ORIGINAL RESEARCH

Evaluation of the risk factors leading to lower extremity amputations in patients with diabetic foot

Dr. Akash Tilwani[1], Proff. Dr. Vineet Choudhary[2], Dr. Himanshu Lambora[3], Dr. Alisha Sheikh[4], Dr. Gaurav Raj Singh[5]

[1,3,4,5]P.G. Resident, [2]Professor, Department of General Surgery, National Institute of Medical Science, Jaipur, Rajasthan, India

Corresponding author
Dr. Akash Tilwani
P.G. Resident, Department of General Surgery, National Institute of Medical Science, Jaipur, Rajasthan, India

ABSTRACT
Background: A considerable number of diabetic foot ulcer (DFU) patients require amputation every year, which worsens their quality of life, aggravates the social burden, and shortens their life expectancy. Considering these negative effects present study aims to evaluate the risk factors leading to lower extremity amputations in patients with diabetic foot. **Methodology:** All patients attending the General surgery OPD/IPD/Emergency Age >18 years with diabetic foot was included in this study.A pre-tested study proforma was used to collect data on demographics, duration of DM and treatment, self-care behaviours, neuropathic symptoms, the presence of intermittent claudication or pain at rest, past history of foot or leg ulcer and amputation. Physical examination with emphasis on the lower limbs were performed to assess for foot deformity (high arch or dropped foot), hammer/claw toe, equinus deformity, cavus deformity, charcot deformity, hallux limitus, pedal oedema, callus, scars of previously healed ulcers, and amputation defects.A provisional diagnosis was established and further investigations were carried out on each patient. In some cases special investigations like CT ANGIO was also done.Management of diabetes and its related non-surgical complications were done under the guidance and supervision of Endocrinologist.After coming to a final diagnosis and evaluating all the risk factors Lower Limb Amputation was planned in indicated cases.All the data collected were subjected to statistical analysis. **Results:** The mean age of overall patients were 56.71 ± 12.240. The majority of the 73.3% male patients are more commonly affected in diabetic foot infections followed by female patients (26.7%).The mean duration of DM of overall patients were 5.993 ± 2.0217.   The mean RBS of overall patients were 183.707 ± 24.1315. The mean HbA1c (%) of overall patients were 6.723 ± 0.7905. The majority of the 69.3% patients were both ulcer with gangrene complaints, followed by 28% patients were only gangrene complaint. Majority of the 51.3% patients for the control of diabetes through OHA therapy, followed by 40% patients through insulin therapy and remaining 8.7% patients for control diabetes through both (OHA+insulin) therapies.61.3% of patients were smoked.Peripheral neuropathy was present in 66% patients. Previous amputation or debridement was present in 76% patients. The hypertension morbidity was found in maximum 56% patients, followed by 10% patients had hypertension with RF, 8% patients hypertension with coronary artery disease and 1.3% patients had hypertension with RF and CAD. There were also 24.7% patients in whom no comorbidities were found. eripheral vascular disease was present in 69.3% patents. Dyslipidemia was found in 55.3% patents. Foot deformity was found in 62.7% patents.Bare foot walking was found in 56.7% patents. **Conclusion:** Glycatedhaemoglobin, Random Blood Sugar, Presence of gangrene, Smoking, Duration of diabetes, Peripheral neuropathy and Dyslipidemiaare considered as predictive factors for major lower extremity amputation in diabetic foot patients.
Keywords: Amputation,diabetic foot ulcer, lower extremity, trauma.

INTRODUCTION
Diabetes mellitus is the most common endocrine disorder known for its multifaceted complications, including diabetic foot ulcers (DFU) which often result in amputation as one of the worst outcomes.[1]Diabetic foot ulcer is most devastating complication of diabetes mellitus affecting 15% of patients. Early effective management of diabetic foot ulcer reduces severity of complications such as avoidable amputations and mortality.[2]
Diabetic foot is defined by World Health Organisation as "The foot of a DM patient that has the potential risk of pathologic consequences, including infection, ulceration, and/or destruction of deep tissues associated with neurologic abnormalities, various degrees of

peripheral vascular diseases and/or metabolic complications of diabetes in lower limb".[2,3]

India is slowly progressing to the top of the world with the largest number of DM subjects and is being anticipated to be the "diabetes capital of the world". According to the Diabetes Atlas 2013 published by the International Diabetes Federation, the number of people with DM in India was 65.1 million, which is expected to rise to 142.7 million by 2035.[4]According to global lower extremity study group, lower extremity amputation (LEA) is de-fined as a complete loss of any part of the lower extremity irrespective of the cause.[5]

DM is responsible for approximately 80% of all non-traumatic amputations performed every year. After a major amputation, 50% of people will need to have the other limb amputated within two year's time. People with a history of diabetic foot ulcer have a 40% greater 10-year death rate than people with DM alone.[6]Compared to healthy persons, diabetes mellitus holds a 15- to 20-fold increased risk of lower extremity amputations (LEA) and the majority of diabetes amputation are reported to be preceded (up to 85%) by a poor healing ulcer.[7]

The pathway to ulceration and finally LEA may include essential contribution from underlying diabetes-related pathophysiology (neuropathy, peripheral arterial disease (PAD), foot deformity and limited joint mobility), initiating environments (trauma), subsequent infection, and healing complications.[8]LEA is performed for various indications including severe soft-tissue infection, osteomyelitis, peripheral arterial occlusionand gangrene.

