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Original Research Article

A study of association of diabetic foot ulcers and peripheral vascular disease

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ABSTRACT

Background: Diabetic foot ulcers (DFU) are a common, costly, complex, and disabling complication of diabetes resulting in lower-extremity amputations. Diabetes Mellitus (DM) is associated with an increase in the incidence of peripheral vascular disease (PVD) compared to non-diabetic subjects. DFU are divided into two types: neuropathic ulcers (NPU) and neuro-ischemic ulcers (NIU). PVD in association with neuropathy leads to neuro-ischemic ulcers (NIU).
Methods: A cross-sectional observational study was conducted for eighteen months period from October 2016 to March 2018, on 120 type-2 DM patients presenting with DFU at tertiary centre in central India. Informed written consent, detailed history was obtained from the patients including duration of diabetes, history of hypertension, smoking, presenting symptoms and other complications related to diabetes. Examination of foot and evaluation for peripheral pulses, ankle brachial pressure index (ABI), neuropathy and blood pressure were done. Laboratory tests for HbA1C, lipid profile, blood urea, serum creatinine and urine albumin creatine ratio (urine ACR) were done. Statistical analysis used: t test, fisher exact test and univariate analysis.
Results: In our study, 1594 patients with T2DM were studied, out of which 120 patients presented with new DFU. Mean age of the patients was 61.5years with an M: F ratio of 1.78:1. NIU was present in 36 and NPU in 84 out of 120 DFU patients. Neuro-ischemic ulcers (NIU) were more common among males (28/78 males vs 8/42 females). NIU was found to have significant association with smoking (25/36 patients), hypertension (28/38 patients) and longer duration of diabetes (13.1 vs 9.2years). Other diabetic complications, retinopathy (26/36 patients) and nephropathy (18/36 patients) were more prevalent in patients with NIU. Dyslipidemia was also found in 58.33% (21/36) patients with NIU however the association was insignificant.
Conclusions: Diabetic foot ulcers are very debilitating complication of diabetes, and a leading cause of amputations all over the world. Because of increased association of peripheral vascular disease with diabetic foot ulcers there is a rise in prevalence of neuro-ischaemic ulcers. Early management of peripheral vascular disease is important to prevent development of neuro-ischaemic ulcers.

Keywords: Diabetic foot ulcer, Neuropathic ulcers, Neuro-ischemic ulcers, Peripheral vascular disease, Type-2 diabetes mellitus

INTRODUCTION

Diabetes is described as "global epidemic" as about 415 million people have diabetes globally which accounts to 1 in 11 people. India has about 40 million patients of diabetes.[1] There is an inevitable rise in diabetes-related complications as a result of the dramatic increase in the worldwide prevalence of diabetes mellitus (DM). Diabetic foot ulcer (DFU) is a chronic complication of diabetes mellitus (DM) of great importance from medical

and social aspects, since it has significant effects on the patient's quality of life. Prevalence of diabetic foot ulcer ranges from 4 to 10% in hospitalized patients.[2-4] Foot ulcers precede about 85% of diabetes-related amputations and it leads to more than half of non-traumatic lower limb amputations.[5] The diabetic foot is biologically compromised. This results from multiple contributing factors. Peripheral neuropathy and ischemia from peripheral vascular disease (PVD) are noted to be the major underlying causes. In the presence of these factors, even moderate ischemia can cause ulcers and impair healing. DFU can be categorized as Neuropathic ulcer (NPU) or Neuro-ischemic (NIU) requiring different treatment and with different prognosis.[6,7] Prevalence of peripheral vascular disease (PVD) is found to be higher in diabetics but data regarding its prevalence is limited.[8] In present study authors have tried to assess the prevalence of PVD in patients with type 2 DM presenting with foot ulcers and compare their clinical profile with those presenting with NPU.

Table 1: The risk factors for diabetic foot ulcers.

