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ORIGINAL ARTICLE

Characteristics of a large cohort of patients with diabetes having at-risk feet and outcomes in patients with foot ulceration referred to a tertiary care diabetes unit

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Key words
Amputation; Diabetic foot; Feet at risk; Foot ulcer

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Abstract

To identify in a large population cohort the clinical and biochemical characteristics of patients with diabetes at risk of foot ulceration and outcomes in those with foot ulcers. All patients with diabetes attending Baqai Institute of Diabetology and Endocrinology from January 2004 to April 2012 included in the study. Clinical, biochemical and socio-demographic data were collected and patients were categorised into those at no risk of ulceration, at risk of ulceration and those with foot ulcer, according to the University of Texas classification. Patients with foot ulceration followed for their final outcome, that is complete healing, persisted non-healed ulcer, lower extremity amputation, lost to follow-up or death. A total of 18 119 patients with diabetes underwent assessment, 3576 (19·7%) patients defined as at high risk for foot ulceration and 3731 (20·6%) presented with foot ulcer. Age, male gender, hypertension, higher glycated haemoglobin (HbA1c), history of smoking and presence of neuropathy were risk factors ($P < 0{\cdot}000$) for foot ulceration. Amputation rate in patients with foot ulceration was significantly related to severity of ulceration at presentation. Preventive foot care practices were followed by 19·02% patients. One thousand eight hundred seventy three (50·2%) patients completely healed, 293 (11%) patients underwent amputation and 397 (10·1%) patients continued to be treated in the foot clinic. All patients with diabetes should be screened for neuropathy to identify those at risk of foot ulceration, as it is the major contributory factor for foot ulceration. The final outcome of foot ulceration was determined by the severity and grade of ulcer at presentation.

Introduction

Foot ulcers are a major cause of morbidity and hospitalisation in patients with diabetes (1). Neuropathy, foot deformity, high plantar pressure, poor glycaemic control, duration of diabetes, male gender and presence of other micro- and macro-vascular complications are contributory factors for foot ulceration (2–4).

The rate of diabetic foot ulceration is higher in developing countries due to various socio-cultural factors such as lack of

Key Messages

- data from Pakistan regarding presentation of diabetic foot ulcers, its characteristics and associated risk factors is scarce
- to the best of our knowledge, this is the largest analysis of patients with diabetes comparing those at low risk with high risk of foot ulceration

- identification of feet at risk is important in the prevention and management of diabetic foot ulcers
- preventive foot care practices are followed by only a minority of patients in a resource constraint society

knowledge regarding diabetic foot care, absence of an effective primary health care system and poor socio-economic status (5). The majority of amputations in patients with diabetes are preceded by foot ulceration; hence, it is important to identify patients at risk of this complication.

In Pakistan, the prevalence of diabetic foot ulceration is between 4% and 10% (6,7) and the amputation rate following foot ulceration although variable is unacceptably high between 8% and 21% (7–9). Data from Pakistan regarding the presentation, associated risk factors and outcome of diabetic foot ulceration are very limited. This study provides robust data regarding diabetic foot disease in Pakistan. We identified patients with diabetes at risk of ulceration and compared the clinical and metabolic characteristics of patients with and without foot ulceration, together with an analysis of outcomes following ulceration.

Methodology

This cross-sectional and follow-up study was conducted at the Baqai Institute of Diabetology and Endocrinology (BIDE), a tertiary care diabetes centre with a specialised foot clinic, from January 2004 to April 2012. All patients with diabetes attending the institute with and without foot problems were included in the study and a history regarding the type, duration and treatment of diabetes were recorded for every patient.

History regarding foot care practices was taken via a structured questionnaire and included questions regarding inspection of feet for dryness, callus, corn, nail cutting technique, bare feet walking, etc. In those with foot ulceration, a detailed history of the cause, duration, history of ulceration, presenting signs and symptoms, previous treatment was recorded at baseline and data on progression was collected.

