

Original Research Article

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Prospective observational study evaluating association of sociodemographic parameters, Wagner's grading, peripheral arterial disease and diabetic peripheral neuropathy with the outcomes of diabetic foot ulcers

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ABSTRACT

Background: The present study was conducted to determine the association of sociodemographic parameters, comorbid conditions and complications of diabetes mellitus (DM) with the treatment outcomes of diabetic foot ulcers.

Methods: The present prospective observational study enrolled 105 participants aged 30-85 years with diabetic foot ulcers presenting to general surgery department during a period of 18 months. Participants who were terminally ill, who had trophic ulcers of Hansen's disease and filariasis and its sequelae were excluded. The study was approved by institutional ethics committee and written informed consent was obtained from all study participants. Data was analyzed using R and the test of significance was chi square test, $p<0.05$ was considered statistically significant.

Results: Higher proportion of male participants and those aged between 50-69 years were encountered. Male participants were of higher age and the mean duration of DM in participants with diabetic foot ulcer was 8 years. The mean HbA1C of study participants was 8.1%, 38.1% participants had high plasma glucose. Foot deformity was observed in 41% participants. 62.9% and 66.7% participants had diabetic peripheral neuropathy and peripheral arterial disease respectively. The mean time required for healing among participants with diabetic foot ulcers was 45.8. Significant association of major amputation with diabetic peripheral neuropathy ($p=0.02$), Wagner's grading ($p<0.001$) and peripheral arterial disease (PAD) ($p=0.006$) was observed.

Conclusions: The presence of diabetic peripheral neuropathy and PAD were risk factors for major amputations in diabetic foot ulcers. Lower Wagner's grading was associated with lower chances of major amputation.

Keywords: Diabetic foot ulcers, Peripheral neuropathy, Wagner's grading, Peripheral arterial disease

INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by persistent hyperglycemia due to reduced insulin secretion, action or both.¹ The global burden of DM has risen four fold and the prevalence in adults has doubled in the past 34 years.² The increase in prevalence has been higher in the low and middle income countries

and diabetes and diabetes related complications impose a major burden on healthcare. India has the second largest population of diabetics though it is considered as the diabetic capital of the world and the prevalence is high in South Indian states especially Kerala.³ Foot ulceration is the most common complication of poorly controlled DM and the annual incidence of diabetic foot ulceration globally is 9.1 to 26.1 million every year.⁴ Indian

prevalence of foot ulceration is ~3% and is considerably lower than those reported among the western population. 15-25% of diabetics develop foot ulcers at least once in their life time and the prevalence is higher in diabetics aged 45 and above and among certain ethnicities.⁵ To date Indians are not considered a high risk ethnicity for foot ulcers but owing to the second largest population of diabetics in India and the explosive rise in diabetic population daily this remains a matter of concern. The risk factors implicated in development of foot ulcers include poor foot care, poor glycemic control, neuropathy peripheral arterial disease (PAD) accompanying DM, calluses, foot deformities, ill-fitting footwear, poor circulation and dry skin.⁵ Diabetic foot ulcers are the most common cause of osteomyelitis of the foot and amputation of lower extremities. The common sites of ulceration are areas which encounter repetitive trauma and pressure sensations.⁶ The pathophysiology of diabetic foot ulceration is a three step process of which the initial stage is the development of callus which results due to neuropathy. Motor neuropathy contributes to formation of ulcers by producing deformities, sensory neuropathy contributes by producing sensory loss resulting in trauma and autonomic neuropathy contributes by producing dryness of skin. All these together with compromised blood flow due to atherosclerosis of small blood vessels result in infections and due to reduction in blood supply the healing process is delayed. Despite considerable progress in treatment modalities of diabetic foot ulcers, prevention and cure of diabetic foot ulcers remain a considerable challenge.⁷ These challenges include the incidence of foot ulcers in a quarter of diabetics, 85% lower limb amputations being preceded by diabetic foot ulcers, 85% of amputations in DM being preventable and being the commonest reason for foot problems and higher health care costs compared to other diabetic complications. Profound infection, gangrene, lower limb ischemia and foot deformities and major etiological factors for lower limb amputations and the prognostic factors include vascularity of the lower limb. Our study aims at determining the association of sociodemographic parameters, comorbid conditions and complications with the treatment outcomes of diabetic foot ulcers.

