Original Article

Diabetic Foot Ulcers in a Tertiary Care Hospital; Risk Factors, Associations and Grades of Presentation

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ABSTRACT

OBJECTIVE: To determine the various risk factors for diabetic foot ulcers and study their associations. To study the grades of diabetic foot ulcers at presentation.

STUDY DESIGN: Comparative descriptive study.

SETTING: Department of Medicine; PIMS Hospital, Islamabad.

STUDY DURATION: 15th July 2012 to 15th Jan 2013.

MATERIAL AND METHODS: 254 cases were selected after informed consent. Study group (A) comprises of 127 cases of type 2 diabetes with diabetic foot ulcer and control group (B) comprises of 127 cases of age and gender matched type 2 diabetics without foot ulcers. Patients having ulcer for ≥4 weeks, who underwent debridement, having serious systemic illness, type I diabetics and non-diabetic patients presenting with foot ulcer were excluded. Age, gender, duration of diabetes, duration of ulcer, glycemic control, presence of neuropathy and vascular disease were documented. Grading and Staging of ulcer was done according to New University of Texas Diabetic Wound Classification. Various risk factors were compared between the two groups. Data analyzed via SPSS version 17 with significant *p*-value < 0.05.

RESULTS: Among 254 cases (68.5 % males & 31.5 % females); mean age was 55.9 ± 10.79 (group A) versus 51.9 ± 11.4 (group B). Mean duration of diabetes was longer in group A (9.36 ± 6.05 years) vs. group B (7.39 ± 4.89 years) ($p = 0.016$). Glycemic control was poor in group A (64.6 %) vs. group B (52 %) ($p = 0.04$). There was significantly more peripheral vascular disease in group A (47.2 %) vs. group B (29 %) ($p = 0.005$). Sensory neuropathy was more in group A (94.5 %) vs. group B (39.4 %) ($p < 0.0001$). Grade-I ulcer was present in 17.32 % cases, Grade-II in 37.79 % and Grade-III in 44.88 %.

CONCLUSION: Neuropathy carries highest risk for diabetic foot ulcer, followed by peripheral vascular disease and poor glycemic control. Therefore diabetic patient must be educate about these risk factor, foot care and self-examination and to have regular screening by clinician. Appropriate glycemic control and timely medical and surgical intervention may reduce morbidity in diabetics.

KEY WORDS: Diabetic foot ulcer, Glycemic control, New University of Texas Diabetic Wound Classification, Peripheral Neuropathy, Peripheral Vascular Disease.

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INTRODUCTION

In the year 2000, global prevalence of type 2 diabetes mellitus was 171 million. By 2030, this figure is expected to be 366 million. A regional study conducted by Ahmed et al shows the prevalence of diabetes in Pakistan to be 8.6 %; 11.1 % in Balochistan & NWFP and 13.9 % in Sindh.[1] Thus, diabetes is now a major challenge faced by developing countries as well.

Foot infections are amongst the most common problems in diabetics. Also the related hospitalizations are almost doubled in diabetics.[2,3] About 15-20% of diabetics experience foot ulcer in a life time and they have 15-45 % greater risk of limb amputation as compared to foot ulcers due to other causes. Local trauma, micro-vascular disease and pressure effects; often in association with the lack of sensation due to neuropathy contributes to pathogenesis of diabetic foot ulcer. The diabetic foot infections vary in severity from superficial cellulitis to chronic debilitating osteomyelitis.[4] Also the restricted joint mobility, poor foot care, improper hygiene, foot deformities and bony prominences further contribute to the risk of ulceration.[5,6]

Diabetics may have peripheral vascular disease involving the large vessels, as well as micro-vascular and capillary disease.[7] Infections in patients with

diabetes are difficult to treat because of vascular insufficiency that leads to poor concentration of antibiotics in the infected tissues. Infections in diabetics are more severe and take longer duration to cure than to equivalent infections in non-diabetics.[8]

Evaluation for etiology of an ulcer is helpful in determining the most appropriate and effective management. Foot ulcers in diabetics are classified as neuropathic, ischemic, or neuro-ischemic, depending on the presence of peripheral neuropathy and arterial disease. Motor and autonomic deficits also contribute to the risk of ulceration.

Reduced sensation in diabetics may substantially lead to impaired sense of touch, vibration, deep pressure, temperature and joint position. Neuropathic ulcers, i.e. the most common type of ulcers result from the effects of tissue-damaging mechanical loads on an insensitive foot.