Some patients with DFU requires LEA because of various reasons like- duration of diabetes mellitus, previous amputation or foot ulceration, poor glycemic control, hypertension, dyslipidemia, presence of PAD, peripheral neuropathy, osteomyelitis, and wound severityare independent predictors for LEA. Additional factors include older age, smoking history, anemia, leukocytosis, hypoalbuminemia, as well as presence of other microvascularand macrovascular comorbidities.[9,10]

This study aimsto evaluate the risk factors leading to lower extremity amputations in patients with diabetic foot.

METHODOLOGY

All patients attending the General surgery OPD/IPD/EMERGENCY Age >18 years with diabetic footwas included in this study. Patients with Presence of DVT, Ulcer and gangrene foot due to non diabetic causes, Signs of acute peripheral arterial thrombosis and Traumatic cases were excluded from the study.

A pre-tested study proformawas used to collect data on demographics, duration of DM and treatment, self-care behaviours, neuropathic symptoms, the presence of intermittent claudication or pain at rest, past history of foot or leg ulcer and amputation. Physical examination with emphasis on the lower limbs were performed to assess for foot deformity (high arch or dropped foot), hammer/claw toe, equinus deformity, cavus deformity, charcot deformity, hallux limitus, pedal oedema, callus, scars of previously healed ulcers, and amputation defects.

A provisional diagnosis was established and further investigations in the form of HBA1C, Admission Plasma Glucose, FBS, Lipid Profile, CBC, ESR, LFT, RFT,ECG,CHEST X-RAY, X-RAY LOCAL PART,2D-ECHO,USG DOPPLER (arterial and venous B/L lower limb,Urine routine examination,Pusculture and sensitivity was carried out on each patient. In some cases special investigations like CT ANGIO was also done.

Management of diabetes and its related non-surgical complications were done under the guidance and supervision of Endocrinologist.

Systemic IV Antibiotics was started as per culture and sensitivity reports.

Regular dressing was done of ulcer with H2O2, Normal Saline, Betadine, EUSOL.After coming to a final diagnosisand evaluating all the risk factors Lower Limb Amputation was planned in indicated cases.Patients who wassign Informed Consent Form on an approved formatwas included in study. Clearance from Institutional Ethical Committee was taken prior to start of the study.Regular clinical follow-up of all the patients were carried out.All the data collected were subjected to statistical analysis by SPSS and Microsoft excel software.

The collected data were analysed with IBM-SPSS statistics software 23.0 Version. Results were presented as means ± standard deviation (SD) and the data were considered significant if p-value was ≤0.05 and highly significant if p- value <0.01.

RESULTS

One hundred and fifty subjects that participated in this study underwent lower extremity amputation. This study shows the comparisons between those who suffered LEA and those who did not.

Table 1: Age distribution

Age Group	No.	Percentage
< 30	7	4.67%
31-40	11	7.33%
41-50	23	15.33%
51-60	42	28.00%
> 60	67	44.67%
Total	150	100%

Mean±SD	56.71±12.240

Majority of the 44.67% patients from the age group of more than 60 years followed by 28% patients from the age group of 51-60 years, 15.33% patients from the age group of 41-50, 7.33% patients from the age group of 31-40 and 4.67% patients from the age of less than 30 years. The mean age of overall patients were56.71±12.240.

Table 2: Gender distribution

Gender	No.	Percentage
Male	110	73.3%
Female	40	26.7%
Total	**150**	**100%**

Above table shows that the majority of the 73.3% male patients are more commonly affected in diabetic foot infections followed by female patients (26.7%).

Table 3: Duration of Diabetes Mellitus

Duration of Diabetes Mellitus	No.	Percentage
< 3 years	8	5.33%
3-6 years	7	4.67%
6-9 years	54	36.00%
> 9 years	81	54.00%
Total	**150**	**100%**
Mean±SD	**5.993±2.0217**	

The more than 9 years duration of diabetes mellitus was majority of the 54% patients, followed by 6-9 years duration was 36% patients, less than 3 years duration was 5.33% patients and 3-6 years duration was 4.67%. The mean duration of DM of overall patients were5.993±2.0217.