METHODS

The present prospective observational study enrolled 105 consecutive participants with type 2 diabetes mellitus (T2 DM) aged 30-85 years in Wagner class (1-5) admitted in general surgery department of Sree Gokulam Medical College and Research Foundation, Venjaramoodu with diabetic foot ulcers requiring surgical intervention during a time period of 18 months between March 2012 to 2014.⁸ Participants treated as outpatient, who were terminally ill, trophic ulcers due to Hansen's disease, filariasis and its sequelae were excluded. Sample size was calculated assuming an α of 0.05 and β of 0.2 and 80% power and 10% attrition rate. The study was approved by institutional ethics committee and written informed consent was obtained from all study participants.

Sociodemographic parameters, history, examination findings (clinical, hematological, biochemical, microbiological and radiological examination) were recorded in case record forms. The total duration of ulcer was obtained from history (duration of lesion prior to hospital admission and duration of lesion from the time of admission to stage of healed ulcer or scar). Ulcer completely covered by healthy granulation tissue and neoepithelialization in the peripheral regions of the ulcer either during hospital stay or during follow up visits was considered as healed ulcer. We did consider the variations in width, size and depth of the ulcers. A completely healed stump or scar was considered as endpoint in participants who underwent amputation. All participants received standard of care with betadine, hydrogen peroxide or normal saline and appropriate antibiotics depending on the culture and sensitivity report. Topical papain, polypropylene glycol, skin graft, debridement, disarticulation and amputation were as per the discretion of the treating surgeon. The outcomes measured were the healing of ulcer with different treatment modalities. Haemoglobin <10 gm% was considered anemia and an ankle brachial pressure index of less than 0.9 was considered suggestive of peripheral vascular disease. Below knee amputation and above knee amputation was considered as major amputation, while toe amputation, fore foot amputation was considered minor amputation. Wagner's grading was used to grade foot ulcers. Data was analysed using free software R and are expressed as proportions and as mean standard deviation (SD) after rounding off to the nearest decimal. The association between various parameters were determined using chi square test and a $p<0.05$ was considered statistically significant.

RESULTS

Sixty-one (63.8%) participants were males and forty-four (41.9%) were females. The mean age of diabetic foot among male participants was 63.8 (9.1) and among female participants was 58.1 (10) years respectively. High prevalence of diabetic foot was observed among participants aged 50-69 years (67.6%). Among male participants, high prevalence of diabetic foot ulcers was observed among those aged 60-69 years and among female participants, high prevalence was observed among those aged 50-59 years (Table 1). The mean duration of DM among the study participants was 8.3 (7.5) years. Seventy-two (68.6%) participants had DM for less than 10 years duration while 24 (22.9%) and 9 (8.6%) participants had DM for 10-20 years and more than 20 years respectively.

The mean HbA1C of the study participants was 8.1 (2.1%). The distribution of HbA1C among study participants is demonstrated in (Table 2). Forty (38.1%) participants had uncontrolled plasma glucose levels. Twenty-eight (26.7%) participants had anemia and were given hematinic and blood transfusion. Foot deformity was observed in 43 (41%) participants which is a

predisposing factor for diabetic foot complications. Bone involvement was observed in 37 (35.2%) participants.

Table 1: Gender based age distribution of diabetic foot.

Age (in years)	Male N (%)	Female N (%)
40-49	4 (3.8)	8 (7.6)
50-59	16 (15.2)	19 (18.1)
60-69	26 (24.8)	10 (9.5)
70-79	11 (10.5)	7 (6.7)
≥80	4 (3.8)	0

Table 2: Distribution of HbA1C among study participants.

HbA1C	N (%)
6-7.9	65 (61.9)
8-9.9	22 (21)
10-11.9	9 (8.6)
≥12	9 (8.6)

Table 3: Proportion of participants according to Wagner's grading.

Wagner's grade	N (%)
I	51 (48.6)
II	12 (11.4)
III	22 (21)
IV	11 (10.5)
V	9 (8.6)

Forty-four (41.9%) participants had single organism and fifty-four (51.4%) had multiple organisms in culture and sensitivity report of the swab from the ulcer. Major proportion of participants were in Wagner's grade I class of ulcer which indicates that early and effective management could reduce the chances of limb loss (Table 3).

Table 6: Association of neuropathy, Wagner's grading and vasculopathy with major amputation.

