ORIGINAL ARTICLE

Prevalence of diabetic foot syndrome amongst population with type 2 diabetes in Pakistan in primary care settings

Amanullah Khan, Nabeea Junaid

Abstract

Objective: To determine the prevalence of diabetic foot syndrome in type 2 diabetes mellitus patients.

Methods: This cross-sectional study was conducted at 25 centres across eight cities in Pakistan from August 2010 to March 2011, and comprised adult type 2 diabetics. The subjects underwent ankle brachial pressure index evaluation for diabetic foot, and neurological assessment using 10g monofilament for sensation and 128Hz tuning fork to elicit vibration.

Results: Of the 230 subjects, 94(40.86%) were males and 136(59.13%) females. The overall mean age was 53.82±9.96 years and mean glycated haemoglobin was 8.81±2.04%. The prevalence of diabetic foot syndrome was 32(13.9%). Based on established diabetic foot risk classification, 37(16.08%) patients were in category-1, 6(2.60%) in category-2, 32(13.91%) in category-3 and 148(64.34%) in category-0. On ankle brachial pressure index assessment, 94(40.86%) patients had impaired values (p<0.9). Sensation was impaired in 50(21.73%) patients, vibrations could not be detected in 37(16.08%), ankle reflexes could not be elicited in 35(15.21%), and foot pulses could not palpated in 28(12.17%) patients.

Conclusions: A high prevalence of diabetic foot syndrome was observed.

Keywords: Diabetic foot/epidemiology, Foot ulcer, Diabetes mellitus Type 2, Amputation, Risk factors. (JPMA 67: 1818; 2017)

Introduction

The burden of diabetes and diabetes-related complications is increasing worldwide. Diabetic foot is a common complication of diabetes and refers to a wide spectrum of symptoms associated with a progressive loss of sensation in feet. The three main pathologies that are associated with diabetic foot syndrome (DFS) are diabetic peripheral neuropathy, peripheral arterial disease and/or infection.[1] The syndrome also encompasses complications like Charcot neuroarthropathy, osteomyelitis, foot ulceration and may lead to the most feared outcome, amputation.[1] The prevalence of foot ulcers is reported to range from 4.0% to10.0% in patients with diabetes, which suggests that lifetime risk of developing foot ulcers in these patients may be as high as 25.0%.[2-4] Of all the non-traumatic lower limb amputations, 8 out of 10 amputations are done in patients with diabetes, out of which 85.0% follow a foot ulcer.[2,5,6] Studies from Pakistan indicate that the prevalence of diabetes foot ulcers ranged from 4.0%[7] to 10.0%.[8] The amputation rate in Pakistan is reported to be high ranging from 21.0%[9] to 48.0%.[10]

Diabetic foot problems are one of the most common reasons for hospitalisation of diabetic patients and impose a significant economic burden on patients, their families and society as a whole. After the appearance of foot ulcers, the cost of care for patients with DFS is 5.4 times higher in the first year and 2.8 times in the second year compared to diabetes patients without foot ulcers.[11] The mean direct cost of major (transtibial or transfemoral) and minor amputations reported in Pakistan in 2005 was Rs46,182±30,742 ($778±518) and Rs50,494±30,488 ($851±514), respectively,[12] which would cost $479±319 and $524±316, respectively, in the current day (2012-13). Patients also suffer from reduced quality of life (QoL). Foot ulcers are reported to cause significantly more pain,[13] result in less mobility[14] and impose restrictions in social functioning and psychological well-being[15] along with burden of treatment regimen.[16,17] Patients with foot ulcer reported significantly (p<0.001) poorer health-related QoL scores, in particular for role limitation-physical, physical functioning, and role limitation-emotional subscales of the Short Form-36 (SF-36) assessment, than patients with diabetes alone.[18]

Since the majority of the amputations in patients with type 2 diabetes mellitus (T2DM) are reported to follow foot ulcers,[6] an understanding of pathways and risk factors is essential to improve QoL, reduce the frequency of ulceration, and ultimately, avoid the amputation of lower extremities. Evidence suggests that peripheral

Sanofi-Aventis Pakistan Limited.