Body mass index (BMI) was calculated after taking the weight of the patient in kilograms and dividing it by the height of the patient in metres squared. The BMI was categorised into normal between 18 and 22, overweight between 23 and 24·9 and obese $\geq 25\ kg/m^2$ (10). Blood pressure was recorded using a standard mercury sphygmomanometer and hypertension was diagnosed if blood pressure was greater than 130/80 mmHg or if the patients were taking any anti-hypertensive medication (11). Retinopathy was diagnosed after dilating the pupil with 1% Mydriacyl (tropicamide 1%) and examined by a trained physician using a keeler Fundoscope (Vista 20) and graded as background, pre-proliferative or proliferative with or without a history of retinal photocoagulation (12). Peripheral neuropathy was quantified by assessing vibration sensation using a 128 Hz tuning fork and a 10 g monofilament applied perpendicularly to the plantar aspect of the first, third and fifth metatarsal heads (13) avoiding any callus, corn or wound site and graded as normal, diminished (lack of perception at any site) or absent (14). Ankle and knee reflexes were assessed using a tendon hammer and graded as normal reinforced or absent. Temperature was graded normal if the patient could distinguish between hot and cold. Pin prick was graded normal if the patient could differentiate between sharpness or a lack of sharpness when the pin was applied proximal to the great toe nail to barely depress the skin or graded abnormal. The neuropathy was quantified using the neuropathy disability score (NDS) (15) with an NDS score ≥ 6 indicating at-risk feet. Osteomyelitis was identified by probe to bone and imaging of the foot using plain X-ray and it was diagnosed if either one or both was present.

All patients underwent assessment of the vascular status by manual palpation of femoral, popliteal, dorsalis pedis and posterior tibial arteries to define patency and were graded as (a) good volume, (b) diminished volume and (c) absent. Peripheral vascular disease of the lower extremities was defined as absent pulsation of either the dorsalis pedis or posterior tibial artery, or both. Inspection of the feet was undertaken for any cutaneous changes, callus, deformities and nail disorders.

Patients with one of the following factors were classified as having feet at risk; diabetic neuropathy, peripheral vascular disease, foot deformity, previous history of foot ulceration, amputation and the presence of corn or callus.

Ulcers were classified according to the University of Texas classification and their sites and sizes were recorded (16).

Outcomes were recorded as complete healing, continuing treatment, lower extremity amputation (LEA) defined as loss of any part of the lower limb, lost to follow-up or expired LEA was classified as major if proximal to tarso-metatarsal joint and minor if distal to this joint (16,17).

Statistical analysis

Data were recorded and analysed on SPSS version 13.0 for Windows. Tables are presented in the form of mean ± SD and count with percentage. Comparison between mean values of groups was obtained by analysis of variance (ANOVA) and then by post hoc Tukey's tests, comparison between percentages was observed by χ^2. Significance was defined as $P < 0{\cdot}05$. Univariate and multivariate logistic regression was used to find the association of foot ulceration with various risk factors.

Results

A total of 18 119 patients with a mean age of $50{\cdot}51 \pm 12{\cdot}24$ years and duration of diabetes of $13{\cdot}09 \pm 7{\cdot}76$ years were studied. Comparisons were made between patients at low risk and high risk of foot ulceration and patients with ulceration (Table 1). Comparing the 3576 (21%) patients at high risk of foot ulceration with the 10 812 (65·5%) at low risk of ulceration, they were older ($53{\cdot}77 \pm 11{\cdot}20$ vs $48{\cdot}73 \pm 12{\cdot}57$ years, $P < 0{\cdot}000$), had a longer duration of diabetes ($15{\cdot}01 \pm 8{\cdot}08$ vs $11{\cdot}82 \pm 7{\cdot}33$ years, $P < 0{\cdot}000$) and a greater prevalence of hypertension (76·9% vs 75·1%, $P < 0{\cdot}05$). Two thousand six hundred and thirty eight (15·5%) patients presented with foot ulceration. They were older ($53{\cdot}5 \pm 10{\cdot}52$ vs. $48{\cdot}73 \pm 12{\cdot}57$ years), had a longer duration of diabetes ($15{\cdot}80 \pm 7{\cdot}83$ vs $11{\cdot}82 \pm 7{\cdot}33$years), and male predominance (71·4% vs 51·8%) compared to low risk patients. Glycated haemoglobin (HbA1c) and serum creatinine were higher in

Table 1 Comparison between patients with diabetes at low risk and high risk of foot ulceration and patients with a foot ulcer*, †

