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Determinants of the Risk for Diabetic Foot Ulceration in Sohag University Hospital

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ABSTRACT

Background: One of the most common complications of diabetes in the lower extremity is the diabetic foot ulceration (DFU). **Objective:** To identify the determinants of the risk for diabetic foot ulceration (DFU) in terms of peripheral neuropathy (PN) or peripheral vascular disease (PVD) among a sample of diabetic foot patients. **Methods:** A cross sectional study included 100 diabetic foot patients attending Sohag University Hospital for follow up during the period from January 2009 to January 2010. They were subjected to complete medical history taking and thorough clinical examination. Diabetic Neuropathy Symptoms (DNS) along with the Diabetic Neuropathy Examination (DNE) scores were used together to define and assess PN. PVD diagnosis was based on identification of claudication pain symptoms; absent or weak foot pulses on palpation of the dorsalis pedis and/or the tibialis posterior arteries; coldness of skin; and finally confirmed by arterial doppler of lower limbs. **Results:** The mean age of the patients was 57.92 ± 9.2 years; 65% were males and 79% lived in rural areas. The majority (79%) had type 2 DM with mean disease-duration of 13.4 ± 6.9 years. Fifty percent of the study patients were smokers and ex-smokers, 33% were hypertensive and 24% had previous history of foot ulceration or amputation. Male gender, old age, low socioeconomic status, smoking, hypertension, type 2 DM, long duration of DM, uncontrolled DM, and previous history of foot ulceration, amputation or other diabetic complications were all significant determinants of PN and PVD; two major risk factors of DFU.

Key words: Diabetic Foot Ulceration (DFU), Peripheral Neuropathy (PN), Peripheral Vascular Disease (PVD)

INTRODUCTION

Knowledge of diabetes dates back to centuries before Christ.(1) Diabetic foot is an umbrella term for foot problems in patients with diabetes mellitus (DM). Infection and/or gangrene of the foot are relatively common in diabetic patients due to arterial insufficiency, diabetic neuropathy and delayed wound healing. Diabetic foot is responsible for up to 50% of diabetes related hospital admissions.(2)

Diabetic foot ulcer (DFU) is one of the common but often neglected complications of diabetes. There is no doubt that people with

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DFU have considerable mortality and morbidity. The risk of death for those with foot ulcers is 12.1 per 100 persons per year-years of follow-up compared to 5.1 in those without foot ulcers.[3] Similarly, the risk for amputation in patients with diabetes is 15 times greater than that for the non-diabetic population and the majority of amputations are preceded by DFU. In addition to increased morbidity and mortality, patients with DFU have a poorer quality of life in comparison to those without ulcers.[4]

Recent studies have revealed that interacting complex mechanisms are involved in the pathogenesis of DFU. There is defective normal healing processes of the tissues.[5] Many chemo-cytokines are involved, including matrix metalloproteinases, serine proteinases, integrins, chemokines, replicative cell senescence, growth factors and adult stem cells.[6] Diabetic patients with tissue injury initially display impairment in the immune system response with reduced chemotactic effects to recruit inflammatory cells into the damaged tissues, thus, slowing down healing and increasing the risk of bacterial infection.[7] Following this initial period, the process switches to an exacerbation of inflammation and proteolysis.[8] The result of prolonged exposure to hyperglycemia also generates glycation of proteins and disturbances of cell responses, thus, further hindering the process of fibrosis and tissue repair.[9] Infection is usually the consequence rather than the cause of diabetic foot ulcers. Infected chronic ulcers may be classified as mild to moderate or severe, when osteomyelitis is involved.[10]

One of the most common complications of diabetes in the lower extremity is the DFU. It is estimated that 15% of patients with diabetes will develop a lower extremity ulcer during the course of their disease.[11] While most ulcers can be successfully treated in the office or outpatient setting, infected and/or ischemic foot ulcers are a major cause for diabetes related hospitalization.[12]

In the United States, the total costs for both direct and indirect health care for persons

with diabetes in 1997 has been estimated to be $98 billion. Costs for ulcer care have been estimated to lie within the range of $4,595 per ulcer episode to nearly $28,000 for the 2 years after diagnosis.[13] The estimated overall total costs in the United States for diabetic foot disease can approach or exceed $6 billion annually.[14]

Egypt is currently among the top 10 countries with the highest prevalence of diabetes and will remain so as 7.6 million Egyptians will have the disease by 2025.[15]

In general, few studies have reported the prevalence of diabetic foot ulceration (DFU) as part of diabetes-related complications and, to our knowledge; there have been very few surveys on DFU risk factors in Egypt.