Correspondence: Nabeea Junaid. Email: nabeea.junaid@sanofi.com

vascular disease, diabetic neuropathy, foot deformity and history of foot ulceration or amputation are associated with the development of diabetic foot ulcers.[19] In addition, high plantar pressure, duration of diabetes, race and gender were found to have significant association with ulcerations in diabetic population.[20]

The management of DFS needs a multidimensional approach involving complementary prevention and treatment strategies. Prevention of DFS through the prolonged use of antibiotics reduces foot ulcer rates and amputations, in addition to improved quality adjusted life years (QALYs), while being cost-effective.[21] Further, early detection of those at risk of developing diabetic foot and proper management of foot problems and its associated complications are known to have substantial economic benefits[22] in terms of reduced treatment cost, particularly the cost of amputation in developing countries.[23] Apart from clinical strategies for using appropriate foot care,[24] improving detection and treatment, improving patient awareness, optimising glycaemic control, and cessation of smoking can be effective in reducing morbidity and mortality of DFS.[25]

A clear evidence-based encompassing data from basic research, clinical management and demographic characteristics of DFS is necessary for the effective implementation of prevention and treatment strategies. Creating context-specific management approaches for DFS, especially in a resource-limited setting like Pakistan, requires a clear understanding of its prevalence, risk classification of affected population, and association with incident risk factors. Currently, statistics of nationwide data on the prevalence of DFS from Pakistan is limited. The current disease registry attempts to address the need for updated and comprehensive information about DFS at primary care settings in Pakistan. The diabetic foot disease registry was primarily undertaken to determine the prevalence of DFS among patients with T2DM in Pakistan. Secondary objectives of the study were to document the profile of patients willing to participate and categorise them according to risk classification, identify the risk factors for foot complications and determine the glycated haemoglobin (HbA1c) levels in these patients. It is expected that this first nationwide study will provide an understanding of the burden of DFS in Pakistan in primary care settings.

Patients and Methods

This cross-sectional study was conducted at 25 centres across eight cities in Pakistan from August 2010 to March 2011, and comprised T2DM patients. The study was a national, multi-centre, non-interventional and cross-sectional disease registry. Data was recorded during a single visit to the primary care centres. Since ethics review committee does not exist at a majority of such clinics, administrative approval was taken from each participating clinic/investigator. Informed consent was obtained from each patient.

Patients aged 18 years or above with T2DM were included in the study. A total of 25 investigators participated in the study who were selected by convenience sampling method. Investigators at each centre recruited 10 consecutive patients who met the inclusion criteria.

Data was recorded on case report forms by the investigators. Demographic characteristics such as age, gender, weight and height were recorded. In addition, data on blood pressure (BP), HbA1c, fasting blood sugar (FBS), duration of diabetes and age at diagnosis were collected.

The proportion of T2DM patients with DFS was evaluated. Additional criteria of evaluation included the profile of patients with DFS and normal feet, risk factors associated with DFS and distribution of patients with DFS across HbA1c levels. A patient with DFS was defined as a person with current and/or healed ulcer and/or gangrene and/or lower limb amputation.

A brief history of previous diabetic foot ulcer, amputation, gangrene, deformity and current ulceration were recorded. Physical examination of both the foot was conducted to assess dryness of skin, cracked skin and discoloration/pigmentation and to observe any infection, callus growth, blister or muscle wasting.

Neurological assessment of the foot was performed using 10g (Semmes-Weinstein) monofilament for sensation, a biothesiometer for ankle reflexes and 128Hz tuning fork to elicit vibration sensitivity. The vascular status of the foot was assessed using ankle brachial pressure index (ABPI) and Doppler ultrasound (Huntleigh dopplex kit, United Kingdom [UK]). The ABPI is the ratio of blood pressure in the lower legs to the blood pressure in the arms. A lower blood pressure in the leg compared to the arm signifies blocked arteries and peripheral vascular disease. An ABPI value >0.9 is considered normal, <0.8 is associated with claudication, and <0.4 is commonly associated with ischaemic rest pain and tissue necrosis. Other parameters such as pinprick sensation and temperature variation between the two feet were also assessed.

