form of numbers and percentages (%). On the other hand, the quantitative data were presented as the mean±SD and as the median with 25th and 75th percentiles (interquartile range). The following statistical tests were applied to the results:

1. The association of the variables which were quantitative was analyzed using an independent t-test.
2. The association of the variables which were qualitative was analyzed using the Chi-Square test. If any cell had an expected value of less than 5 then Fisher's exact test was used.

For statistical significance, p-value of less than 0.05 was considered statistically significant.

Results

Out of the 75 patients in the study, 58 patients were male whereas 17 were female, depicting a male preponderance. Most of the patients were in the age group of 40-50 years. A total of 40 patients required amputation. The most common mode of presentation for patients who underwent amputation was Cellulitis (92.5%).

Table 1: Association of Random Blood Sugar Levels and Duration of Diabetes with Amputation

Random blood sugar levels	Patients with amputation (n=40)	Patients without amputation (n=35)	Total
< 200	7	18	25
>200	32	17	50
Mean ± SD	271.4 ± 88.32	215.37 ± 83.27	245.25 ± 89.94
Range	108-457	98-505	98-505
Duration of diabetes mellitus(years)			
< 6years	6	29	27
> 6 years	34	6	40
Mean ± SD	10.47 ± 5.52	3.8 ± 2.83	7.96 ± 5.79
Range	1-25	0-16	0-25

X-rays showed bony deformities with osteomyelitis changes in 57.5% of patients and were found to be statistically significant. Wound culture analysis was suggestive of gram-negative bacterial growth in 82.5% of patients.

Table 2: Association of Foot Deformity with Amputation

X-ray findings	Patients with amputation	Patients without amputation	Total	P-value
Normal	17	31	48	<.0001
Deformity	23	4	27	
Total	40	35	75	

On further examination, sensory and vascular impairment was found in 50% and 47.5% respectively. Doppler was suggestive of biphasic and monophasic waveforms implying impaired blood flow in 75% of patients with amputations.

Table 3: Association of Sensory Examination and Peripheral Pulses with Amputation

Sensory examination	Patient with amputation	Patient without amputation	Total	P-value
Normal	20	30	50	0.001
Impaired	20	5	25	
Total	40	35	75	
Peripheral pulses				
Normal	21	27	48	0.027
Feeble/ Absent	19	8	27	
Total	40	35	75	

On multivariate analysis, factors that were statistically significant for amputation were the duration of diabetes (6 years) (p-value<0.0001; mean ± SD 7.96 ± 5.79), random blood sugar(mg/dL) above 200 (p-value=0.006; mean ± SD ± 245 ± 89.94), presence of X-ray deformity (<0.0001) and Wagner's classification of IV, V (p = 0.0001).

Table 4: Association of Wagner's Grade with Amputation

Wagner's grade	Patients with amputation	Patients without amputation	Total
0	0	9	9
I	0	1	1
II	7	8	15
III	9	11	20
IV	20	6	26
V	4	0	4

Gram-negative infections with the most common being pseudomonads, *E. coli* and *Klebsiella*, impaired sensory examination (p-value=0.001) and impaired vascular status as evident with abnormal peripheral pulses (p-value=0.027) were found statistically significant. Ankle-Brachial Index < 0.9 (p-value=0.0001; mean ± SD 0.9± 0.3) and USG doppler suggestive of the monophasic waveform (p = 0.001) were significant risk factors for amputation statistically.

Table 5: Association of USG Doppler Findings and Peripheral Pulses with Amputation

Doppler waveform	Patients with amputation	Patients without amputation	Total
Normal doppler	10	20	30
Biphasic	15	13	28
Monophasic	15	2	17
Total	40	35	75
Doppler Changes			
Normal	3	5	8
Atherosclerotic	10	9	19
Atherosclerotic + oedema	10	3	13
Oedema	17	18	35
Total	40	35	75

Patients presenting with ulcer or gangrene in addition to the modes of presentation had a significantly higher risk of amputation (p-value=0.003 and p-value<0.0001, respectively). The most prevalent addiction amongst the population was tobacco

consumption (p=0.951), with the most common comorbidity associated being hypertension. Age, gender, level of HbA1C, WBC levels, addiction, comorbidities, and history of amputation had no significant association.

Discussion

In our study, the amputation rate was 53.3%. The mean age group of our study was between the 5th and 7th decade with a male preponderance. Several factors were studied to find their statistical significance leading to amputation, which was shown by multivariate analysis. These were chronicity of diabetes mellitus, poor glycaemic control, presence of foot deformity, higher Wagner's grade (IV, V) and presence of infection, neuropathy and vasculopathy. [7,8]

A study done by Lin et al. showed very wide differences in the incidence of lower extremity amputation in the literature (ranging from 10.02% to 58.85%), and the total incidence rate was 30.84%. The literature shows that amputation rates in diabetic feet range from approximately 18.2 % (Pscherer et al.) to as high as 50.6 % (Chaudhary et al.). The amputation rates vary as per the design of the study. The high amputation rate in our study was attributed to a greater number of patients presenting with high Wagner's grade, being a referral centre for complex diabetic foot surgery. [9,10]

