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Original Research Article

Evaluation of risk factors for lower extremity amputation in diabetic foot ulcer: a hospital based observational study in Northern India

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ABSTRACT

Background: The present prospective observational study was done to analyse the risk factors leading to minor or major lower extremity amputation (LEA) in diabetic patients.
Methods: A 139 patients were divided into Group A (n=113) and Group B (n=26) who underwent minor and major LEA respectively.
Results: Majority of the patients in group B were from rural and lower socioeconomic background. Duration of diabetes (p=0.017) and of DFU was significantly longer in group B (P <0.001) The pro-portion of patients with Wagner Grade 4 and 5 ulcer were significantly higher in group B than in group A (P <0.001) Wound infection and maggots were significantly higher in group B though polymicrobial infection was higher in group A. Biochemical investigations were abnormally altered but difference between two groups was not significant.
Conclusions: Socioeconomic burden on the society due to LEA can be reduced by making diabetic patients aware of foot hygiene, regular medical check-up for control of diabetes and associated complications.

Keywords: Amputation, Diabetes, Foot hygiene, Infection

INTRODUCTION

Diabetes is increasing at an alarming rate in the form of global epidemic. There was an estimated 451 million people with diabetes worldwide in 2017 and these figures are expected to increase to 693 million by 2045.[1]

In developing countries like India the diabetic population was estimated as 32 million in 2000 and is expected to rise to 80 million ,the largest number in the world by the year 2030.[2] Micro and macro vascular complications associated with diabetes affect quality of life , increases the cost of living and global healthcare burden. Diabetic foot ulcer (DFU) is one of the commonest diabetic complications responsible for hospitalization.

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.[3] Amputation rates vary widely across the world and within the country. Rates range between 0.7 per 1000 in eastern asian population to 31 per thousand in US prima Indians. Compared to healthy persons (0.29%), diabetes has 10-30 times more risk of LEA (2.8%).[4,5] Every 30 seconds a lower limb is lost somewhere in the world as a consequence of diabetes.[6] A 60% to 80% of non-traumatic LEA are being reported in diabetics and 85% of LEA in diabetics are preceded by a poor healing diabetic foot ulcer (DFU).[7-9]

The prevalence of DFU is 4-10% and the risk of developing diabetic foot infection during life-time in a

diabetic is as high as 15% to 25%.[4] Major factors responsible for DFU include com-promised blood supply due to peripheral microvascular disease, with lack of sensation due to peripheral neuropathy. Both these factors in turn predispose to repetitive trauma and super imposed infection. Other contributory factors include older age, smoking, duration of diabetes, hypertension and dyslipidemia. Cultural habits, barefoot walking, poor footwear, poverty, illiteracy, ignorance about foot care make Indian population at greater risk to amputation. Approximately 20% of the DFU lead to some level of amputation.[10] The major concern is that the incidence of diabetic related LEA is increasing due to growing diabetic population worldwide and prolonged life expectancy.

Though there are well defined risk factors for DFU development, limited data is available as to factors which predict its progression to minor or major LEA.

A minor LEA is defined as any amputation distal to the ankle joint, whereas a major LEA was any amputation through or proximal to the ankle joint.[11] Several potential risk factors like age, sex, duration and control of diabetes, depth of ulcer, severity of infection, associated co morbidities for LEA have been cited in the literature but there are inconsistencies between the studies. The present study was done with the objective to determine the potential predictors of major and minor LEA in patients with DFU.

METHODS

It was a hospital based prospective observational study on 139 patients to assess the risk factors associated with severity of amputation with diabetic foot ulcer. They were divided into two groups. Group A (n=113) and group B (n=26) who underwent minor and major LEA respectively.

Exclusion criteria

- Patients on immunosuppressive therapy or radiotherapy were excluded from the study.

The demographic data of the patients including age, sex, place from where they came, their education status was recorded. All patients were evaluated for time span of disease, control of diabetes, duration and depth of diabetic foot ulcer (DFU).