Mild foot ulcers precede most of the non-traumatic amputations in people with diabetes. According to the International Diabetes Federation and the International Working Group on the Diabetic Foot,[14] it is possible to reduce amputation rates by between 49% and 85% through a care strategy that combines: prevention; the multi-disciplinary treatment of foot ulcers; appropriate organization; close monitoring; and the education of people with diabetes and healthcare professionals.[16] Thus, it is essential that foot care services, which are very scarce in Egypt, be urgently initiated to cope with the rapidly increasing prevalence of diabetes and its complications among Egyptians.

The aim of the present work was to identify the determinants of the risk for DFU in terms of peripheral neuropathy (PN) or peripheral vascular disease (PVD) among a sample of diabetic foot patients in Sohag University Hospital.

SUBJECTS AND METHODS

A cross-sectional study included 100 patients diagnosed with diabetic foot and attending Sohag University Hospital for follow up during the period from January 2009 to January 2010. A written consent was taken from all enrolled patients after approval of the study by the Ethical committee at Sohag Faculty of Medicine. Every participant was

subjected to the following tools and techniques:

1. Structured interview questionnaire to collect the following data:
   - Name, age, sex, occupation, marital status, residence, and history of smoking.
   - Type of diabetes, duration of diabetes, therapeutic history and diabetic control.
   - Presence of vascular symptoms such as cramps and/or claudication and neuropathic symptoms such as tingling, numbness, and burning sensation with a 'stocking and glove' distribution.
   - Previous history of foot ulceration or amputation. History of systemic hypertension or other diabetic complications.

1. Clinical examination of the foot to identify PN, PVD or other risk factors of diabetic foot ulceration such as callus and oedema.[16] Both feet were examined for signs of vasculopathy and neuropathy including skin status (color, thickness, dryness, cracking, atrophic changes, and decreased hair growth). PN was assessed by vibratory, monofilament, muscle strength and tendon reflex testing. Pressure, pain, vibration and joint position sensitivities were evaluated bilaterally. For pressure perception, the 10 g Semmes-Weinstein monofilaments was used on 4 sites of the foot. These sites were without callus, notably the pulps of the hallux and metatarsal heads of first, third and fifth toes. The site was considered sensate if the patient responded, "yes" upon contact with the monofilament and insensate if there was no response.

   For vibration perception, a 128 Hz tuning fork was applied at 3 sites on the foot; the pulp of the hallux, the lateral and the medial malleoli. The patient was asked to describe what he felt. If he/she described a feeling of vibrations, the site concerned was considered normal. If he/she described anything other than vibrations, the site concerned was considered

abnormal. In addition, pin-prick perception on the dorsal surface of the great toe and the index finger were evaluated. Neuropathy was further assessed by examining the tendon reflexes bilaterally and testing for muscle strength by examining for extension of the knee and dorsiflexion of the foot.

Diabetic Neuropathy Symptoms (DNS) along with the Diabetic Neuropathy Examination (DNE) scores were used together to define and assess neuropathy.[16] The DNS score is a four-item validated symptom score, with high predictive value to screen for PN in diabetes. Symptoms of unsteadiness in walking, neuropathic pain, paraesthesia, and numbness are elicited. The presence of one symptom is scored as 1 point; the maximum score is 4 points. A score of 1 or higher is defined as positive for PN.

The DNE score is a sensitive and validated hierarchical scoring system. The score contains two items concerning muscle strength, one concerning reflexes, and five concerning sensation (eight total items). Each item is scored from 0 to 2 (0 for normal and 2 for severely disturbed). The maximum score is 16 points. A score of >3 points is defined as positive for PN.

Neuropathy was considered to be present if DNS score was >0 and/or the DNE score was >3.[16] Lower limb ischemia or PVD was ascertained by the examining physician through palpation of the dorsalis pedis and the tibialis posterior pulses when one or more foot pulses were judged absent with or without symptoms of lower-limb claudication and/or amputation or gangrene were present.

2. Investigations were done to all studied patients namely; fasting blood glucose level. Also, arterial Doppler of lower limbs was done if PVD was suspected clinically.