Table 4: Random Blood Sugar

Random Blood Sugar (mg/dl)	No.	Percentage
< 175	8	5.33%
175-200	19	12.67%
200-225	58	38.67%
> 225	65	43.33%
Total	**150**	**100%**
Mean±SD	**183.707±24.1315**	

The random blood sugar (> 225 mg/dl) was majority of the 43.33% patients, followed by less than 200-225 mg/dl was 38.67% patients, 175-200 mg/dl was 12.67% patients and less than 175 mg/dl random blood sugar was 5.33% patients. The mean RBS of overall patients were 183.707±24.1315.

Table 5: HbA1c (%)

HbA1c (%)	No.	Percentage
< 6%	1	0.67%
6-7%	35	23.33%
8-9%	44	29.33%
> 9%	70	46.67%
Total	**150**	**100%**
Mean±SD	**6.723±0.7905**	

The percentage of HbA1c (more than 9%) was found majority of the 46.67% patients, followed by 8 to 9% was 29.33% patients, 6-7% was 23.33% patients and less than 6% of HbA1c was only 0.67% patients. The mean HbA1c (%) of overall patients were 6.723±0.7905.

Table 6: Presenting Complaints

Presenting Complaints	Frequency	Percent
Infected ulcer	4	2.7%
Gangrene	42	28.0%
Ulcer+Gangrene	104	69.3%
Total	**150**	**100.0%**

Out of 150 patients, majority of the 69.3% patients were both ulcer with gangrene complaints, followed by 28% patients were only gangrene complaint.

Table 7: Diabetes Control

Diabetes Control	Frequency	Percent
OHA	77	51.3%
Insulin	60	40.0%
OHA+Insulin	13	8.7%
Total	**150**	**100.0%**

Majority of the 51.3% patients for the control of diabetes through OHA therapy, followed by 40% patients through insulin therapy and remaining 8.7% patients for control diabetes through both (OHA+insulin) therapies.

Table 8: Smoking

Smoking	Frequency	Percent
Yes	92	61.3%
No	58	38.7%
Total	**150**	**100.0%**

Out of 150 patients, maximum 61.3% of patients were smoked.

Table 9: Peripheral Neuropathy

Peripheral Neuropathy	Frequency	Percent
Yes	99	66.0%
No	51	34.0%
Total	**150**	**100.0%**

Out of 150 patients, peripheral neuropathy was present in 66% patients.

Table 10: Previous Amputation or Debridement

Previous Amputation or Debridement	Frequency	Percent
Yes	114	76.0%
No	36	24.0%
Total	**150**	**100.0%**

Out of 150 patients, the previous amputation or debridement was present in 76% patients.

Table 11: Comorbidity

Comorbidity	Frequency	Percent
Hypertension	84	56.0%
Hypertension with CAD	12	8.0%
Hypertension with RF	15	10.0%
Hypertension with RF and CAD	2	1.3%
No comorbidity	37	24.7%
Total	**150**	**100.0%**

The hypertension morbidity was found in maximum 56% patients, followed by 10% patients had hypertension with RF, 8% patients hypertension with coronary artery disease and 1.3% patients had hypertension with RF and CAD. There were also 24.7% patients in whom no comorbidities were found.

Table 12: Peripheral Vascular Disease

Peripheral Vascular Disease	Frequency	Percent
Yes	104	69.3%
No	46	30.7%
Total	**150**	**100.0%**

Peripheral vascular disease was present in 69.3% patents.

Table 12: Dyslipidemia

Dyslipidemia	Frequency	Percent
Yes	83	55.3%
No	67	44.7%
Total	**150**	**100.0%**

Dyslipidemia was found in 55.3% patents.

Table 13: Foot Deformity

Foot Deformity	Frequency	Percent
Yes	94	62.7%
No	56	37.3%
Total	**150**	**100.0%**

Foot deformity was found in 62.7% patents.

Table 14: Bare Foot Walking

Bare Foot Walking	Frequency	Percent
Yes	85	56.7%
No	65	43.3%
Total	**150**	**100.0%**

Bare foot walking was present in 56.7% patents.

Table 14: Univariate predictors of amputation

	OR	Sig.	95% CI	
			Lower Bound	Upper Bound
Duration of DM (years)	.660	**< 0.01**	.387	1.126
RBS	1.198	**< 0.01**	1.001	1.435
HbA1c (%)	19.007	**< 0.05**	1.664	217.093
Presenting complaint	2.921	**< 0.05**	1.345	6.614
Diabetes Control	3.233	.808	.278	37.644
Smoking	94.973	**< 0.01**	3.428	2631.036
Peripheral Neuropathy	1.142	**< 0.01**	.042	31.253
PVD	10.967	.484	.000	20078663.166
Dyslipidemia	.399	**<0.05**	.043	3.751
Foot Deformity	.000	.107	.000	819.280
Bare Foot walking	5.987	.664	.236	152.137

Above table shows univariate predictors of amputation among the study participants. Subjects with glycated hemoglobin were 19 times more likely to suffer LEA (95% CI 1.664–217.093; P<0.05). Patients who had duration of DM (P<0.01), RBS (P < 0.01), presenting complaints (P<0.05), smoking (P<0.01) and pheripheral neuropathy (P<0.01) were approximately 1 time, 1.5 time, 3 times, 95 times, and 1.5 as likely to undergo LEA respectively.

