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Original Research Article

Risk factors of amputation in diabetic foot infections

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ABSTRACT

Background: Diabetes is the most common underlying cause of foot ulcers, infection, and ischemia, leading to hospitalization and the most frequent cause of non-traumatic lower extremity amputation. Despite well-defined risk factors for diabetic foot ulcer development, limited data are available as to which factors predict amputation in a diabetic foot ulcer episode. Therefore, to predict lower limb amputation occurrence and to determine the factors associated with the risk of amputation in diabetic patients, we conducted this study.
Methods: A hospital based longitudinal study was carried out to assess the risk factors associated with amputation in diabetic foot infection. Patients with foot infections, who were either a diagnosed case of diabetes mellitus or were diagnosed at the institute were included in the study. We excluded patients receiving immunosuppressive therapy or radiotherapy, and infections at or above the ankle joint. Study factors were demographic details, biochemical parameters, Wagner grading, peripheral neuropathy as evaluated by nerve conduction test and vasculopathy as assessed by Ankle brachial index. The primary outcome factor was amputation. The data was presented as descriptive statistics and analyzed by dividing the patients into amputation and non-amputation group, and univariate and multivariate analysis was done.
Results: A total of 64 patients were included in the study, out of which the amputation rate was 39.1%. Poor glycemic control, osteomyelitis, vasculopathy, peripheral neuropathy and Wagner grading were statistically significant.
Conclusions: In the present study, poor glycemic control, vasculopathy, peripheral neuropathy and higher Wagner grade are significant risk factors for amputation in diabetic foot infections.

Keywords: Diabetic foot, Diabetic foot infection, Lower extremity amputation, Diabetic neuropathy, Diabetic vasculopathy, Wagner grading system

INTRODUCTION

Diabetes is the most common underlying cause of foot ulcers, infection, and ischemia, which are among the most serious complications of diabetes, leading to hospitalization and the most frequent cause of non-traumatic lower extremity amputation.[1] Compromise of blood supply from micro vascular disease, often in association with lack of sensation because of neuropathy, predisposes persons with diabetes mellitus to foot infections.[2] Patients with diabetes are 15 to 30 times more likely to have an amputation than are patients without diabetes.[3] The incidence of diabetic foot is increasing due to the increased prevalence of diabetes and the prolonged life expectancy of diabetic patients.

Despite well-defined risk factors for diabetic foot ulcer development, limited data are available as to which factors predict amputation in a diabetic foot ulcer episode. Several risk factors for amputations among diabetics have been cited in the literature. However, there are inconsistencies between the studies.

There are numerous classification systems for diabetic foot ulcer outcome prediction, but only few studies evaluated their reliability or external validity.[4] These classification systems are essential tool for assessing and selecting treatment and for improving communication among health care professionals.[5] Thus, a single or simplified classification system, which includes the most accurate predictive factors for amputation, would facilitate decision-making.

Therefore, to predict lower limb amputation occurrence and to determine the factors associated with the risk of amputation in diabetic patients, we conducted this study.

METHODS

A hospital based longitudinal study was conducted at Lata Mangeshkar Hospital, Nagpur, a tertiary care hospital from September 2015 to August 2017. The aim of the study was to assess the risk factors associated with amputation in diabetic foot infectios. The inclusion criteria were patients with foot infections defined as infection of soft tissue in diagnosed case of diabetes mellitus with or without treatment and newly-diagnosed diabetics, above 18 years of age and of either gender. We excluded patients receiving immunosuppressive therapy or radiotherapy, infections at or above the ankle joint, or ulcers due to causes other than diabetes mellitus. Formal written informed consent was obtained from all patients. The study was approved by the Ethical committee of the hospital.

The study factors were demographic details of all patients including age, gender, smoking history, and any recent history of trauma to the foot.

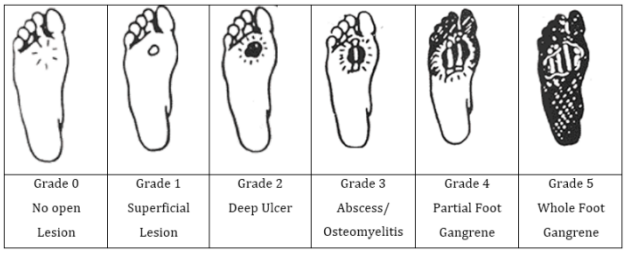

Figure 1: Wagner grading system.