Data analysis

Data were computed and analyzed using the Statistical Package for Social Sciences (SPSS) version 10. Between-groups comparisons were assessed using the chi-square test for nominal variables and the

student t-test for ordinal data. Statistical significance was assessed at p≤0.05. All calculated p- values were two-tailed.

RESULTS

The study included 100 patients with diabetic foot. The mean age of the patients was 57.92 ± 9.2 years; 63% were above the age of 55 years. Most of the sample were males (65%). More than one third of the samples (35%) were farmers, about 37% without certain job, 14% were workers and 14% were employees. About 79% of the sample were rural residents and 21% of them were urban ones. The governorates and towns were considered as urban areas while the villages and hamlets were considered as rural areas.

Table 1 shows that current smokers constituted 41% of the studied patients with diabetic foot, while ex-smokers rated 9%. Half of the sample were ever smokers. All females in the study were non-smokers while 76.9% of males were ever smokers.

Table 1. Smoking rates among the studied males and females

Smoking	Sex				Total		*p*-value[a]
	Male		Female				
	No.	%	No.	%	No.	%	
Smoker	41	63.1	0	0	41	41	< 0.001
Non smoker	15	23.1	35	100	50	50	< 0.001
Ex-smoker	9	13.8	0	0	9	9	< 0.001
Ever-smokers	50	76.9	0	0	50	50	< 0.001
Total	65	100	35	100	100	100	

a Chi square test

Table 2 reveals that the percentage of type 2 DM of the study sample was 79% and type 1 was 21%. Only 8% of the sample had duration of diabetes less than 4 years, while 62% of the sample had duration of diabetes between 10 and less than 20 years. About 11% of the studied sample had duration of diabetes more than 20 years. Fifty three percent of the sample was treated by oral hypoglycemic

drugs, 25% were treated by insulin and 22% of cases started the treatment by oral hypoglycemic drugs for a while then shifted to insulin therapy because they were uncontrolled on the oral therapy (Table 3).

As regards type 1 DM, 95.2% of cases were treated by insulin and only one case was treated by oral therapy at first then shifted to insulin therapy. On the other hand, most cases of type 2 DM were treated by oral hypoglycemic drugs (67.1%) and 26.6% of cases started by oral therapy for a while then shifted to insulin. Only 6.3% of cases of type 2 DM started the treatment by insulin therapy.

Table 2. Relation between duration and type of diabetes among the studied sample

Duration of diabetes (years)	Type of diabetes				Total		*p*-value[a]
	Type 1		Type 2				
	No.	%	No.	%	No.	%	
0-4	0	0	8	10.1	8	8	<001
5-9	1	4.8	18	12.8	19	19	<001
10-14	3	14.3	31	39.2	34	34	<001
15-20	11	52.4	17	21.5	28	28	<001
20-30	6	28.6	5	6.3	11	11	<.001
Total	**21**	**100**	**79**	**100**	**100**	**100**	

[a] Chi square test

Table 3. Therapeutic history of the studied sample and its relation to type of diabetes

Therapeutic History	Type of diabetes				Total		*p*-value[a]
	Type 1		Type 2				
	No.	%	No.	%	No.	%	
Oral hypoglycemic	0	0	53	67.1	53	53	<.001
Insulin therapy	20	95.2	5	6.3	25	25	<.001
Start by oral therapy then shift to insulin	1	4.8	21	26.6	22	22	<.001
Total	**21**	**100**	**79**	**100**	**100**	**100**	

[a] Chi square test

The percentage of hypertension among the studied sample was 33%. Most cases of type 1 DM were not hypertensive (90.5%), while 39.2% of cases of type 2 were hypertensive (Table 4). Twenty three percent of the total sample had previous history of diabetic foot ulcer which was complicated with foot amputation. Only 1% of cases had previous history of diabetic foot ulcer that was not complicated by amputation. Cardiac complications were encountered among 18% of the studied sample who received treatment for ischemic heart disease, while 4% of cases suffered from diabetic nephropathy and 2% suffered from diabetic retinopathy (Table 5).

Results of the present work showed that most of the sample (58%) had fasting blood glucose level ranging from 130 to 249 mg/dl, 26% had fasting blood glucose level of 250-399 mg/dl, while 4% had fasting blood glucose level >400 mg/ dl.