Following the examination of diabetic foot, patients were classified into four categories according to the cumulative risk stratification accepted by international working

group on diabetic foot.[26] Patients with no evidence of neuropathy were considered as category 0, patients with neuropathy but no evidence of foot deformity or peripheral vascular disease were considered as category 1, patients with neuropathy with evidence of deformity or peripheral vascular disease were considered as category 2 and patients with history of foot ulceration or lower extremity amputation were considered as category 3.

Based on a previous study from Pakistan, the incidence of diabetic foot ulcers in patients with T2DM in Pakistan was taken as 10.0%.[8] For 95% confidence interval (CI), at 4.0% margin of error, a sample size of 216 patients was required to estimate the point prevalence to within 14%. Accounting for inaccurate completion of case report forms as well as withdrawal after consent, a sample size of 250 was determined. Descriptive statistics was used for all analyses. All categorical variables were presented as proportions and percentages. Continuous variables were reported as means with standard deviations. Skewed data was presented as median. Chi-square independent test and t-test were used to compare the proportions differences and mean differences between patients with and without DFS. P<0.05 was considered statistically significant. All statistical analyses were carried out using SPSS 18.0.

Results

Of the 250 patients enrolled, data was analysed for 230(92%) patients as 6(2.4%) patients refused to participate after giving consent and 14(5.6%) were not evaluated for DFS.

There were 94(40.86%) males and 136(59.13%) females with an overall mean age of 53.82±9.96 years and mean duration of diabetes being 7.87±5.50 years. The mean FBS in the study population was 160.63±62.19 mg/dL and HbA1c was 8.81±2.04%. The systolic and diastolic BP was 135.13±18.97 mmHg and 86.17±10.19 mmHg, respectively, and body mass index (BMI) was 28.89±5.05 kg/m2.

DFS was observed in 32(13.91%) patients (95% CI: 10.03% - 18.98%) patients. On the basis of international consensus on diabetic foot risk classification, 37(16.1%) patients were in category 1, 6(2.60%) in category 2, 32(13.91%) in category 3 and 148(64.34%) in category 0 (Figure-1).

The most common findings observed on physical examination of foot were dryness of skin in 91(39.56%), cracked skin 71(30.86%) and discoloration/pigmentation 36(15.65%). A history of diabetic foot ulcer was observed in 15(6.52%) of patients whereas 20(8.69%) patients had ulceration at the time of diagnosis. Moreover, only 1(0.43%) patient presented with gangrene and 3(1.3%) with amputation. Neurological assessment of foot showed that sensation was impaired on monofilament

Table-1: Findings on assessment for diabetic foot syndrome in patients with diabetes (N=230).

Parameters	n (%)
Physical examination of feet	
Dryness of skin	91 (39.56)
Cracked skin	71 (30.86)
Discoloration/pigmentation	36 (15.65)
Ingrown toe nails	24 (10.43)
Infection	23 (10.00)
Callus	21 (9.13)
Blister	13 (5.65)
Muscle wasting	22 (9.56)
Neurological assessment	
Sensation absent on monofilament examination	50 (21.73)
Pinprick sensation absent	23 (10.9)
Ankle reflexes absent	35 (15.21)
Vibration absent	37 (16.08)
Vascular assessment	
Varied temperature gradient	38 (16.52)
Foot pulses (by palpation) absent	28 (12.17)
Impaired ABPI (<0.9)	94 (40.86)
Extreme findings	
Previous history of diabetic foot ulcer	15 (6.52)
Current ulceration	20 (8.69)
Amputation	3 (1.30)
Gangrene	1 (0.43)
Deformity	11 (4.78)

ABPI: Ankle brachial pressure index.

Table-2: Comparison of profiles between patients with diabetic foot syndrome and normal feet.

Baseline characteristics	DFS (n=32)	Normal feet (n=198)	p value
Age, years	52.81 ± 9.27	53.98 ± 10.09	0.54
Weight, kg	78.56 ± 16.19	73.57 ± 14.43	0.08
Height, cm	160.62 ± 10.84	159.81 ± 9.63	0.70
BMI, kg/m^2	29.54 ± 5.1	28.81 ± 5.05	0.51
BP systolic, mm Hg	134.87 ± 18.61	135.18 ± 19.07	0.93
BP diastolic, mm Hg	87.74 ± 10.23	85.92 ± 10.19	0.36
Duration of diabetes, years	8.93 ± 4.59	7.70 ± 5.62	0.24
Age at diagnosis, years	43.75 ± 10.07	45.71 ± 11.89	0.38
FBS, mg/dL	175.81 ± 75.27	158.16 ± 59.66	0.14
HbA1c, %	9.37 ± 2.34	8.72 ± 1.98	0.09

All values are represented as mean±standard deviation
DFS: Diabetic foot syndrome
BMI: Body mass index
BP: Blood pressure
FBS: Fasting blood sugar
HBA1c: Glycated haemoglobin.