All infections were classified according to the Meggitt-Wagner grading system (Figure 1). Baseline investigations including hemoglobin (Hb), Glycosylated hemoglobin (HbA1c), total leucocyte count (TLC), serum creatinine and fasting blood sugar levels were collected. X-ray of foot was done to assess features of osteomyelitis. Peripheral arterial disease (PAD) was evaluated by measuring ankle brachial index (ABI) using a hand held doppler. Peripheral neuropathy was assessed using RMS computerized system, on which it was defined as a delay of >45 m/sec. The main outcome factor was amputation which was defined as the complete loss in the transverse anatomical plane of any part of the lower limb.

Statistical analysis

After confirming the normality of the data, the continuous variable were analyzed using student 't' test and categorical variables was analyzed using Chi Square and Fischer Exact test. The data was divided into amputation group and non-amputation group and univariate and multivariate analysis was done to identify the predicting factors statistically associated with amputation.

RESULTS

A total of 64 patients were included in the study, male: female ratio was 3:1 and the mean age was 55.57±10.44 years. Amongst the 64 patients, 25 (39.1%) underwent amputation, out of which 10 (40%) underwent below knee amputation while 60% patients had Ray amputation. History of Smoking and recent history of trauma to the foot was present in 48% of patients who underwent amputation. Amongst the various blood investigations, only Fasting blood sugar and glycosylated hemoglobin were statistically significant (Table 1).

Table 1: Univariate analysis of laboratory parameters.

Parameters	Amputated n=25	Non-Amputated n=39	P value
Hb	10.07±2.3	10.43±2.18	0.53 (NS)
TLC	14424±6827	11925±5026	0.09 (NS)
FBS	232±100	188±70	0.04 (S)
HbA1c	10.02±2.32	8.82±2.3	0.04 (S)
S. Creatinine	1.45±0.71	1.16±0.44	0.052 (NS)

The patients were arbitrarily divided into 2 groups according to the Wagner grading system (lower grade – Wagner grade 0 to 2; Higher grade – Wagner grade 3 to 5), and it was observed that out of the 26 patients in higher grade, 22 (84.6%) patients underwent amputation while out of the 38 patients in lower grade, 3 (7.9%) patients underwent amputation. These results were statistically significant (p=0.000) showing high amputation rate in Wagner grade 3 and above.

Six patients had radiographic features suggestive of osteomyelitis and all of them required amputation.

A total of 44 (68.75%) patients had sensory-motor neuropathy on electrophysiological studies, out of which 22 (50%) underwent amputation, while out of the 20 patients with normal conduction studies, 3 (15%) patients

underwent amputation. These results were statistically significant (p=0.008), thus suggesting that neuropathy is a risk factor for amputation (Table 2).

Table 2: Association of amputation with peripheral neuropathy.

Electrophysiological Tests	Amputation		Total (%)
	Yes (%)	No (%)	
Normal study	3 (15.0)	17 (85.0)	20 (100.0)
Sensory motor neuropathy	22 (50.0)	22 (50.0)	44 (100.0)
Total	25 (39.1)	39 (60.9)	64 (100.0)

Peripheral arterial disease was assessed using ABI, which was arbitrarily divided into two groups, one with ABI ≤0.9, and another with ABI >0.9 (Normal). A total of 25 patients (39.1%) had values ≤0.9, out of which 20 patients (80%) underwent amputation while out of the 39 patients (60.9%) with normal ABI, 5 patients (12.8%) underwent amputation. These results were statistically significant (p=0.001) (Table 3).

Table 3: Association of ABI with amputation.

Ankle Brachial Index	Amputation		Total (%)
	Yes (%)	No (%)	
≤0.9	20 (80)	5 (20)	25 (100)
>0.9	5 (12.8)	34 (87.2)	39 (100)
Total	25 (39.1)	39 (60.9)	64 (100.0)

When these significant predictive factors were analyzed in a multivariate analysis, only Wagner grading system was shown to be strongly associated with amputation (Table 4).

Table 4: Multivariate analysis.

