


## The risk of micro and macrovascular disease in Egyptian patients with diabetes and peripheral arterial disease

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### ABSTRACT

**Aim:** The aim of this study was to assess the prevalence of micro- and macrovascular disease in Egyptian patients with diabetes mellitus (DM) and peripheral arterial disease (PAD).

**Methods:** The study included 161 Egyptian patients with DM and PAD (91.3% had type 2 DM and 67.1% were females). Mean diabetes duration was  $14.2 \pm 5.2$  years. Full history, clinical and fundus examination as well as laboratory investigations were done. PAD was diagnosed through assessment of ankle/brachial index (ABI) by Doppler ultrasonography.

**Results:** ABI was  $<0.9$  in 33.5% and  $>1.3$  in 66.5% of patients. A significant positive correlation was found between abnormal ABI and diabetes duration, ischemic heart disease (IHD), diabetic retinopathy and neuropathy, foot ulcers, elevated blood pressure (BP), creatinine, urine albumin/creatinine ratio (ACR) and triglycerides and a significant negative correlation with HDL. Multivariate regression analysis revealed that the independent predictors for PAD in patients with  $ABI < 0.9$  were neuropathy, creatinine, triglyceride, LDL, urine ACR and low HDL, and in patients with  $ABI > 1.3$  were IHD, neuropathy, elevated diastolic BP and triglyceride.

**Conclusion:** The risk of micro- and macrovascular disease is high in Egyptian patients with diabetes and PAD. Early diagnosis and good control of risk factors could reduce PAD progression.

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### KEYWORDS

Peripheral arterial disease; diabetes; microvascular; macrovascular; ankle/brachial index

## 1. Introduction

Diabetes mellitus (DM) is a non-communicable disease with micro- and macrovascular complications that affect the patients' quality of life. Delayed diagnosis and lack of management resources in the developing countries cause a major impact on diabetes management [1]. The risk of severe and early peripheral arterial disease (PAD) in patients with diabetes is compounded by the diffuse nature of the vascular affection. Multiple factors contribute to the development of PAD in DM. These factors include age, smoking, arterial hypertension, obesity, insulin resistance and dyslipidemia [2]. The aim of this study was to assess the prevalence of micro- and macrovascular disease in Egyptian patients with DM and PAD.

## 2. Methods

The study included 161 Egyptian patients with DM and PAD (91.3% had type 2 DM and 67.1% were females). They were recruited after screening 500 patients (62.8% were females) with DM for PAD. Mean age of the study patients was  $56.5 \pm 11.9$  and mean diabetes duration was  $14.2 \pm 5.2$  years. Their medications included metformin, sulfonylurea, DDP 4 inhibitors, insulin, angiotensin-converting enzyme inhibitors, angiotensin receptor

blockers, statins and aspirin. They were recruited from the outpatient clinics at Cairo University hospital. Exclusion criteria included those with DM duration  $<5$  years, patients with major foot deformities or PAD due to causes other than DM. Clinical registry sheet included full history (sex, age, smoking history, diabetes duration and medications). The presence of microvascular complications (retinopathy, sensory neuropathy and nephropathy) and PAD (previous vascular surgery or amputation of the limb) were also included. All participants provided written informed consents. The study protocol was approved by Cairo University ethical committee and review board.

Clinical examination included assessment of blood pressure (BP) and peripheral pulsations, foot examinations and testing for deep and superficial sensations (using 10 gm monofilament, Seims Weinstein Tape 6 points). Hypertension (HTN) was diagnosed when systolic BP was  $\geq 140$  or diastolic BP  $\geq 90$ . Fundus examination and electrocardiogram were also done. Glycated hemoglobin (HbA1c), blood urea, serum creatinine, urine albumin/creatinine ratio (ACR) and lipid profile were measured. Radiological examination of the foot was done to rule out osteomyelitis. Doppler ultrasonography was used to assess Ankle/Brachial index (ABI).

Patients were supine for at least 5 minutes. ABI was estimated as systolic pressure over the tibial arteries/systolic pressure over the brachial artery. PAD was diagnosed when ABI was <0.9 or >1.3 [3].