	Low risk of ulceration	High risk of ulceration	Foot ulcer
$n = 18\,119$	10 812 (59·7%)	3576 (19·7%)	3731 (20·6%)
Male	5605 (51·8%)	1776 (49·7%)***	2678 (71·7%)*
Female	5207 (48·2%)	1800 (49·7%)	1053 (28·3%)
Age (years)	48·73 ± 12·57	53·77 ± 11·20*	53·52 ± 10·56*
Age > 65 years	1151 (10·6%)	675 (18·9%)*	585(15·7%)*
Duration of diabetes (years)	11·82 ± 7·33	15·01 ± 8·08*	15·76 ± 7·80*
Body mass index (kg/m^2)	27·30 ± 5·41	28·30 ± 6·15*	26·69 ± 5·27*
Systolic blood pressure (mmHg)	128·34 ± 20·79	132·88 ± 23·12*	134·42 ± 21·08*
Diastolic blood pressure (mmHg)	80·86 ± 11·15	80·68 ± 12·51	83·29 ± 11·15*
Hypertension (≥130/80 mmHg)	8118 (75·1%)	2751 (76·9%)***	2799 (75%)
Smoking	1545 (14·3%)	582 (16·3%)**	759(20·3%)*
HbA1c (%), mmol/mol	9·46 ± 2·24, 80 ± 1	9·85 ± 2·36*, 84 ± 2	9·84 ± 2·32*, 84 ± 2
Serum creatinine (μmol/l)	1·04 ± 0·38	1·15 ± 0·54*	1·29 ± 0·73*
Total cholesterol (mmol/l)	4·83 ± 1·09	4·74 ± 1·11***	156·44 ± 41·52*
HDL (mmol/l)	0·99 ± 0·19	0·98 ± 0·19*	34·80 ± 7·82*
LDL (mmol/l)	3·02 ± 0·70	2·95 ± 0·70**	100·89 ± 25·87*
Triglyceride (mmol/l)	1·99 ± 1·04	1·96 ± 1·05	139·17 ± 92·03*

CI, confidence interval; HbA1c, glycated haemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

*Data presented as mean ± SD and *n* (%); neuropathy disability score score ≥ 6 indicate high-risk feet.

†All patients with significant neuropathy were considered at risk of foot ulceration.

* $P < 0·001$, ** $P < 0·01$ and *** $P < 0·05$, comparing low risk of ulceration with high risk of ulceration group and patients with foot ulcer.

Table 2 Preventive foot care practices among patients with foot ulcer

Variables	Yes	No
Daily inspection of feet	21·38%	78·61%
Proper nail cutting technique	31·08%	68·91%
Use of proper foot wear	9·52%	90·47%
Use of socks	45·16%	54·83%
Use of moisturiser for feet	36·46%	63·53%
Bare foot walking	40%	60%

those with ulceration compared to patients with a low risk of ulceration while total cholesterol, triglycerides and low-density lipoprotein (LDL) were lower in patients at risk of ulceration compared to the low-risk patients.

Preventive foot care practices were observed in only 19% patients with foot ulcer. Twenty-one per cent patients daily inspected their feet, while 9·5% patients were using proper foot wear. Similarly proper, nail cutting technique was practiced by 31% patients, use of moisturiser on feet was seen in 36% patients while 40% patients were walking barefoot (Table 2).

On logistic regression analysis, age, male gender, history of smoking, duration of diabetes and presence of hypertension were significant risk factors ($P < 0·0001$) for patients with foot ulceration compared to low risk patients (Table 3).

With regard to the site of ulceration, toes were involved in 1225 (46·4%) of the patients, metatarsal head in 526 (19·9%), heel in 387 (14·7%), mid foot in 379 (14·4%) malleoli in 82 (3·1%) and other sites in 39 (1·47%) patients.

The patients with foot ulceration were classified according to the University of Texas classification system. Seven hundred and fifty five (28·62%) patients presented with stage 1B, followed by 613 (23·23%) and 360 (13·64%) patients in stage 1A and 3B respectively. Ninety-one (30·33%) patients underwent amputation of 235 (8·90%) patients who presented with stage 3D ulceration followed by 75 (25%) with stage 3B (Table 4).

Table 4 shows the outcome of patients with foot ulceration. Of 3731 patients, 1873 (50·2%) completely healed and 293 (11·10%) patients underwent amputation. Seventy five (2·0%) patients expired and 1093 (29·2%) were lost to follow-up (Table 5).

Discussion

This study provides a large analysis of patients with diabetes comparing those at low risk with high risk for foot ulceration in relation to risk factors and also defines the outcomes of patients with foot ulceration at a tertiary care diabetes centre in Karachi, Pakistan. It builds on our recent data assessing outcomes in a smaller cohort of patients (18).