	Unstandardized coefficients		Standardized coefficients	Sig.
	B	Std. error	Beta	
(Constant)	2.769	0.240		0.000
FBS	0.000	0.001	-0.032	0.721
HbA1c	-0.027	0.018	-0.134	0.132
Wagner Grading	-0.238	0.041	-0.712	0.000

a. Dependent variable: amputation

DISCUSSION

Diabetic foot infections are a common and potentially serious problem in persons with diabetes. Despite well-defined risk factors for diabetic foot ulcer development, limited data are available as to which factors predict amputation in a diabetic foot ulcer episode.

In this study, the overall rate of amputation in diabetic patients was 39.1%. Similar high rate of amputation was also reported by Yesil et al (37.1%), Uysal et al (33.2%), Wang et al (29.6%), Jeon et al (48.9%).[6-9] This is likely because most of the patients in this study presented to the department of surgery when infection or ischaemic change had already occurred, and so the overall amputation rate was relatively high. Also the percentage of distal amputation was higher as compared to below knee amputation (40%), which could be due to decreased perfusion distally, thus leading to delay in wound healing, and also increased occurrence of osteomyelitis of phalanges.

Risk factors for amputation in terms of diabetic complications have been investigated intensively and can be used to define the risk assessment models. Risk factors for lower extremity amputation among patients with diabetes include age, sex (male), comorbidities such as hypertension, chronic complications such as vasculopathy, nephropathy, duration of diabetes, sensory neuropathy and HbA1c. However, inconsistent results have been reported and the risk factors have not yet been clarified.

The most important finding in our study was that poor glycemic control had increased risk for amputation. A raised fasting blood sugar level was statistically significant for amputation in the present study. In an Iranian study, Shojaiefard reported that FBS was on the higher side in patients who required amputation as compared to the ones who did not require amputation.[10] Similar results were observed by Pemayun et al in their study conducted in Indonesia.[11]

Few studies have shown that levels of blood glucose over periods of time, as assessed by HbA1C, would be a better predictor for amputation. The level of HbA1c is directly related to the average glucose concentration over the life span of the hemoglobin. In the present study, the strong association of HbA1c with amputation could reflect a greater pathogenic role of chronic hyperglycemia probably via neuropathy, autonomic dysfunction, PAD, and susceptibility to infection. The United Kingdom prospective diabetes study reported that the hazard ratio of death from amputation declines 43% when HbA1c declines by 1%.[12]

It was reported in this study, that Wagner Grade was strongly associated with amputation as compared to other risk factors on multivariate analysis. Oyibo et al reported that the Wagner grade significantly correlated with the risk of amputation.[13] Calhoun et al reported that increased Wagner grade was associated with a higher treatment failure.[14] Ulcers of Wagner grades 4 and 5 denote the presence of local or diffuse gangrene, which are usually

due to a combination of ischemia and infection. It is thus not surprising that grade 4 and 5 ulcers were very strongly associated with amputation in our study. In a Turkish cohort, Yesil et al reported that Wagner grade (Wagner grade 4 and 5) was a strong predictor for amputation.[6]

PAD is a manifestation of widespread systemic atherosclerosis, characterized by atherosclerotic occlusive disease of the lower extremities and is one of the macro vascular complications highly prevalent in adult diabetic patients. Various studies reported PAD was an independent risk factor associated with prevalent foot complications in patients with diabetes and an independent factor related to major amputation in neuroischaemic/ischemic ulcers as in this study. Thus, low ABI is a risk factor for amputation as it indicates decreased perfusion to the foot.

Peripheral neuropathy was statistical significant (<0.008) for amputation in the current study and is a major risk factor for amputation. Due to peripheral neuropathy, there is loss of sensation. As a result, neuropathic changes, such as foot deformity, decreased protective sensation and skin fissures, caused by diminished sweating lead to formation of diabetic foot infections, which leads to further damage ultimately leading to gangrene formation. Diabetic neuropathy develops as consequence of chronically elevated blood sugar levels, which cause vascular and metabolic abnormalities.

CONCLUSION

In the results of our analysis, poor glycemic control, peripheral arterial disease, peripheral neuropathy and higher Wagner grade are significant risk factors for amputation in diabetic foot infections. Strict control of diabetes, which is the primary disease, is first of all required for the risk reduction.

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