Patients were assessed for co morbidities including dyslipidemia, hypertension, peripheral neuropathy, peripheral arterial disease and nephropathy. Wound culture swab, lower limb color doppler and blood parameters including fasting blood sugar, glycated hemoglobin (HbA1c), lipid profile, renal profile were investigated in each patient.

DFU were classified according to Wagner system. Grade 0 hyperkeratosis below or above the bony prominences, Grade 1: overlying skin and subcutaneous tissue is ulcerated, Grade 2: lesions are deeper to penetrate till tendon, bone or joint capsule. Grade 3: osteomyelitis is present, Grade 4: gangrene of some portion of toes or forefoot and Grade 5: entire foot is gangrenous.[12]

Diabetic neuropathy was defined as inability to perceive pressure with 10g using a nylon mono-filament test at three sites (two planter and one dorsal) with patient's eyes closed. Peripheral artery disease was assessed by palpating dorsalis pedis and posterior tibial pulses. It was confirmed by doing color doppler of lower limb vessels.

RESULTS

Prospective observational study conducted on 139 patients were divided into two groups, group A (n=113) and group B (n=26) who underwent minor and major lower extremity amputation (LEA) respectively.

Table 1: Demographic data.

Variables	Group A (N=113)	Group B (N=26)	P value
Males	78 (69)	23 (88.4)	P=0.045
Females	35 (31)	3 (11.6)	
Mean age	(61.39±6.12)	(67.31±5.37)	P<0.001
Urban	15 (24.8)	4 (15.4)	
Rural	85 (75.2)	22 (84.6)	P=0.305
Level of education <10	86 (76.1)	24 (92.3)	
>10 class	17 (23.9)	2 (7.6)	P=0.067
Awareness of foot care	104 (92.03)	25 (96.15)	P=0.464

A 69% in group A and 88.4% in Group B were males. The mean age in group B (67.31±5.37) was significantly higher in group A (61.39±6.12) (p<0.001).

Majority of them 85 (75.2%) in group A and 22 (84.6%) in group B were from lower socio-economic status and rural back-ground (p=0.305) number of patients who had not studied till 10th class was 86 (76.1%) in group A and 24 (92.3%) in group B.

Difference in the level of education in two groups was statistically significant. (p = 0.067). 104 (92.03%) patients in group A and 25 (96.15%) were not aware of foot care or foot wear. (p= 0.464) (Table 1).

Mean HbA1c in group B (10.6±1.044) was significantly higher than in group A (8.4± 0.773) (p<0.001) (Figure 1).

Mean duration of diabetes was 8.75 ±2.11 years in group A and 9.9±2.55 years in group B. The difference was statistically significant (p=0.017) (Figure 2).

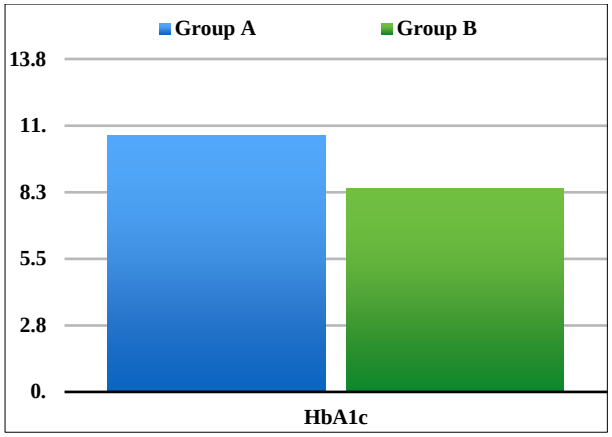

Figure 1: Correlation of HbA1c with grade of amputation.

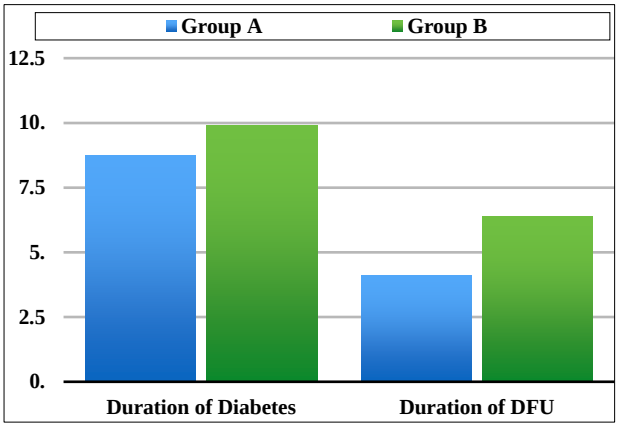

Figure 2: Correlation of duration of diabetes and of diabetic foot ulcer with grade of amputation.