Among diabetics, the peripheral arterial disease characteristically affects the vessels between the knee and ankle. Mechanical damage to poorly perfused, fragile and friable tissues typically causes ischemic ulcers. The foot injury that initiates ulcers could be traumatic or may result from repetitive mechanical stress (i.e. walking bare foot or improper footwear) or continuously applied pressure (i.e. usually unperceived by the patient). Thermal injury, insect or animal bites is another cause particularly in developing countries. Restricted joint mobility, poor foot care, and foot deformity resulting in bony prominences also contribute to the risk of ulceration.[9]

Several risk factors have been studied as predictors of amputation in diabetics with foot ulcers. Earlier identification and modification of these risk factors is important to reduce the morbidity. Most of these risk factors are readily identifiable from the history and physical examination. This includes history of previous foot ulceration, neuropathy, foot deformity and vascular disease. In a community based study of 1300 type 2 diabetic patients by Davis et al, it was concluded that incidence of lower extremity amputation was 3.8 per one thousand patient-years. The predictors of limb amputation in diabetics were foot ulceration, ankle brachial index < 0.9, elevated glycated hemoglobin (HbA1C) and peripheral neuropathy.[10]

This study was conducted to determine various regional risk factors associated with diabetic foot ulcers in a tertiary care hospital and study their association and also to document various grades and stages of ulcers when presenting to the tertiary care hospital. The rationale of the study was to provide better understanding and the possible interventions required for primary and secondary prevention in diabetics particularly in a developing country like Pakistan.

MATERIALS AND METHODS

This comparative study was conducted at Dept. of Medicine, PIMS Islamabad from 15th July 2012 to 15th January 2013 after ethical approval from the institutional review committee. Adult patients (≥ 18 years) with type 2 diabetes presenting to diabetic foot clinic and outdoor Medicine department, with recent diabetic foot ulcer (i.e. < 4 weeks) were included in group A by after informed consent. 127 age and gender matched type 2 diabetics without foot ulcer cases were included in group B as control. We used non-probability consecutive sampling. Patients with type 1 diabetes, those who underwent debridement or surgical procedure, having serious systemic illness (i.e. renal failure, liver cirrhosis, congestive cardiac failure and malignancy), non-diabetic patients presenting with foot ulcer and having other causes of neuropathy (i.e. leprosy) were excluded. Diabetic foot was defined as foot ulcer, cellulitis or deep abscess in type 2 diabetes patients.

Demographic information (i.e. age, gender and contact address) was obtained. Duration of diabetes, duration of ulcer and history of previous hospitalizations due to foot ulcers was documented. Glycemic profile was reviewed and labeled as satisfactory at HbA1c ≤ 7 % as per criteria of American Diabetic Association (ADA).

Patients were clinically assessed for presence of sensory neuropathy by Semmes-Weinstein 10-g monofilament and for loss of vibratory sensation by 128 Hz tuning fork. Vascular insufficiency was assessed by clinical examination of lower limb pulses followed by arterial Doppler examination in those with weak or absent pulses. X-ray of the foot was advised as per indication to assess underlying bone involvement. On the basis of these, diabetic foot ulcer was classified according to New University of Texas (NUOT) Diabetic Wound Classification **(table I)**.[11] All this information was documented on a specially designed proforma.

Data was analyzed by Statistical Package for Social Sciences (SPSS) version 17. Mean and standard deviation was calculated for quantitative variables (i.e. age, duration of diabetes and duration of ulcer); and frequencies and percentages for qualitative variables (i.e. gender, glycemic control, previous history of hospitalization due to ulcer, sensory neuropathy, peripheral vascular disease and ulcer grade). Chi-square test was used to identify differences between gender, neuropathy, vascular insufficiency, mode of treatment for diabetes and un-satisfactory glycemic control. Independent sample t-test was used to compare mean age and duration of diabetes between two groups and results presented in the form of tables. P-value < 0.05 considered as statistically significant.