A large number of patients with diabetes (21%) presenting for general diabetes care were at risk of foot ulceration and 15·5% presented with a foot ulcer. The reported estimates for feet at risk vary widely (5–80%) depending on the population studied, methodology applied and age group (19). Furthermore, because this study was conducted at a tertiary care diabetes centre with a specialised foot clinic, the number of patients at risk of ulceration will be expected to be higher than the general population.

The most common risk factor for ulceration was neuropathy, which is a well-recognised risk factor for the development of diabetic foot ulceration (13). Preventing foot complications begins with identifying feet at risk. The insidious nature of neuropathy emphasises the importance of regular assessment of the diabetic foot. Increasing age, poor glycaemic control and poor vision may contribute to the development of foot ulceration (20) as demonstrated in numerous observational

Table 3 Logistic regression analysis of comparison between patients with diabetes at low risk and high risk of foot ulceration and patients with a foot ulcer*

	Univariate model			Multivariate model		
Risk factors	Odds ratio†	Odds ratio‡	Odds ratios§	Odds ratio†	Odds ratio‡	Odds ratios§
Male	0·917 (0·850–0·989)	2·317 (2·112–2·541)	2·563 (3·324–2·826)	0·958 (0·872–1·052)	2·325 (2·085–2·593)	2·508 (2·209–2·847)
Age (years)	1·037 (1·033–1·040)	1·034 (1·030–1·038)	1·0 (0·995–1·004)	1·024 (1·019–1·028)	1·016 (1·012–1·021)	0·990 (0·985–0·995)
Duration of diabetes (years)	1·056 (1·051–1·061)	1·067 (1·061–1·073)	1·012 (1·006–1·018)	1·041 (1·035–1·047)	1·061 (1·054–1·068)	1·019 (1·012–1·026)
Body mass index (kg/m^2)	1·031 (1·025–1·038)	0·975 (0·966–0·985)	0·952 (0·943–0·961)	1·044 (1·036–1·052)	0·987 (0·977–0·996)	0·953 (0·943–0·963)
Systolic blood pressure (mmHg)	1·010 (1·008–1·012)	1·014 (1·012–1·016)	1·003 (1·001–1·005)	1·007 (1·005–1·010)	1·009 (1·006–1·012)	1·001 (0·998–1·004)
Diastolic blood pressure (mmHg)	0·999 (0·995–1·002)	1·019 (1·015–1·023)	1·019 (1·015–1·023)	0·991 (0·987–0·996)	1·016 (1·010–1·022)	1·024 (1·018–1·030)
Smoking	1·176 (1·059–1·305)	1·652 (1·482–1·842)	1·376 (1·220–1·552)	1·228 (1·088–1·387)	1·083 (0·959–1·224)	0·893 (0·772–1·032)

*Data is presented as odds ratio (95% confidence interval).
†Obtained by comparing low risk of ulceration with high risk of ulceration group.
‡Obtained by comparing low risk of ulceration with foot ulcer group.
§Obtained by comparing high risk of ulceration with foot ulcer group.

Table 4 Presentation of foot ulcers according to the University of Texas (UT) classification

Grade	Stages	No. of patients*	Without amputation	Amputation†
Grade 0				
None	Stage A	44	40	4 (1·33%)
Infection	Stage B	105	104	1 (0·33%)
Ischaemia	Stage C	6	2	4 (1·33%)
Both	Stage D	14	13	1 (0·33%)
Grade 1	Superficial wound not involving tendon, capsule or bone			
None	Stage A	613	574	39 (13%)
Infection	Stage B	755	715	40 (13·33%)
Ischaemia	Stage C	32	32	0 (0%)
Both	Stage D	137	129	8 (2·67%)
Grade 2	Wound penetrating to tendon or capsule			
None	Stage A	2	1	1 (0·33%)
Infection	Stage B	250	230	20 (6·67%)
Ischaemia	Stage C	19	14	5 (1·67%)
Both	Stage D	53	45	8 (2·67%)
Grade 3	Wound penetrating to bone or joint			
None	Stage A	1	1	0 (0%)
Infection	Stage B	360	285	75 (25%)
Ischaemia	Stage C	12	1	3 (1%)
Both	Stage D	235	144	91 (30·33%)

*Patients who completed the follow-up.
†Data presented as *n* (%).