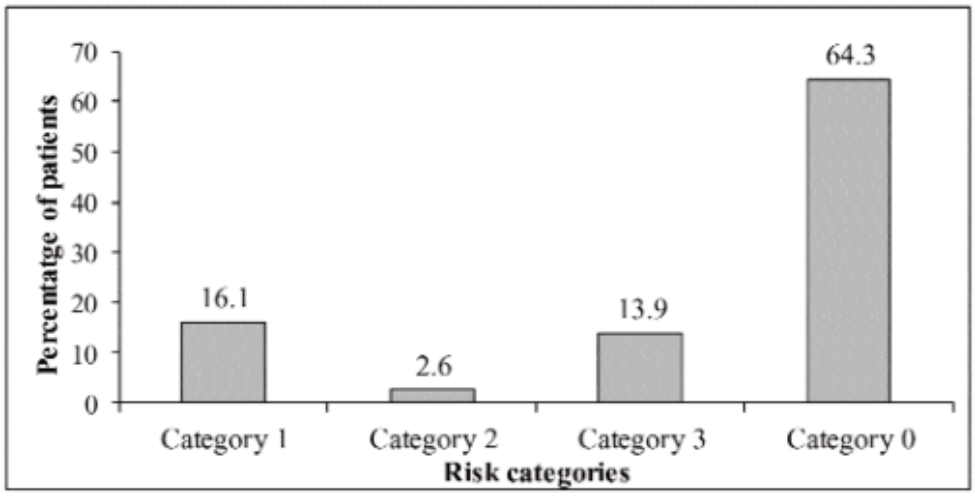
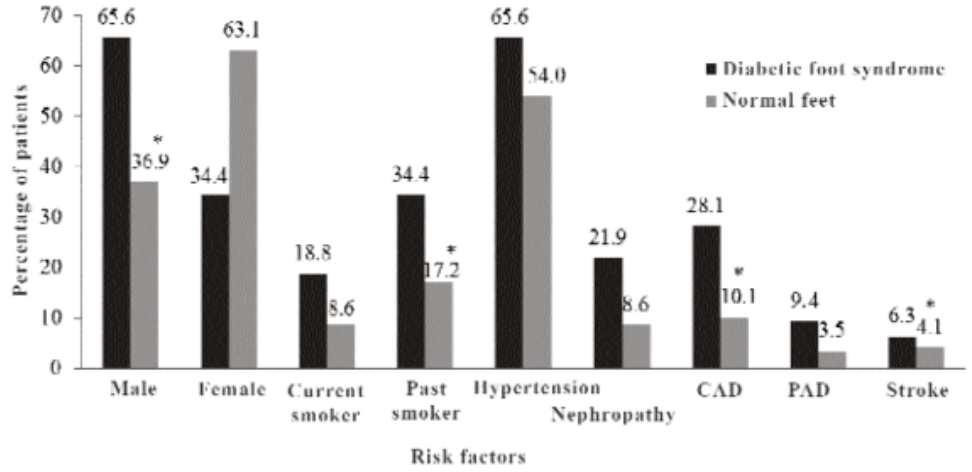


Figure-1: Categorisation of patients based on international consensus on diabetic foot risk classification.



***Signifies statistically significant difference, p <0.05.**
CAD: Coronary artery disease
PAD: Peripheral artery disease.

Figure-2: Comparison of risk factors between patients with diabetic foot syndrome and normal feet.

Table-3: Distribution of patients with DFS across HbA1c levels (N=32).