RESULTS

Total 254 cases were included; 127 diabetics with foot ulcer (group A) and 127 diabetics without foot ulcer (group B). There were 40(31.5%) females and 87 (68.5%) males in group A and 44(34.6%) males and 83(65.4%) females in group B giving insignificant difference in gender between the two groups (p = 0.594). Mean age was 55.9 ± 10.79 (group A) versus 51.9 ± 11.4 years (group B). Mean duration of diabetes was significantly longer in group A (9.36 ± 6.05 years) as compared to group B (7.39 ± 4.89 years) (p = 0.016). The glycemic control was un-satisfactory in group A (64.6 %) as compared to group B (52 %) (p = 0.042). Sensory neuropathy was significantly more in group A (94.5 %) vs group B (39.4 %) (p < 0.0001; **table II).** Peripheral vascular disease was significantly more in group A (47.2 %) as compared to group B (29 %) (p = 0.005). On the basis of ankle brachial index (ABI) calculated by Doppler studies of group A, mild vascular disease was present in 17 %, moderate in 21.2 % and severe in 8.7 %. In group B, there was mild disease 15 %, moderate in 12.6 % and severe in 1.6 % **(table III).** According to NUOT Classification, Grade-I ulcer was present in 17.32 % (0.7 % Stage I-A, 11.02 % Stage I-B, 3.14 % Stage I-C, 2.36 % Stage I-D); Grade-II in 37.79 % (0.7 % Stage II-A, 26.77 % Stage II-B, 1.57 % Stage II-C, 8.66 % Stage II-D); Grade-III in 44.88 % (2.36 % Stage III-A, 22.83 % Stage III-B, 0.7 % III-C, 18.89 % Stage III-D) (p = 0.004; **table IV**).

TABLE I: NEW UNIVERSITY OF TEXAS CLASSIFICATION[12]

	GRADE-1	GRADE-II	GRADE-III
Stage-A	Non ischemic non infected superficial wound	Non-ischemic non infected wound penetrating to tendon or capsule	Non-ischemic non infected wound penetrating to bone or joint
Stage-B	Non-ischemic infected superficial wound	Non-ischemic infected wound penetrating to tendon or capsule	Non-ischemic infected wound penetrating to bone or joint
Stage-C	Ischemic non- infected superficial wound	Ischemic non- infected wound penetrating to tendon or capsule	Ischemic non-infected wound penetrating to bone or joint
Stage-D	Ischemic infected superficial wound	Ischemic infected wound penetrating to tendon or capsule	Ischemic infected wound penetrating to bone or joint

TABLE II: DEMOGRAPHIC FEATURES AND ASSOCIATED RISK FACTORS IN DIABETICS WITH FOOT ULCER IN COMPARISON TO DIABETICS WITHOUT FOOT ULCERS (n=254)

Variables		Group A (With Ulcer) n =127	Group B (Without ulcer) n =127	p-value
Age (years) Mean ± SD		55.9±10.79	51.9±11.4	0.098**
Duration of diabetes (years) mean ± SD		9.36± 6.05	7.39±4.89	0.016**
Peripheral neuropathy n(%)		120 (94.5%)	50(39.4%)	<0.0001*
Gender n (%)	• Male • Female	87(68.5%) 40(31.5%)	83(65.4%) 44(34.6%)	0.594*
Glycemic control n (%)	• Satisfactory • Unsatisfactory	45 (35.4%) 82 (64.6%)	61(48%) 66(52%)	0.042*
Vascular insufficiency n(%)	• Normal • Mild • Moderate • severe	67(52.8%) 22(17.3%) 27(21.3%) 11(8.75%)	90(71%) 19(15%) 16(12.6%) 2(1.6%)	0.005*
Mode of treatment for diabetes	• Oral Hypoglycemics • Insulin • Combination therapy • Diet control only	47(37%) 41(32.3%) 37(29%) 2(1.6%)	63(49.6%) 31(24.4%) 26(20.5%) 7(5.5%)	0.038*

*(Chi-square test *; Independent sample t-test **)*

TABLE III: PATIENTS WITH DIABETIC FOOT ULCER IN DIFFERENT STAGES OF ULCER ACCORDING TO NEW UNIVERSITY OF TEXAS CLASSIFICATION (n=127)

		Ulcer Grade			Total
		Grade-I	Grade-II	Grade-III	
Stage of ulcer	Stage-A	1 (0.7%)	1 (0.7%)	3 (2.36%)	5 (3.93%)
	Stage-B	14 (11.02%)	34 (26.77%)	29 (22.83%)	77 (60.62%)
	Stage-C	4 (3.14%)	2 (1.57%)	1 (0.7%)	7 (5.51%)
	Stage-D	3 (2.36%)	11 (8.66%)	24 (18.89%)	38 (29.92%)
Total		22 (17.32%)	48 (37.79%)	57 (44.88%)	127 (100%)

p-value<0.0001; test of significance Chi-square test

TABLE IV: PERIPHERAL VASCULAR DISEASE WITH RESPECT TO GENDER OBSERVED IN PATIENTS WITH AND WITHOUT FOOT ULCER (n=254)