Mean duration of diabetic foot ulcer was 4.1±0.78 months in group A and 6.38 ±0.9 months in group B. The difference was statistically significant. (p<0.001) (Figure 2).

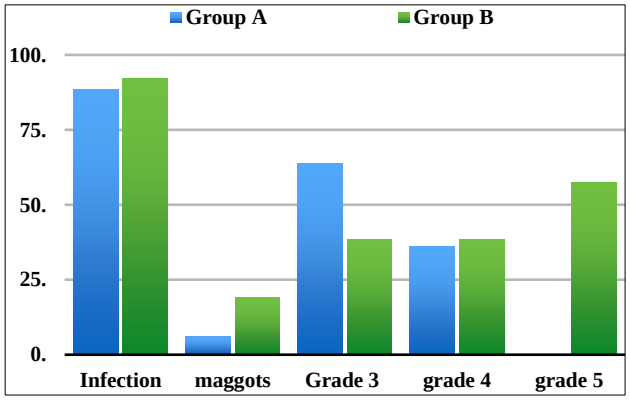

Figure 3: Showing role of infection and depth of wound with severity of amputation.

Culture from the wound was positive in 100 patients (88.5%) in group A and 24 patients (92%) in group B. In 78 (78%) patients in group A and 12(50%) in group B more than one organism was detected. Most common organism was *staphylococcus aureus* (95%) less frequent were *Staphylococcus epidermidis* (2%) streptococcus (1%) Klebsiella species (1%) and pseudomonas species (1%) Maggots were present in 5 (6%) patients in group A and 5 (19%) in group B patients. It was statistically significant p=0.033 (Figure 3).

A 72 (63.8%) patients in Group A had wagner grade 3 while 41 (36.2%) had grade 4 DFU whereas in group B 1(4%) had Wagner grade 3, 10 (38.4%) had Grade 4 and 15(57.6%) patients had Wagner's grade 5 DFU. The difference was statistically significant (p = 0.001) (Figure 3).

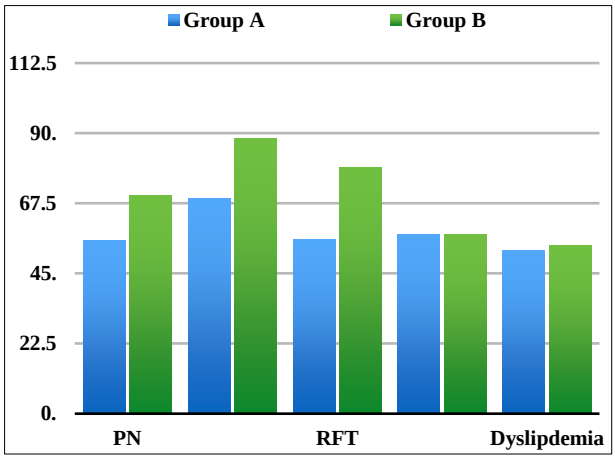

Figure 4: Correlation of systemic factors with severity of infection.

In present study patients with peripheral neuropathy were significantly higher in group B 20 (70%) than in group A 63 patients (55.7%) (p=0.047) whereas 78 patients (69.03%) in group A and 23 (88.4%) in group B had peripheral vascular disease. The difference was again statistically significant p <0.001 Similarly impaired renal function was statistically significantly higher in group B 79% than in group A 56% (p =0.047) (Figure 4).

Authors observed that dyslipidemia in Group A 59(52.3%) and Group B 14(53.9%) (p=0.88) and hypertension in group A 65 (57.5%) and Group B 15 (57.6%) p=0.987 were not statistically significant. p=0.987 (Figure 4).