Poor glycaemic control in the form of random sugars more than 200 mg/dl was found to be a significant risk factor for amputation as uncontrolled sugars provided a favourable environment for bacterial growth. This was accentuated by the chronicity of diabetes which was found as a statistically significant factor for amputation. A study by Shojaiefard et al. showed that the mean of random blood sugar in patients with amputation was 264.53 ± 96.00 mg/dl and in patients with non-amputation it was 285.71 ± 91.81mg/dl (p-value = 0.744). These results were like the findings of our study. Both conditions cause accelerated atherosclerosis and further reduce the blood supply to the wound, thus reducing the healing of the ulcer. [11]

Diabetes causes neuropathy and vasculopathy leading to repeated trauma and the presence of a neglected wound due to loss of pain sensation**.** This neuropathic foot is further complicated due to the impaired vascular status of the patient as evidenced by ABI. In our study, the proportion of patients with Ankle-Brachial Index <0.9 was significantly higher in patients with amputation compared to patients without amputation. ABI of 0.9 to 1.3 was considered normal. An ABI <0.9 is suggestive of arterial occlusion, <0.5 signifies rest pain and <0.3 signifies imminent necrosis. An ABI of > 1.3 was seen with calcific arteries owing to their incompressibility. Thus, the lower the ABI value, the more the arterial occlusion. The more the occlusion, the less the blood supply, hence contributing more to the chronicity. The proportion of patients with feeble or absent peripheral pulses was significantly higher in patients with amputation compared to patients without amputation (p-value=0.027). A study done by Mehraj et al. showed that 62.8% had absent or diminished peripheral pulses.

Table 6: Multivariate Analysis of the Risk Factors for Patients with and without Amputations

Parameters	P-value
Duration of diabetes	<0.0001
Bony deformity	<0.0001
Wagner's grades 3,4 & 5	<0.0001
Impaired sensory status	<0.001
Impaired peripheral vascularity	<0.001

On further investigation using ultrasonography doppler, the presence of monophasic waveform was significantly higher in patients with amputation. This indicated reduced and restricted blood flow to the limb. A study done by Wu et al. showed that univariate predictors of lower limb amputation were ulcer duration more than 1 month prior to hospitalization ($P<$ 0.001), peripheral arterial disease ($P<$ 0.001), Wagner grade ≥ 4 ($P<0.001$), wound infection (P 0.041), proteinuria (P 0.021), leucocytosis (P 0.001) and osteomyelitis ($P < 0.001$). On multivariate regression, only three variables emerged as significant independent predictors of lower limb amputation and these include ulcer duration of more than 1 month (O.R. 10.3, 95% C.I. 4.055-26.132), peripheral arterial disease (O.R. 2.8, 95% C.I. 1.520-5.110) and presence of osteomyelitis (O.R. 5.6, 95% C.I. 2.930-10.776). [12,13]

In our study, the distribution of addictions was comparable between the two. Despite tobacco consumption being a confounding factor and the most common addiction in the populations, there was no statistical significance in addiction and amputations. [14]

In literature, a high Wagner's grade and the presence of bony deformity were found as major predisposing factors for amputation. The deeper the wounds and deformities, the more the chance of osteomyelitis and well-established gram-negative infection with bone involvement. In our study, a high Wagner's grade and the presence of gram-negative bacterial infection was found as a statistically significant factor for predicting the risk of amputation. A study done by Namgoong et al. showed that patients with gram-negative bacteria grown on wound culture had a significantly higher rate of amputation, a result that was like our study's finding. The study done by Neto et al. showed that the presence of deformities, ulceration and amputation was recorded in 45.9%, 25.3% and 12.9% of patients respectively. The predictors for diabetic foot were male gender and the presence of neuropathy. In addition, studies done by Guo et al. and Chuan et al. reported amputation rates greater than 25% in diabetic foot ulcer patients. [15]

The strength of our study lies in the fact that as a prospective study, follow-up of patients was observed. Since the study was conducted in a single centre, the sample size was limited with a possibility of selection bias. Being a tertiary health care centre, this was a centre for referral of complex diabetic foot surgery with a high Wagner's grade, hence the result might not apply to populations at the primary health care centre. Further studies with a larger population are required to validate the results of this study. [16]

Conclusion

Lower extremity amputation is the most serious and costliest complication of diabetic foot ulcer. Chronicity of diabetes mellitus, poor glycaemic control, presence of bony deformities, high Wagner grade ulcer, infected wound at the time of presentation and presence of neuropathy and vasculopathy are important risk factors predisposing for amputation in diabetic foot ulcer. Patients with one or more of the above risk factors should undergo a thorough evaluation, aggressive management, and vigilant surveillance. To prevent amputation, a multidisciplinary approach consisting of an endocrinologist, general surgeons, and occupational and physiotherapists working as a team is of prime importance.

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