HbA1c levels (%)	n (%)	Odds ratio	p value
<7	6 (18.75)	-	-
7.1 - 8.0	3 (9.37)	1.69	0.48
8.1 - 9.0	4 (12.50)	1.40	0.62
9.1 - 10.0	6 (18.75)	0.64	0.48
>10	13 (40.62)	0.44	0.12

HBA1c: Glycated haemoglobin
DFS: Diabetic foot syndrome
Reference category for odds ratio, HbA1c <7.0%.

examination in 50(21.73%) patients, ankle reflexes could not be elicited in 35(15.21%) and vibrations could not be detected by 37(16.08%) patients. Further, the assessment of vascular status in the study population revealed that most patients 94(40.86%) had an impaired ABPI value (<0.9), 38(16.5%) had varied temperature gradient between the two feet and foot pulses (by palpation) were absent in 28(12.17%) patients. The mean ABPI values for the left and right feet were 0.98±0.13 and 0.97±0.13, respectively (Table-1).

No statistical difference was observed in the age (p=0.54), systolic (p=0.93) and diastolic (p=0.36) BP, duration of diabetes (p=0.24), FBS (p=0.14) and HbA1c (p=0.09) between patients with DFS and normal feet (Table-2).

DFS was found across all levels of HbA1c, and there was no statistically significant difference in the odds ratio of number of patients with DFS with HbA1c <7.0% and HbA1c ≥7.0%. FBS was higher in patients with DFS compared to those with normal feet, though not significant (175.8 mg/dL vs. 158.2 mg/dL, p<0.14). Among patients with DFS, 26(81%) had HbA1c >7.1% (Table-3).

Comparison of risk factors between patients with DFS and normal feet showed significant difference in gender (p=0.002), smoking history (p=0.02), coronary artery disease (CAD) (p=0.01) and stroke (p=0.03) (Figure-2). Among all the patients, hypertension 128(55.65%), history of smoking 45(19.56%) and CAD 29(12.60%) were the most common risk factors associated with DFS.

Although the relative proportion of patients taking only OADs was similar between patients with DFS 19(59.37%)

Table-4: Comparison of treatment between patients with diabetic foot syndrome and normal feet.

Treatment (n=198)	DFS (n=32)	Normal feet
OADs only	19 (59.37)	129 (65.15)
Monotherapy	4 (21.05)	27 (20.93)
Two OADs	12(63.15)	81 (62.79)
>2 OADs	3 (15.78)	21 (16.27)
Insulin only	0 (0.0)	7 (3.53)
OADs + insulin	13 (40.62)	59 (29.79)

All values presented as n (%).
DFS: Diabetic foot syndrome
OADs: Oral anti-diabetic drugs.

and normal feet 129(65.15%), a higher proportion of patients with DFS received OADs + insulin 13(40.62%) (Table-4).

The most common OADs prescribed in the study population were metformin 196(85.21%), glimepiride 102(44.34%) and thiazolidinediones 36(15.65%).

Discussion

The current study demonstrated that there was a high prevalence (13.9%) (95% CI: 10.0% - 18.9%) of DFS in patients with T2DM in Pakistan. One-third of the patients were at high risk of DFS in the study population. Dryness of skin, cracked skin, and discoloration/pigmentation were most commonly observed on foot examination. On neurological examination, most of the patients were found to have loss of protective sensation of foot and impaired ABPI score. Significant differences in the risk factors such as gender, past smoking, CAD and stroke were observed in patients with and without DFS. Incidence of DFS was found across all levels of HbA1c.

The prevalence of DFS in T2DM patients observed in the current study is substantially higher than previous reports of 4.0%[7] and 10.0%[8] from Pakistan. Although the sample size used in the current study was smaller than previous studies (n=2,199),[8] the recruitment of patients from a wide geographic area (spanning eight cities of Pakistan) ensures greater applicability of the current data. The results were similar to the studies from the Indian sub-continent, where 15% prevalence of neuropathy was reported.[27] Lower prevalence rates of 2.8% and 8.5% for DFS were found in patients with T2DM from Germany[28] and UK,[29] respectively. This underscores the low importance given to the care of serious diabetic complications, in the public healthcare system of developing countries. Hence an early diagnosis of disease through periodic screening in patients with T2DM is a crucial step towards preventing foot ulceration and reducing disease burden.