General / systemic contributions	Local issues
Uncontrolled hyperglycaemia	Peripheral neuropathy
Duration of diabetes >10yrs	Structural foot deformity
Peripheral vascular disease	Trauma
Dyslipidemia	Poorly fitted shoes
Blindness or visual loss	Callus
Chronic renal disease	History of prior ulcer/ amputation
Older age	Prolonged elevated pressures
High body mass index	Limited joint mobility

Etio-pathogenesis of DFU

The development of diabetic foot ulcers is associated with multiple risk factors as per recent studies.[9,10] These risk factors are as follows: gender (male), duration of diabetes longer than 10 years, advanced age of patients, high Body Mass Index, and other comorbidities such as retinopathy, diabetic peripheral neuropathy, peripheral vascular disease, glycosylated haemoglobin level (HbA1c), foot deformity, high plantar pressure, infections, and inappropriate foot self-care habits.[9-12] (Table 1, Figure 1).

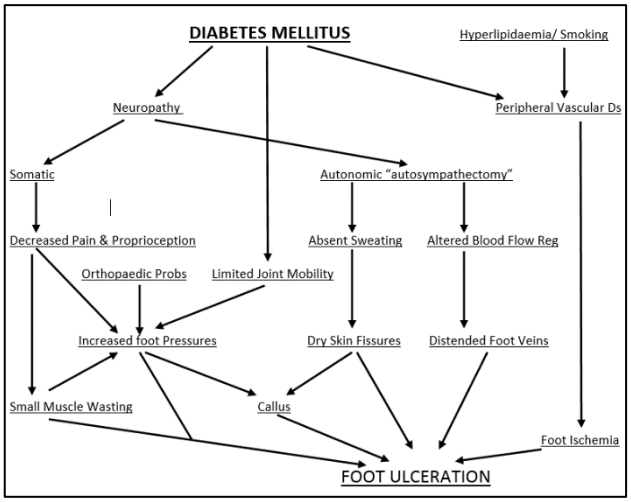

Figure 1: Aetiology of diabetic foot ulcer (Boulton et al).[13]

METHODS

This is a non-interventional, cross-sectional observational study, conducted for eighteen months period from October 2016 to March 2018, on 120 type-2 DM patients presenting with foot ulcers at our centre situated in central India.

A total of 1594 patients with T2DM visited the medicine out-patient department (OPD) and surgical OPD in the study duration, out of which 120 presented with new foot ulcers. The DFUs were graded according to University of Texas diabetic wound classification system (Table 2). Patients with only calluses without ulceration, non-diabetic patients with foot ulcers and patients with previous amputation of foot/leg were excluded from the study.

Table 2: University of Texas diabetic wound classification system.

	Grades			
Stages	**0**	**I**	**II**	**III**
A	Pre-or post-ulcerative lesions Completely epithelialized	Superficial wound not involving tendon capsule or bone	Wound penetrating to tendon or capsule	Wound penetrating to bone or joint
B	With infection	With infection	With infection	With infection
C	With ischemia	With ischemia	With ischemia	With ischemia
D	With infection and ischemia	With infection and ischemia	With infection and ischemia	With infection

After obtaining an informed written consent, detailed history was obtained from the patient including duration of diabetes, history of hypertension, smoking, presenting symptoms and other complications related to diabetes. Examination of foot, peripheral pulses, and blood pressure was done.

The variable, diabetic foot ulcer (DFU) was defined by the break of skin continuity in any region below the ankle of any depth level with or without complications in people affected with diabetes. It also included gangrene and necrosis. Neuropathy was defined as inability of the patient to detect 10gm nylon monofilament on more than one site or vibration perception threshold more than 25volts. Neuropathy was determined by using Tuning fork (loss of vibration), 10gm nylon monofilament and tendon reflex testing. Vibration perception threshold was measured using biothesiometer.