Comorbidity	Major amputation		P value
	Yes (%)	No (%)	
Neuropathy	Present	12 (11.4)	0.02 [†]
	Absent	1 (0.01)	
Wagner's grade	I	0	<0.001 [‡]
	II	1 (1)	
	III	1 (1)	
	IV	4 (3.8)	
	V	7 (6.7)	
PAD	Present	13 (12.4)	0.006 [‡]
	Absent	0	

[†]Indicates significant association between groups probably indicating the lower proportion of participants without neuropathy who required major amputation; [‡]indicates significant association between groups probably indicating the lower proportion of participants with Wagner's grade I who did not require major amputation; and [‡]indicates significant association between groups probably indicating the lower proportion of participants without PAD who required major amputation.

Sixty-six (62.9%) participants had diabetic peripheral neuropathy. PAD was observed in 70 (66.7%) participants. History of regular alcohol consumption was present in 23 (21.9%) and history of smoking was present in 8 (7.6%) and history of both smoking and alcoholism was present in 19 (18.1%) participants. History of impairment in vision implying diabetic retinopathy was present in 25 (23.8%) participants. Previous history of ischemic heart disease was present in 38 (36.2%) participants and history of systemic hypertension was present in 63 (60%) participants. The mean time required for healing among participants with diabetic foot ulcers was 37.7 (45.8%) days (Table 4). Majority of participants (41.9%, n=44) required dressing and debridement, the treatment modalities advocated for diabetic foot ulcers is demonstrated in (Table 5).

Table 4: Time required for ulcer healing among study participants.

Time required for healing (days)	N (%)
<30	52 (49.5)
30-89	36 (34.3)
90-120	13 (12.4)
>120	4 (3.8)

Table 5: Treatment modalities used for diabetic foot ulcer among study participants.

Treatment undertaken	N (%)
Dressing alone	2 (1.9)
Dressing and debridement	44 (41.9)
Dressing, debridement and split skin thickness graft	12 (11.4)
Toe amputation	28 (26.7)
Fore foot amputation	6 (5.7)
Below knee amputation	9 (8.6)
Above knee amputation	4 (3.8)

Significant association of major amputation with diabetic peripheral neuropathy ($p=0.02$), Wagner's grading ($p<0.001$) and PAD ($p=0.006$) was observed (Table 6).

DISCUSSION

Foot ulceration is one of the leading causes of hospital admission in DM and is the most common non-traumatic cause of lower limb amputation. Peripheral neuropathy, peripheral vascular disease and susceptibility to infection are the three most important causes for development of diabetic foot ulcers. The major etiological factors of amputation in DM are profound infections, gangrene, foot deformities and lower limb ischemia and vascularity is the most important prognostic factor for diabetic foot ulcers. Selection of the proper amputation level is crucial not only to preserve the maximal length of the viable extremity, but to minimize morbidity and mortality when overly distal amputation is selected, the blood supply might be inadequate for wound healing which may require repetitive surgeries. Repeated amputation is associated with higher rates of morbidity or mortality, should be avoided whenever possible. The problems associated with overly proximal amputation is difficulty in ambulation without appropriate prosthesis.⁹ Ischemia in diabetic foot can be tricky since warmth maybe perceived due to autonomic neuropathy. The lack of autonomic tone in the capillary circulation cause shunting of blood from arteries to veins resulting in a foot that feels warm with bounding pulses and dilated veins. Absence of claudication pain due to autonomic neuropathy may worsen the diabetic foot even more. Often patients with diabetic foot ulcers undergo multiple debridement's with no signs of healing eventually leaving the surgeon with the only option, amputation. This process requires prolonged hospital stay which result in imposition of an economic burden on the family with risk of other complications such as anemia, hypoproteinemia, bedsores, hospital acquired infections. weight loss and psychological problems accompany prolonged hospital stay.¹⁰

64% of the participants were males, which could be due to the higher prevalence of DM among males or due to the previously reported higher risk of diabetic foot ulcers among males.^{11,12} Elderly women (>80 years) are reported to be at higher risk of developing diabetic foot and the risk increases with the presence of calluses and claw toe increasing the risk by at least 2 fold.¹² Physical activity is considered protective among women while the use of insulin, presence of sensory complaints was associated with higher risk among men. The lower proportion of elderly participants could also be a reason for the lower proportion of female participants in our study. The mean age of male participants with diabetic foot was higher than female participants, though the reverse is expected. This could only be explained on the basis of the location of the hospital which is in a rural area where the access to the hospital is still difficult to elderly females, however high the literacy rate is. High