### 2.1. Statistical methods

Data were coded and entered using the statistical package for the Social Sciences (SPSS) version 25 (IBM Corp., Armonk, NY, USA). Data were summarized using mean, standard deviation, median, minimum and maximum for quantitative variables and frequencies (number of cases) and relative frequencies (percentages) for categorical variables. Comparisons between groups were done using unpaired *t*-test in normally distributed quantitative variables while non-parametric Mann–Whitney test was used for non-normally distributed quantitative variables [4]. For comparing categorical data, Chi-square ( $\chi^2$ ) test was performed. Exact test was used instead when the expected frequency is less than 5 [5]. Logistic regression was done to detect independent predictors of ABI [6]. P-values <0.05 were considered statistically significant.

### 3. Results

HTN was diagnosed in 52.2% and ischemic heart disease (IHD) in 23% of the study group. Mean systolic BP was 129 ± 20.4 mmHg and mean diastolic BP was 80 ± 11.8 mmHg. Mean HbA1C was 8.1 (65 mmol/mol) ±1.7%. Mean HbA1C in patients with ABI <0.9 was 8.4% (68 mmol/mol) and 8.0% (64 mmol/mol) in those with ABI >1.3. Urine ACR was high in 50.9% of our patients. Loss of superficial sensation was found in 37.9% and loss of vibration sense in 44.1% of the patients. Evidence of diabetic retinopathy was detected in 68.3% and foot deformities in 32.3% while 7.5% of the patients had foot ulcers. Dorsalis pedis pulsations were lost in 12.4% of patients.

ABI was <0.9 in 33.5% and >1.3 in 66.5% of patients. A significant positive correlation was found between abnormal ABI and diabetes duration, IHD, retinopathy, neuropathy, foot ulcers, elevated blood pressure (BP), creatinine, urine albumin/creatinine ratio (ACR) and triglycerides and a significant negative correlation with HDL. Multivariate regression analysis revealed that the independent predictors for PAD in patients with ABI < 0.9 were neuropathy creatinine, triglycerides, low HDL (P < 0.001 for all) LDL (P < 0.01) and urine ACR (P < 0.05). In patients with ABI >1.3 the independent predictors for PAD were IHD, lost superficial sensations (P < 0.001 for both), elevated diastolic BP, lost deep sensations (P < 0.05 for both) and triglycerides (P < 0.01). No significant difference was found between males and

**Table 1.** Demographic data of the studied group.

		abnormal ABI	
		n	%
<b>Sex</b>	<b>male</b>	53	32.9%
	<b>Female</b>	108	67.1%
<b>Type of DM</b>	<b>Type 1</b>	14	8.7%
	<b>Type 2</b>	147	91.3%
<b>HTN</b>		84	52.2%
<b>IHD</b>		37	23.0%
<b>Smoking</b>		41	25.5%
<b>High Urine ACR</b>		82	50.9%
<b>Diabetic Retinopathy</b>		110	68.3%
<b>Foot deformity</b>		52	32.3%
<b>Lost DP Pulses</b>		20	12.4%
<b>Foot Ulcers</b>		12	7.5%
<b>Lost Superficial Sensations</b>		61	37.9%
<b>Lost Vibration Sense</b>		71	44.1%

n, number of patients; DM, diabetes mellitus; HTN, hypertension; IHD, ischemic heart disease; ACR, albumin/creatinine ratio; DP, dorsalis pedis; ABI, ankle/brachial index.

**Table 2.** Multivariate regression analysis for patients with ABI < 0.9.

	P value	OR	95% CI	
			Lower	Upper
<b>Neuropathy</b>	<0.001*	15.904	3.760	67.271
<b>Nephropathy</b>	<0.05*	4.169	1.043	16.675
<b>Creatinine</b>	<0.001*	11.502	4.271	30.977
<b>TG</b>	<0.001*	1.016	1.008	1.023
<b>LDL</b>	<0.01*	0.984	0.974	0.995
<b>Low HDL</b>	<0.001*	0.919	0.880	0.960

ABI, ankle/brachial index; OR, odds ratio; CI, confidence interval; TG, triglycerides; LDL, low-density lipoprotein; HDL, high-density lipoprotein; \*, significant.