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 minor and major amputations in 139 patients.

In present study 81.2% (group A) underwent minor amputations and 19.8% (group B) had major amputation. Of the major amputation all were below knee amputation while toe amputation was the commonest amongst minor amputation (80%). Mean age of patients in group A and group B was 61.39±6.12 and 67.31±5.37 respectively. It was statistically significantly higher in group B (p<0.001).

Similar to present study Ozan et al, also found that the mean age of patients in major amputation group was significantly higher than in minor amputation group but Abbott et al, reported higher incidence of major amputation in younger age group probably because they were more mobile and more predisposed to trauma.[13,14] Amputations following DFU have been reported higher in male patients than in females in litera-ture.[9,15-18] In present study also male patients were more than female patients in group A (69%) as well as in group B (88.4%). Similar to Ozan et al, we also concluded that major amputation was significantly higher in male patients.[13]

In present study majority of the patients were illiterate, from lower socio-economic status and rural background 85 (75.2%) in group A and 22 (84.6%) in group B p=0.305.

Number of patients who had not studied till 10th class was 86 (76.1%) in group A and 24 (92.3%) in group B. Difference in the level of education in two groups was statistically significant p = 0.067.

A 92.03% patients in group A and 96.15% were not at all aware for foot care or foot wear which they should be using for they are being diabetic. Difference in both the groups was not significant (p= 0.464). Longer duration, uncontrolled diabetes, associated co morbidities, poor foot care con-tribute to development of DFU. Further ignorance, careless attitude, improper follow up leads to subsequent infection and associated complications which ultimately end up in some grade of amputation.

In present study poor glycemic control was one of the major common factors amongst both the groups though mean HbA1c was significantly higher in major (10.6±1.044) than in minor LEA group (8.4± 0.773) (p <0.001).

Where Lehto et al, reported that HbA1c levels and the risk of amputation increases largely in a linear fashion Ozan et al found no significant differences between the major and minor amputation groups in terms of HbA1c levels.[19,13]

HbA1c above 9.0±2.1,10.4%, and 8 % was respectively observed by Imran et al, Vishvanathan Vet al, Pemayun TG et al, in patients who had underwent LEA.[15,16,20]

Diabetic foot ulcer leading to major amputation significantly increases with increasing duration of diabetes.[12,21,22] In present study mean duration of diabetes was significantly higher in group B than in group A (p=0.017). Contrary to this other researcher claimed that the duration of diabetes is not a baseline factor that predicts amputation.[20,23-25]

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 months) than in group A (4.1±0.78 months) p <0.001.[13]

Infection may not be the cause of DFU, but ulcers are susceptible to superadded infection and leading to dreaded complication of LEA. In present study, infection was found to be equally significant risk factor for both grades of amputation. Culture from the wound was positive in 100 patients (88.5%) in group A and 24 patients (92%) in group B. The difference between two groups was not statistically significant (p=0.572).

On the contrary Ozan et al, found significantly higher levels of C-reactive protein (CRP), marker of acute infection in major LEA group than minor LEA group. Similarly, in other studies elevated levels of baseline reactants of acute infection, ESR, WBC count , CRP were observed as independent predictors of major amputations.[13,23,26] However a study similar to ours did not find Cr, glucose and WBC levels to be significant risk factors for major amputations.[27] Pittet et al, and Upchurch et al, showed that elevated CRP levels were useful in signaling severe infection and predicting limb loss but did not mention it's correlation with grade of amputation.[28,29]

Vishvanathan V et al, in a multicentric study also concluded that infection was the major cause of amputation in India however Pemayun et al, did not reveal a strong association of infection and LEA thus substantiating that a septic foot does not inevitably lead to LEA and may explain the role of severe infection as dependent rather than independent of risk factors.[16,20]

Most common organism found in present study was *staphylococcus aureus* (95%) Latif et al, and Ozan et al, recorded positive culture in 69.1% and 95% cases respectively and most common organism in their study was also staphylococcus aureus.[18,13]

More than one organism was detected in78% (78) patients in group A and 50% (12) in group B Similar findings were reported by Ozan et al.[13]

Maggots were present in 5 (6%) patients in group A and 5 (19%) in group B patients. It was statistically significant p=0.033.