Absent pulses were defined as absence of both Posterior tibial artery and Dorsalis pedis artery pulses in the affected foot. Peripheral vascular disease (PVD) was defined by an Ankle brachial blood pressure Index (ABI) less than or equal to 0.91. Foot ulcers were categorized as ischemic when peripheral pulses were absent, but the sensation was intact, neuropathic when sensation was absent, but the peripheral pulses were intact and neuro-ischemic when both sensation and peripheral pulses were absent. NIU was defined as ulcer in patient with ABI <0.9. Dyslipidemia was defined as per ADA 2016 guidelines.[14]

Laboratory tests for HbA1C, lipid profile, blood urea, serum creatinine and urine albumin creatine ratio (urine ACR) were done. HbA1c values indicated the metabolic control as indicated. HbA1c <7% were taken as good metabolic control. HbA1c 7-10% were taken as fair control. HbA1c >10% were taken as poor metabolic control. The statistical analysis used was t test and Fisher exact test and univariate analysis.

RESULTS

Neuro-ischaemic ulcers (NIU) were diagnosed in 36 patients and the rest 84 had Neuropathic ulcers (NPU). Mean age of the patients in our study was 61.5 years with an M: F ratio of 1.78:1 (78 male and 42 female). NIU were more common among male patients as compared to female patients (28 out of 78 males vs 8 out of 42 females). In present study average duration of diabetes was 11.8 years. The average duration of diabetes was found to be longer in patients with NIU, i.e. 13.1 years as compared to 9.2 years for those with NPU.

Table 3: Risk factors comparison among neuropathic and neuro-ischemic ulcers.

Risk Factor	Neuropathic ulcers NPU (n= 84)	Neuro-ischaemic ulcer NIU (n= 36)	Stats analysis
Duration of diabetes	9.2±8.16yrs	13.1±12yrs	't'=2.0689, d.f = 118 P = 0.0407, Significant
Male gender (n=78)	50 (64.10%)	28 (35.90%)	Fisher exact test p=0.05, Non-significant
Smoking (n=40)	15 (17.85%)	25 (69.44%)	Fisher exact test P<0.0001, Extremely significant
Hypertension (n=65)	37 (44.04%)	28 (77.77%)	Fisher exact test P=0.0007, Extremely significant
Dyslipidemia (n= 54)	33 (39.28%)	21 (58.33%)	Fisher Exact Test P=0.0717, Non-significant
Retinopathy (n=69)	43 (51.19%)	26 (72.22%)	Fisher exact test P=0.0437, Significant
Nephropathy (n=48)	30 (35.71%)	18 (50%)	Fisher exact test P=0.1592, Non-significant

Out of 120 patients, 40 had a history of smoking. 25 out of 36 patients (69.5%) having NIU were smokers as compared to only 15 out of 84 (17.85%) of those having NPU, indicating a strong association between smoking and NIU. Hypertension was found in 54% (65 out of 120) patients, 77.7% (28/36) patients with NIU were hypertensive whereas only 44% (37/84) patients having NPU were found to have hypertension. The median HbA1c levels for NPU and NIU were 9.1% and 10.5% respectively. The association of smoking, hypertension and duration of diabetes with NIU was found to be highly significant (Table 3).

In 82 out of 120 patients (68%) other diabetic complications like retinopathy and nephropathy were coexistent. Retinopathy (26/36 patients) and nephropathy (18/36 patients) were more prevalent in patients with NIU. Dyslipidemia was found in 45% (54 out of 120)

patients. 58.33% (21/36) patients with NIU were having deranged lipid profile whereas only 39.28% (33/84) patients having NPU were found to have deranged lipid profile however the p value was insignificant. The prevalence of complications among patients having NIU was 86.1% (31 out of 36) whereas it was only 58.3% (49 out of 84) among those having NPU however the p value was insignificant (Table 3).