Fifty five percent of the total studied sample had diabetic neuropathy which was diagnosed according to DNS and DNE scores. Meanwhile, 24% of the sample were diagnosed with PVD based on identification of claudication pain symptoms; absent or weak foot pulses on palpation of the dorsalis pedis and/or the tibialis posterior arteries; coldness of skin; and finally confirmed by arterial doppler of lower limbs (table 5, 6).

Table 4. Hypertension among the studied sample and its relation to type of diabetes

	Type of diabetes						
	Type 1		Type 2		Total		*p*-value[a]
	No.	%	No.	%	No.	%	
Hypertensive	2	9.5	31	39.2	33	33	0.007
Not hypertensive	19	90.5	48	60.8	67	67	0.009
Total	**21**	**100**	**79**	**100**	**100**	**100**	

[a] Chi square test

Table 5 illustrates the association between PN and some socio-demographic and medical variables. It indicates that some variables were significantly more encountered among patients with PN namely; male gender (65.5%, p<0.05), rural residence (81.8%, p<0.05), smoking (43.6%, p<0.05) and type 2 diabetes (74.5%, p<0.05). Also, long duration of diabetes and previous history of foot ulceration or amputation were significant variables (p<0.005). About 36.4% of cases with recent diabetic foot complication and diabetic neuropathy had past history of foot ulceration or amputation. The presence of other diabetic foot complications such as ischemic heart disease (IHD), diabetic nephropathy and retinopathy were also significant factors associated with diabetic neuropathy (p<0.05). Nearly one quarter of the studied diabetic foot patients (24%) had PVD.

Table 6 shows the association between PVD and some socio-demographic and medical variables. It indicates that PVD can be predicted by several factors. Among these factors were: male gender (79.2%, p=0.007), hypertension (37.5%, p =0.001), old age of 55 years or more (75%, p =0.02). Smoking was also an important predicting factor for PVD, 62.5% of cases were smokers or being an ex-smoker (p=0.04). Also the presence of other diabetic complications such as diabetic nephropathy, diabetic retinopathy, and hypertension were important risk factors for PVD in patients with diabetic foot (p=0.03). Long duration of DM was highly significantly associated with PVD (p=0.001), 75% of cases had duration of diabetes more than 10 years. Only 3% of cases of the studied sample received prior foot care knowledge, all of them were employees and living at urban areas. No one of the studied sample had history of previous usage of therapeutic footwear.

Table 5. The association between PN and some socio-demographic and medical variables.

Variables	Presence of PN		Absence of PN		*p*-value
	(n=55)	(%)	(n=45)	(%)	
Sex					
Male	36	65.5	29	64.4	<0.05
Female	19	34.5	16	35.6	
Residence					
Rural	45	81.8	34	75.6	<0.05
Urban	10	18.2	11	24.4	
Age group					
40-54	19	34.5	18	40	>0.05
55-69	26	47.3	20	44.4	
70-84	10	18.2	7	15.6	
Type of DM					
Type 1	14	25.5	7	15.6	<0.05
Type 2	41	74.5	38	84.4	
Smoking					
Smoker	24	43.6	17	37.8	
Non-smoker	29	52.7	21	46.7	<0.05
Ex-smoker	2	3.6	7	15.6	
Previous history of foot ulcer or amputation					
Positive	20	36.4	4	8.9	0.003
Negative	35	63.6	41	91.1	
History of IHD	10	18.2	8	17.8	<0.05
Diabetic retinopathy	3	5.5	1	2.2	
Diabetic nephropathy	1	1.8	1	2.2	
Duration of DM					
0-4 years	1	1.8	7	15.6	
5-9 years	7	12.7	12	26.7	
10-14 years	21	38.2	13	28.9	0.004
15-19 years	19	34.5	9	20.2	
20-30 years	7	12.7	4	8.9	
Therapeutic history					
Insulin therapy	23	41.8	30	66.7	
Oral hypoglycemic	15	27.3	10	22.2	0.007
Oral shift to insulin	17	30.9	5	11.1	

PN, peripheral neuropathy; IHD, ischemic heart disease

Table 6. PVD in relation to some socio-demographic and medical variables.