Table 5 Outcome of patients with foot ulceration

Outcome	*n* = 3731*
Completely recovered	1873 (50·2%)
Minor amputation	
Toe amputation	219 (5·8%)
Transmetatarsal amputation	17 (0·45%)
Major amputation	
Above ankle amputation	50 (1·3%)
Above knee amputation	7 (0·18%)
Under treatment	397 (10·1%)
Lost to follow-up	1093 (29·2%)
Expired	75 (2·0%)

*Data presented as *n* (%).

studies (3,21). In this study, we show a relationship between foot ulceration and the duration of diabetes and hypertension, similar to previously identified risk factors (4,9).

Among patients with foot ulceration, a large proportion had a history of foot ulceration, consistent with previous studies (16,17,19,22).

Most of the patients presented with neuropathic ulcers followed by neuro-ischaemic ulcers, but pure ischaemic ulcers were rare in our study population. A purely ischaemic foot with no concomitant neuropathy is rarely seen in patients with diabetes (22). Hence, neuropathy is the major precipitating factor for foot ulceration (23). While the prevalence of neuropathy is common, the prevalence of peripheral vascular disease is generally low in Asian Indians (19). This finding needs further evaluation with vascular assessment using dopplers and angiography but was beyond the scope of this study.

Male gender predominance in this study is consistent with previously reported studies (4,6,7). Similarly, most of the patients with a foot ulcer had diabetes for more than 10 years with poor glycaemic control. Although this study together with other studies (4) found that diabetes duration was related to the risk of developing foot ulceration, others have not found this association (4). Similarly, triglyceride, cholesterol and LDL levels were lower in patients with ulceration compared to the group at low risk of ulceration. However, the majority of patients with foot ulceration were taking lipid-lowering agents that may explain the lower blood lipid levels in this group.

The majority of our patients with foot ulceration presented with advanced pathology (UT stage C and D) resulting in a high amputation rate. The incidence and prevalence of LEA in patients with diabetes vary widely across the world (15,23) from 0·03% in countries like Denmark to 0·86% in the USA to as high as 33% in Africa (23). The reported prevalence of amputation from India is about 3% (22). In Pakistan despite a comparable prevalence of foot ulceration, the amputation rate has been reported to be as high as 8–21% (6,8,24). In this study, 11·10% of patients required LEA. In our study, 28% patients were either lost to follow-up or were referred to a public sector hospital due to financial reasons. This may have important implications as the final outcome of these patients is not known. Many factors have been suggested to contribute to this unacceptably high rate of LEA such as severity of disease at presentation, increasing age, poor socio-economic conditions and lack of diabetes care in primary care, with late referral and hence poorer outcomes once patients reach secondary and tertiary care units (20,22).

Preventative foot care practices were followed by only 19·02% of the studied population. This may be multifactorial including lack of awareness regarding foot care, use of improper foot wear and bare feet walking. The percentage of patients following good foot care practice is much lower in our study population than reported in other studies from India and around the world (25,26). This observation is important as foot ulceration leading to amputation, is potentially preventable (16). With adequate education, preventive foot care practices and attention to foot wear, incidence of ulceration and amputation can be reduced by 44–85% (26).

The major limitation of our study is that it is not population based and represents patients referred to a tertiary care centre. Final outcome of patients who lost to follow-up was not known. This limitation of population selection was unavoidable. Furthermore, neuropathy and vascular assessment was done using conventional clinical methods. However, the main strength is the sample size with accurate characterisation and grading of ulceration and a high follow-up rate.

Foot complications in patients with diabetes can be managed with an integrated multidisciplinary team. The most important step in preventing diabetic foot complications is the recognition of feet at risk and the early recognition and treatment at the level of primary care followed by prompt referral to the multidisciplinary team. This is more important in a resource constrained society like Pakistan as the economic and psychological impact of diabetic foot ulceration and amputation is considerable (27).

Conclusion

All patients with diabetes should be screened to identify those at risk of foot ulceration, as neuropathy is the major contributory factor for foot ulceration. The final outcome of foot ulceration was determined by the severity and grade of ulcer at presentation along with the presence of other micro- and macro-vascular complications. This emphasises the importance of education to both patients and primary care practitioners to allow earlier referral and timely intervention to reduce or limit these unacceptably high amputation rates.

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