DISCUSSION

Based on the WHO criteria, diabetic foot is defined as infection, ulceration and/or destruction of deeper tissues associated with neurological abnormalities and various degrees of PVDs of the lower limb.[15] DFU is one of the most serious complications of diabetes. Of all non-traumatic amputations, approximately 50% are performed on diabetics for complications of diabetic foot like non-healing ulcers and gangrene. PVD is a common associated condition in patients with T2DM. Around 14% of the patients with T2DM in western countries suffer from PVD, but in India, these figures vary between 4% and 15%.[16,17] Peripheral atherosclerosis observed in patients with the DM is typically more distal in distribution and often more extensive, involving distal popliteal, the tibial, and metatarsal vessels of lower limbs are most commonly and severely affected.[18] The three main factors leading to diabetic foot ulceration - neuropathy, microangiopathy and large vessel disease - gives rise to a similar array of abnormalities of microvascular function - limited vasodilatory reserve, impaired postural vasoconstriction, impaired pressure regulation, and maldistribution of blood flow.[19]

Diabetic foot ulcers were found in 120 out of 1594 T2DM patients visiting authors' out-patient department, making the prevalence of 7.52% in our study of the central Indian population. The prevalence of DFU (in T2DM patients) in various studies conducted in different countries ranged between 1.0% and 4.1% in the United States, 4.6% in Kenya, 11.7% in Nigeria, 20% in Iran and 20.4% in Netherlands.[20-24] The prevalence was found to be 8.02% in a study of the north Indian population.[8] As per recent studies, the prevalence of NIU is rising and is found to be ranging from 23.3% to 30.5 %.[21, 25] In present study, 30% of patients with diabetes with new ulcers were having NIU and 70% were having NPU. In present study, mean age of patients was 61.5years, which was in agreement with findings of other studies.[8,26,27] Aging increases the propensity of skin to damage, because of decreased angiogenesis and increased sepsis.

In present study, authors found male predominance (78 male patients vs. 42 female patients) with a male to female ratio of 1.85:1 which was similar with other studies.[8,26,28] Increased number of male patients may be due to their smoking habits. In our study the mean duration of diabetes in patients with NPU and NIU was 9.2 and 13.1years respectively. The mean duration of diabetes reported by other studies ranged from 8-14 years.[8,27] So it is suggested that there is increased risk of neuropathy as well as NIU with increased duration of T2DM.

The risk factors associated with NIU were longer duration of diabetes, male gender, smoking, hypertension, dyslipidemia and poor glycemic control (median HbA1c of 10.5%). Similar risk factors were also reported to be associated by other studies.[8,21,27] In present study, dyslipidemia was found in 45% (54 out of 120) patients, 58.33% patients with NIU and 39.28% patients having NPU were found to have deranged lipid profile, which was similar to results of Memon H et al, i.e. 55.11% and Mithal A et al.[29,30] Early detection and differentiation of diabetic foot ulcers into ischemic and non-ischemic is needed due to modifiable risk factors associated with neuro-ischaemic ulcers. To reduce the chances of amputations, aggressive management of NIU is required.

In diabetic patients having peripheral vascular disease, always look and properly address other complications like CAD, retinopathy and nephropathy. Peripheral pulse examination should be done in all patients with DM and ABI should also be measured in addition to clinical evaluation in patients presenting with DFU. Patients should be advised evaluation of leg vessels by peripheral Doppler study and or peripheral angiography when ABI is less than 0.9. And the patient should be advised to stop smoking and educated about the importance of proper diabetic foot care. A multidisciplinary approach is required for DFU with PVD patients involving physician/ diabetologist, podiatrist, general surgeon, vascular surgeon, plastic reconstructive surgeon, orthopaedic surgeons, cardiologist, rehabilitation physician and orthopaedic shoe maker should be used to treat such patients.

CONCLUSION

Diabetic foot ulcers are very debilitating complication of diabetes, and a leading cause of amputations all over the world. There is a rise in prevalence of neuro-ischaemic ulcers because of increased association of vascular disease with diabetic foot ulcers. Early management of peripheral vascular disease is important to prevent development of neuro-ischaemic ulcers. To research the role of PVD and other risk factors in the genesis of the diabetic foot ulcers, multivariate studies are recommended.

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