DISCUSSION

Diabetics are prone to foot complications and if associated with co morbidities it can rapidly progress and lead towards amputation which is not only a health problem but also a socioeconomic burden severely affecting quality of life. The present study was aimed to assess the risk factors in patients which led to amputation and not amputations in 150 patients.

In the present study, all amputation were below knee amputation. The mean age of patients in lower extremity amputation was 56.71±12.240.In contrast to a Turkish study[11], we observed no significant association between age and LEA. Our observation is supported by many other studies which had demonstrated a lack of association between age and LEA in patients with DFU.[12,13]

Amputations following DFU have been reported higher in male patients than in females in literature.In our study also males are more commonly affected in diabetic foot infections and amputation rates are also higher compared to females. Similar to Ozan et al, we also concluded that major amputation was significantly higher in male patients.[14]

Diabetic foot ulcer leading to major amputation significantly increases with increasing duration of diabetes.In present study mean duration of diabetes mellitus was 5.993±2.0217 years. Contrary to this other researcher claimed that the duration of diabetes is not a baseline factor that predicts amputation.Similar to findings of Ozan et al, in present study also mean duration of DFU was significantly higher in group B (6.38±0.9 years) than in group A (4.1±0.78 years) (P<0.01).[14]

In present study, the random blood sugar ((> 225 mg/dl) was majority of the 43.33% patients and mean RBS of overall patients were 183.707±24.1315 (OR 1.198, 95%CI 1.001 1.432; p<0.01).The poor glycemic control is one of the major common factors in LEA.This study shows that mean HbA1c was significantly higher in LEA (p<0.01).Similar results found that Lehto et al[15], studied the HbA1c levels and the risk of amputation increases largely in a linear fashion and Ozan et al found significant differences between the major and minor amputation groups in terms of HbA1c levels.[14]Other similar studies was observed by Imran et al, Vishvanathan Vet al[17], Pemayun TG et al, in patients who had underwent LEA.[16]

The hospitalized DFU patients with foot gangrene had an approximately 6.5-fold higher risk of amputation.

Foot gangrene was caused by deficient blood supply to tissues due to arterial stenosis or occlusion that further led to localized necrosis and tissue death. The presence of ulcer with gangrene in 69.3% patients are going for amputation.Similar results shows that Yesil S et al. presence of gangrene in 66.3% with diabetic ulcer.[18]

In the present study, mostly 51.3% patients are control of diabetes through the oral hypoglycemia agent, followed by 40% patients are control of diabetes through insulin drug and remaining 8.7% patients are control through both OHA and insulin drug. The prospective study conducted by Adler et al, reported that treatment with OHA and insulin is independent risk factors for LEA in patients with DM.[19]

It is a known fact that peripheral neuropathy, peripheral vascular disease and dyslipidemia are the potential risk factors for foot complications. In the present study, LEA patients presented with more diabetic complications that included peripheral neuropathy (P<0.01)and dyslipidemia (P<0.05). It was statistically significant results shows that Ozanet al[14], observed peripheral neuropathy and dyslipidemia as the most important risk factors for LEA but it was statistically not significant for major or minor LEA.Like other developing countries, in the absence of vascular intervention and revascularization services, PVD was the most significant factor responsible for major LEA in present study. Similar data has been reported in previous studies.ZubairM et al[20], Pemayun TG et al[16], demonstrated that dyslipidemia was associated with risk of LEA.

In the present study, the presence of foot deformity was the majorcontributing factor to barefoot dynamic plantar pressure in high-risk diabetic patients. Difference in the level of foot deformity and barefoot walking with amputation was statistically not significant (P>0.01), which were similar to other recent studies.[77,78]

CONCLUSION

Glycatedhaemoglobin, Random Blood Sugar, Presence of gangrene, Smoking, Duration of diabetes, Peripheral neuropathy and Dyslipidemiaare considered as predictive factors for major lower extremity amputation in diabetic foot patients.Interestingly, most of these identified predictors of LEA are factors that can be quickly assessed by the patient's bedside. We believe that the findings in this study would assist general practitioners identify high risk patients who may benefit from early referral to specialist centers, and also guide foot care specialists in taking appropriate and timely clinical decisions. This may go a long way in reducing LEA rate in people with DFU in our environment.

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