Stratification of patients at risk for DFS is used to facilitate risk group assignment and design preventive and monitoring strategies.[26] Alarmingly, one-third of the study population was at risk of foot ulcer, classified into categories 1-3 according to the international consensus on diabetic foot risk classification. Amongst these, 13.9% patients were already at high risk of "extreme degree of foot complications" (category 3) with ulcers and amputations. This might be due to the longer duration of diabetes in the study population, and perhaps the presentation of advanced stage of disease at the time of diagnosis. Compared to the current study, a recent observation from a large cohort of patients with diabetes (between 2004 and 2009) from Pakistan identified around 10.0% of patients with 'feet at risk'.[30] Another cohort study, which evaluated the prevalence and incidence of foot pathology showed very high proportion of Mexican Americans (40.9%) and non-Hispanic whites (41.3%) to be at risk of DFS.[3]

The identification of gender, long-term complications of diabetes, smoking and CAD as the risk factors of DFS in the current study is in agreement with previous studies from Pakistan[30,31] and Germany.[28] Varied temperature gradient observed in the study population may also contribute to an increased risk of foot ulceration as reported in previous studies.[32] In addition, socio-cultural factors such as barefoot walking,[33] poor socio-economic conditions and inadequate facilities for diabetes care in resource-constrained societies are known to aggravate the incidence of foot ulceration.[34] Evidence from previous studies from Pakistan suggest that other factors such as poor knowledge about diabetic foot care and low education and literacy rates are associated with poor foot care practices.[35,36] A high incidence of risk factors warrants prudent strategies for prevention and management of DFS in patients with T2DM. This is particularly important considering the negative impact of DFS on QoL and associated economic burden on the patient and society. Further, early detection along with glycaemic control, awareness of foot care and appropriate footwear, and providing multidisciplinary approach to wound care can reduce the rate of lower extremity amputations by more than 50.0%.[37,38]

Evidence suggests that age and duration of diabetes are risk factors for ulceration and amputation[28,29] and are a cause of concern in the current population as well. High mean HbA1c and FBS was seen among all patients and distribution of patients with DFS across all levels of HbA1c was observed in the current study indicating poor glycaemic control. It also implies that a low HbA1c

(<7.0%) does not necessarily mean no complications; people with low HbA1c levels have equal odds of being affected with foot complications. About four out of five patients in the current study had poor glycaemic control (HbA1c>7.0%) — a trend which is confirmed by reports of poor glycaemic control from previous Pakistani studies.[31] This indicates increased risk of foot ulceration among all patients with diabetes. There is a need to optimise the treatment of DFS based on glycaemic control. The role of enhanced glycaemic control in preventing neuropathy[39] and in wound-healing rate[40] is well-established.

Management of diabetes using insulin prevents or delays the onset of complications including diabetic neuropathy.[41,42] The relative risk of developing DFS in patients with diabetes is lower (hazard ratio=0.61, p=0.0405) with insulin glargine therapy compared to neutral protamine Hagedorn insulin therapy.[43] The low prescription of insulin (34.3%), alone or in combination with OADs observed in the study population might contribute to the high prevalence of DFS. For optimal treatment of diabetic foot ulcer, adequate revascularisation of the affected area, debridement of wound, infection control and mitigating pressure of the ulcer through off-loading together with quantification of neuropathy, plantar foot pressure, and vascular status is recommended.[25] Prevention strategies using antibacterial regimens are reported to reduce rate of ulceration and improve quality adjusted life years in patients with DFS.[21]

Conclusion

A high burden of DFS was found in patients with T2DM in Pakistan. The current burden was further aggravated by the high proportion of population at risk of DFS, a significant minority of which is prone to high risk of "extreme degree of foot infections". A point of further concern is the low rate of prescription of insulin in patients with DFS in Pakistan. This implies low awareness of appropriate treatment options even in healthcare providers dealing with patients' routine care. Considering the poor glycaemic control, associated risk factors of DFS and existing treatment in the population, there's a need for early diagnosis and optimisation of treatment for the management of not only diabetes but also foot complications in this population.

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Conflict of Interest: At the time of conducting the study and manuscript development, Amanullah Khan and Nabeea Junaid were employed by Sanofi-Aventis Pakistan Limited. The latter is still working there.

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