In present study, 53% patients in group A had Wagner grade 3 while 47% had grade 4 DFU whereas in group B only 4% had Wagner grade 3, 38.4% had grade 4 and 57.6% patients had grade 5 DFU. It was statistically significant (p=0.006).

Similar to this Imran et al, observed that the frequency of minor and major amputation increases with the higher grades of DFU.[15] Ozan et al, also concluded that the proportion of patients with grade 4 was higher in the major LEA Group than in minor LEA group.[13] Yesil S et al, and Latif et al, observed most frequent amputations in patients with grade 3 and 4 Wagner DFU.[23,18] Most recently Sadriwala QS et al, also reported that Wagner Grade was strongly associated with amputation as compared to other risk factors on multivariate analysis.[30] It is a known fact that peripheral neuropathy and peripheral vascular disease are the potential risk factors for foot complications. In present study 63 patients (55.7%) in group A and 20 (70%) in group B had peripheral neuropathy. It was statistically significant. Ozan et al, observed peripheral neuropathy (43%) as the most important risk factor for LEA but it was statistically not significant for major or minor LEA.[13] An 89 patients (78%) in group A and 23 (89%) in group B in present study had peripheral vascular disease. Like other developing countries, in the absence of vascular intervention and revascularization services, PAD was the most significant factor responsible for major LEA in present study. Similar data has been reported in previous studies.[9,20] Most recently peripheral artery disease was reported as independent risk factor for DFU and its progression to amputation by Mills and Amstrong DG et al.[31,10] Ozan et al, found PAD in 56% cases but the rate was not significantly different between two groups of minor and major amputation.[12] A study from Sudan reported that significant factors associated with major LEA included ischaemia, neuropathy, depth of wound and grade of infection. Vishvanathan V et al, also confirmed that approximately 85% of their study subjects had the presence of neuropathy and 35% had PVD and retinopathy. A 21.4% and 24.2% had nephropathy and cardiovascular disease respectively.[16] The amputation is reported to be ten times higher in patients with end stage renal disease than without dialysis. Previous studies showed that elevated serum creatinine levels were useful in predicting limb loss.[32-34] In present study also renal function was impaired in 56% (63) patients in group A and 79% (20) in group. End stage renal disease was significantly higher in (75%) patients with major amputation. Reports regarding the role of hypertension as a predictor of LEA is conflicting. In present study 65 (57.5%) in group A and 15 (57.6%) in group B were hypertensive. Difference between two was statistically insignificant. While Zubair M et al, Pemayun TG et al, have shown an association of LEA with hypertension but on the contrary study conducted by Lehto et al, reported that hypertension was not a significant predictor for LEA incidence.[19,20,25]

In present study 59 (52.3%) in group A and 14 (53.9%) in group B were dyslipidemia. The difference between two groups was not statistically significant. Zubair M et al, Pemayun TG et al, demonstrated that dyslipidemia was associated with risk of LEA whereas Chaturvedi et al, from the WHO multinational study failed to demonstrate that serum cholesterol, LDL-cholesterol, and HDL-cholesterol as significant risk factors for LEA.[20,25,35] Jain et al, also concluded that three patients (8.82%) who underwent major amputation had diabetes alone, 14 patients (41.18%) had diabetes and hypertension and 17 patients (50%) had diabetes, hypertension and dyslipidemia.[17]

CONCLUSION

After identifying male sex, duration and control of diabetes, duration of ulcer, infection and se-verity of diabetic foot ulcer, peripheral neuropathy ,peripheral arterial disease as definite independent risk factors for major lower extremity amputation, authors conclude that to decrease social-economic burden on the society and to avoid psychological trauma to the patient, amputation rate and grade of amputation can be minimized essentially by patient education, proper foot care and multidisciplinary team effort to control DM, to prevent diabetic foot ulcer, to adequately treat DFU and to prevent it's recurrence by keeping in mind and managing associated peripheral artery disease, peripheral neuropathy, chronic renal disease.

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