		With ulcer			Without ulcer			Total n=254
		Male n=87	Female n=40	total n=127	Male n=83	Female n=44	total n=127	
Peripheral vascular disease	Normal **(0.90-1.30)**	48 55.2%	19 47.5%	67 52.7%	61 73.5%	29 66%	90 71%	157 61.8%
	Mild **(0.70-0.89)**	13 14.9%	9 22.5%	22 17%	8 9.6%	11 25%	19 15%	41 16%
	Moderate **(0.40-0.69)**	18 20.7%	9 22.5%	27 21.2%	12 14.5%	4 9%	16 12.6%	43 16.92%
	Severe **(<0.40)**	8 9.2%	3 7.5%	11 8.7%	2 2.4%	0 0%	2 1.6%	13 4.7%
***p*-value**		0.71			0.09			254 100%

Test of significance Chi-square test; p< 0.05 is significant.

DISCUSSION

Diabetic foot ulcer is a frequently seen cause of morbidity in patients with diabetes mellitus and also the leading cause of lower extremity amputations. Complications usually begin with an unrecognized foot ulcer in a diabetic patient with an insensitive foot that gets infected, leading to significant morbidity.

The mean age of the patients with diabetic foot ulcer in current study was 55 years. Motley et al found mean age of 57.9 years in a study conducted in Texas USA.[12] Shahbazian et al also found comparable mean age of 53.8 years in an Iranian study.[13] These studies were performed in different health care centers with variation in quality of care; yet the comparable mean age suggests that diabetic foot ulcer is possibly time-dependent with contribute of environmental and local factors. Although the age of onset of diabetes varies in different continents across the world, however with the increasing age, skin becomes more fragile and sensitive that may be the intrinsic contributory factor for development of chronic wounds. Also, the aging cells do not proliferate rapidly and may not have an adequate response to stress in terms of gene up regulation of stress-related proteins.

Among the patients presenting with diabetic foot, there were higher number of males (68.5 %) as compared to females (31.5 %). These results are comparable to an international study conducted by Mohanasoundaram et al that shows the prevalence of diabetic foot ulcer to be 65 % in males and 35 % in females.[14] The possible reasons could be the improper hygiene, inadequate foot care and type of foot wear among males. This can be explained by the reason that most of the women in Pakistan are restricted to domestic activities, while men are engaged in occupational activities with higher risk of mechanical trauma and infection. Current study also confirms this preponderance of men.

The mean duration of diabetes was 9 years in patients with diabetic foot and it was significantly longer as compared to diabetics without ulcer. A study conducted by Hussain et al showed mean duration of diabetes to be 13 years in patients with foot ulcer and 9 years in patients without foot ulcer.[15] Zain et al concluded that long standing diabetes, male gender and overweight are risk factors for diabetic foot ulcers.[16] Thus, it can be conclude that with the longer duration of diabetes there are more chances of developing diabetes related complications like neuropathy and vascular insufficiency leading to vicious cycle of foot deformities, pressure areas and ultimately foot ulceration.

Glycemic control was un-satisfactory in 64.6 % of diabetics with foot ulcer and 52 % of diabetics without foot ulcer. Study conducted by Ahmed et al in Jeddah Saudi Arabia showed poor glycemic control in 66 % of diabetics.[17] A regional study conducted by Shams et al shows poor glycemic control in 75 % diabetics.[18] Hussain et al found mean HbA1C of 12 % in patients with diabetic foot ulcer versus 10.5 % in those without foot ulcer.[1616] Patients with diabetes tolerate infection poorly and infection adversely affects their glycemic control. This repetitive phenomenon further worsens the glycemic control that affects the host's response to infection.[19] Over all glycemic control was poor in both study groups. Possible reasons could be non-compliance or improper management plan leading to development of complications at an early stage and making them prone to infections.