Variables	Presence of PVD		Absence of PVD		*p*-value
	(n=24)	(%)	(n=76)	(%)	
Sex					
Male	19	79.2	46	60.5	0.007
Female	5	20.8	30	39.5	
Hypertension					
Present	9	37.5	24	31.6	0.001
Absent	15	62.5	52	68.4	
Age (years)					
40-54	6	25	31	40.8	0.02
55-69	10	41.7	36	47.4	
70-84	8	33.3	9	11.8	
Smoking					
Smoker	11	45.8	30	39.5	0.04
Non-smoker	9	37.5	41	53.9	
Ex-smoker	4	16.7	5	6.6	
Positive history:					
Ischemic heart disease	9	37.5	9	11.8	0.03
Diabetic retinopathy	1	4.2	3	3.9	
Diabetic nephropathy	1	4.2	1	1.3	
Type of DM					
Type 1	4	16.7	17	22.4	>0.05
Type 2	20	83.3	59	77.6	
Duration of DM (years)					
0-4	2	8.3	6	7.6	
5-9	4	16.7	15	19.7	
10-14	7	29.2	27	35.5	0.001
15-19	8	33.3	20	26.3	
20-30	3	12.5	8	10.5	

PVD, peripheral vascular disease; DM, diabetes mellitus

DISCUSSION

DFU is one of the common but often neglected complications of diabetes. It is considered one of the most serious complications of diabetes. There is no doubt that people with DFU have considerable mortality and morbidity.[16]

Identifying diabetic patients at risk for DFU is very important in preventing this common and serious complication of diabetes and to decrease its effect on diabetic patients and the community in general.[17]

This study has been conducted to identify two major risk factors of DFU namely; PN and PVD and their determinants. The studied

sample showed that 55%, 24% and 1% had diabetic PN, PVD and previous history of foot ulcer respectively. These results when compared to data from near-by countries show that, the situation in Egypt seems to be alarming. In one study in the Gulf area, the prevalence of neuropathy, PVD and foot ulcer was found to be 36.6%, 11.8% and 5.9% respectively.[17] The lower prevalence of ulcers in our study could be explained by the late presentation of the cases and the lack of well-developed foot care programs.

In general few studies were done to assess the risk factors of diabetic foot in Egypt and the world. This is the first study conducted in our university to assess and evaluate socio-demographic and medical factors that determine the risk for DFU in terms of PN and PVD.

The present study revealed that about 65% of the study population were males. Male gender predominance was consistent with many earlier studies as that of Emad et al, (2009) [18] who found that most of the studied patients in his study that was done to assess risk factors of diabetic foot in Suez Canal University were males (67%).

Also Fatma et al, (2007)[17], in Al-Ain University Hospital at United Arab Emirates, found that about 56.8% of the sample were males. It is possible to suggest that males have more daily activities than females in our locality so, they are more liable to foot trauma and hence they are commoner in diabetic foot ulceration.

This study showed that most of the population were old age, 63% of the population were above 55 years old. Mean age in this study was 57.92 ±9.2.

Most cases of type 1 DM developed diabetic foot complication after duration of DM more than 15years (81%) and no cases developed diabetic foot complication before 5 years.

About thirty nine percent of type 2 DM patients in our study developed foot complication after 10-15 years from the disease onset while 27.8% of cases

developed diabetic foot complication after duration of DM more than 15 years and 10.1% developed foot complication before 5 years duration. As regards foot amputation, 23% of our study patients had this hard experience, when compared to other international data, this raises a major alarm urging a better care for diabetic foot in our community.[19]

People at greatest risk of diabetic foot complications can easily be identified by careful clinical examination of the feet so, education and frequent follow-up is indicated for these patients.[20] Diabetic foot ulcers is a leading cause of amputations, affect 15% of people with diabetes.[21] Thanks to foot-care programs, the incidence of diabetic foot amputation is decreasing in developed countries and was found to be 2.4 per 1000 diabetes-patients in Norway.[21]

Conclusively, male gender, old age, low socioeconomic status, type 2 DM, smoking, hypertension, increased duration of DM, previous history of foot ulceration, amputation or other diabetic complications, uncontrolled DM, were main determinants of the risk for DFU as evidenced by two major risk factors namely diabetic neuropathy and PVD. Awareness of the determinants of the risk for DFU is an inevitable step on the way to achieve a competent Foot-care system for diabetic patients in our community that would decrease morbidity and mortality, as well as, the economic burden in Egypt.

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