prevalence of diabetic foot ulcers was observed in the ages between 50-69 years, higher proportion of male participants were at higher age compared to female participants. This is also contrary to previous reports and published literature. This can only be explained on the basis of the lower hospital access to elderly females. The mean duration of diabetes mellitus among study participants was 8.3 years, which was lower than previous reports of 9.96 years which indicates poor glycemic control among diabetic Keralite's which would predispose them to foot ulcerations early. Only 8.6% participants had diabetes mellitus for more than 20 years, this is contradicting the popular belief that diabetic foot ulcers are common among long standing diabetes mellitus. The higher prevalence of diabetic foot ulcers among diabetics with shorter duration of DM indicates the shifting trend of diabetic foot ulcers among those with shorter duration of DM. This could be due to the changes in phenotype of DM from older to younger owing to urbanization, fast food culture, sedentarism and other life style changes.

The mean HbA1C of study participants was 8.1% which indicates poor glycemic control for diabetics since ADA recommended glycemic levels is $<7\%$. 38% participants were having uncontrolled DM, ~18% participants were having very high baseline HbA1C ($>10\%$). This could indicate the lower awareness regarding glycemic control, the complications of DM and their association among rural population of Kerala. 38% participants had anemia which could be due to constant blood loss from the ulcer site, during debridement and cleaning. Foot deformity is a predisposing factor for diabetic foot ulcers, was present in 41% participants. Foot deformities in DM mellitus is due to peripheral neuropathy and a complex interplay between sensory, motor and autonomic components of peripheral neuropathy. The damage to innervation to the intrinsic muscles of the feet results in development of imbalance between flexion and extension causing abnormal bony prominences which leads to pressure points and subsequent skin loss and ulceration. Autonomic neuropathy worsens the existing condition by reducing sweating and resulting in dryness, subsequent fissuring and infections. Loss of sensations over the lower extremities lead to lower identification of ulcers and prolongs the ulcer duration and increases the chances of infection. Charcot arthropathy, is a typical condition where there is laxity of the small joints of the feet predisposing to ulceration where there is an interplay of sensory, autonomic and motor components of diabetic peripheral neuropathy. Bone involvement was observed in 35% participants which indicates the need for early intervention in participants with diabetic foot ulcers. Long standing diabetic foot ulcers lead to spread of infection to the bone and subsequent osteomyelitis.

51% participants had more than one organism in the culture and sensitivity report. Common organisms causing infections in diabetic foot ulcers are *Staphylococcus aureus*, *Streptococcus*, *Enterococcus*,

Enterobacteriaceae, Klebsiella, Hemophilus influenza, Pseudomonas. Polymicrobial infections are common in chronic and deep ulcers and the common organisms reported are *Pseudomonas* and multidrug resistant gram negative organisms.¹³ 48% participants were in Wagner's grade I (superficial ulcers) which indicates timely intervention could prevent limb loss in those patients. 62% participants had diabetic peripheral neuropathy, given the time taken for development of ulcers peripheral neuropathy would be a common finding in these patients. Also, peripheral neuropathy by predisposing to ulcer formation would be an anticipated finding in these patients. Similarly, peripheral arterial disease was a finding in 68% participants, being a lead contributor to peripheral occlusive vascular disease, it is rather a common finding among participants with foot ulcers. Smoking and alcohol consumption predispose to PAD thus increasing the risk of diabetic foot ulcers were seen in ~50% participants. Visual impairment probably attributing to diabetic retinopathy was observed in 24% participants which could also be attributed to senile cataract observed among elderly. Ischemic heart disease was seen in 36% participants which is an expected finding since DM is considered as a coronary artery risk equivalent.¹⁴ Systemic hypertension was observed among 60% participants, which is contrast to previous observations of protective effect of hypertension on diabetic foot ulcers.¹⁵ This could also be due to the use of angiotensin converting enzyme inhibitor use among the cohort which could explain the protective effect.

The average duration for wound healing was 45 days and 41% participants required dressing and debridement alone for the ulcer. Significant association between diabetic neuropathy and major amputation was observed ($p=0.02$) indicating a positive association between neuropathy and major amputation. None of the participants with superficial ulcers (Wagner's grade I) underwent major amputation ($p<0.001$) indicating lower the Wagner's grading lower the chances of amputation. None of the participants without PAD underwent major amputation ($p=0.006$) indicating the correlation of PAD and major amputation.

Limitations

Small sample size and lack of long term follow up are the limitations of the present study.

CONCLUSION

The presence of diabetic peripheral neuropathy and PAD were risk factors for major amputations in diabetic foot ulcers. Lower Wagner's grading was associated with lower chances of major amputation.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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