Current study shows higher prevalence of sensory neuropathy in diabetics with foot ulcer (i.e. 94.5 %) vs. those without ulcer (39.4 %) (**table II**). Also, it was more commonly seen in 40-60 years age group. A South Indian study conducted by Dhanasekaran et al, showed diabetic neuropathy in 63.2 % of diabetic foot ulcers.[20] Another study by Al-Mahroos et al showed that diabetic patients with foot ulcers had more severe neuropathy and higher vibration perception thresholds values than patients without foot ulcers.[21] Neuropathy is a micro-vascular complication enhanced by poor glycemic control, and development of neuropathy can be delayed by good glycemic control. The patients with neuropathy had longer mean duration of ulcers, more advanced ulcer stage and higher mean glycated hemoglobin levels. Importance of good glycemic control has been emphasized by these findings as a key aspect of primary intervention in diabetic foot ulcer management. The detection of neuropathy before the development of its complications is the best way to prevent diabetic foot infections.[22]

(Doppler studies, based on Ankle brachial index (ABI), showed peripheral vascular disease to be more common (47.2 %) in diabetics with foot ulcer. (**table III**).

These results are comparable with study by Prompers et al that found peripheral vascular disease in 49 % of patients with new foot ulcer.[23] The decreased circulation leads to poor tissue oxygenation and impaired wound healing. Moreover, infections in these patients are difficult to treat because of inappropriate therapeutic concentrations of antibiotic(s) in the infected tissue. The anaerobic organisms can easily colonize the ulcers leading to resistant infections.[24] In a study by Micheal Edmonds, it has earlier been suggested that lower limb tissue levels of antibiotics can be markedly decreased as a result of impaired perfusion in peripheral vascular disease and revascularization improves wound healing.[25] It is open to speculation whether aggressive revascularization will improve control of infection in these patients. A significant relation between peripheral arterial disease, infection and poor outcome has also been observed in a study by Cardoso et al that suggested the peripheral arterial disease to be an independent predictor of infection-related mortality in a large cohort of outpatients with type 2 diabetes mellitus.[26]

Early recognition and management of risk factors responsible for development and poor healing of diabetic foot ulcers is important for reducing morbidity in diabetics. The most important of these risk factors are previous foot ulceration, neuropathy (loss of protective sensation), foot deformity, and peripheral vascular disease. The significance of these risk factors has earlier been confirmed by the results of a study that was conducted in a community of 1300 type 2 diabetes cases by Davis et al.[8] The incidence of lower extremity amputation in this study was 3.8 per 1000 patient-years. Predictors of amputation were foot ulceration, ankle brachial index < 0.9, elevated HbA1C and neuropathy.

According to NUOT classification, majority of patients (44.8%) in our study presented late in due course of their disease with deep ulcerations i.e. Grade III, while 37.7% in Grade II & fewer patients (17%) presented with Grade I (**table IV**). This late presentation was also seen in a study by Edo et al where less than 10% of the patients presented to hospital within 7 days of developing a foot ulcer.[27] A regional study conducted by Ali et al in Karachi also found more diabetics with advanced grade of ulcer (62 % in Grade II; 29.9 % in Grade III) and very few presenting earlier (7 % in Grade I).[28] Late presentation to health care facility may result from various factors notably ignorance of complications of diabetes like neuropathy,, self care at home, patronage of chemist/pharmacist, lack of funds for health expenses, and fear of limb amputation if they came to the hospital.

Also, in patients with diabetic neuropathy, ulcers usually remain unnoticed at an early stage due to blunted

pain perception and present late once they penetrate deep producing pain and functional debility. The severity of foot ulcer at presentation is a major risk factor for limb amputations as previously shown in a study by Van Battum et al in which predictors of minor amputation were depth of the ulcer, peripheral arterial disease, infection and male gender. The rate of minor amputation correlated strongly with disease severity score at the moment of presentation to the foot clinic.[29] In view of these authors they recommend early access to health care facility by diabetics to reduce the risk of amputation by timely intervention.

The strengths of current study are an appropriate sample size and study design that provides opportunity to compare the risk factors between two groups and advanced investigations like Doppler ultrasound to assess the severity of vascular disease. Also we used New University of Texas (NUOT) classification which incorporates both the grading and staging of diabetic foot ulcer along with the presence or absence of infection. There are certain limitations of this study like lack of randomization and further prognosis or final outcome in the form of minor or major amputations, morbidity and mortality.

CONCLUSION

Very few diabetics present at initial stage of ulcer and there is need to educate patients to seek early medical and surgical opinion. The diabetics having prolonged history of diabetes, poor glycemic control, neuropathy and peripheral vascular disease should be considered at risk for diabetic foot ulcer. The high prevalence of neuropathy and peripheral vascular disease observed in this study points to need for regular examination by clinician and to educate diabetics about foot care and daily self-examination. Appropriate preventive measures, good glycemic control and timely intervention may reduce the morbidity in diabetics.

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