**Table 3.** Multivariate regression analysis for patients with ABI > 1.3.

	P value	OR	95% CI	
			Lower	Upper
<b>ABI&gt;1.3 IHD</b>	<0.001*	7.333	3.428	15.685
<b>Lost Superficial Sensations</b>	<0.001*	2.569	1.442	4.577
<b>Lost Deep Sensations</b>	<0.05*	2.014	1.158	3.502
<b>DBP</b>	<0.05*	0.972	0.950	0.995
<b>TG</b>	<0.01*	1.006	1.002	1.010

ABI, ankle/brachial index; OR, odds ratio; CI, confidence interval; IHD, ischemic heart disease; DBP, diastolic blood pressure; TG, triglycerides; TG, triglycerides; LDL, low-density lipoprotein; HDL, high-density lipoprotein; \*, significant.

females in any of the studied parameters. The results of the study are summarized in Tables 1–3.

### 4. Discussion

Patients with PAD are either asymptomatic or complain of atypical symptoms. So screening is essential to reach the right diagnosis [7]. Asymptomatic disease can progress to the symptomatic phase, with intermittent claudication, which could negatively affect the quality of life [8]. PAD is also an indicator of generalized atherosclerosis and thus carries a high risk for cardiovascular morbidity and mortality [9]. DM is an important risk factor for severe and early PAD [2]. The strong correlation between diabetic retinopathy and carotid intima-media thickness as

a marker of atherosclerosis in Egyptian patients with type 2 DM has been previously reported by our group [10]. Fiordaliso et al. reported that capillary microangiopathy is present in both neuro-ischemic and neuropathic diabetic foot skin. They concluded that the predominance of arteriolar occlusions with neuro-ischemia indicated the existence of small vessel disease that slowed the healing process of foot ulcer [11]. Early Diagnosis of PAD would help to identify and modify the risk factors of cardiovascular disease in patients with DM.

The aim of this study was to assess the prevalence of micro- and macrovascular disease in Egyptian patients with DM and PAD. Our results showed that that ABI was  $<0.9$  in 33.5% and  $>1.3$  in 66.5% of patients. A significant positive correlation was found between abnormal ABI and diabetes duration, IHD, diabetic retinopathy and neuropathy, foot ulcers, elevated BP, creatinine, urine ACR and triglycerides and a significant negative correlation with HDL. HTN and IHD were found in 52.2% and 23% of our patients respectively, while diabetic nephropathy and retinopathy were detected in 50.9% and 68.3% of the patients, respectively. Loss of superficial sensation was found in 37.9% and loss of vibration sense in 44.1% of the patients. Jambart et al. reported that 53.7% of the 3989 participants with diabetes, in a multi-ethnic study in several Middle East countries, met the criteria of painful neuropathy [12].

Foot deformities and ulcers were found in 32.3% and 7.5% of patients with PAD, respectively. Dorsalis pedis pulsations were lost in 12.4% of patients with PAD. Superficial sensory loss (detected by monofilament) was found in 37.9% while deep sensory loss was detected in 44.1% of patients with PAD.

No significant correlation could be found, in our study, between  $ABI < 0.9$  or  $> 1.3$  and HbA1C. Aronow et al. reported that the higher the HbA1C levels in patients with diabetes and PAD, the higher the prevalence of severe PAD. But the mean HbA1C level in their 224 patients was 9.1% (76 mmol/mol) in comparison to 8.4% (68 mmol/mol) in our patients with  $ABI < 0.9$  and 8.0% (64 mmol/mol) in those with  $ABI > 1.3$  [13].

Our study showed significant correlation between PAD and peripheral neuropathy, retinopathy and nephropathy. Xu et al. studied the association between albuminuria and PAD in 1386 Chinese patients with DM. They reported that high normal urine ACR was associated with increased prevalence of PAD [14]. Wattanakit et al. also reported that the presence, but not magnitude, of albuminuria is an important risk factor for PAD in patients with DM [15].

Multivariate regression analysis revealed that the independent predictors for PAD in patients with  $ABI < 0.9$  were neuropathy creatinine, triglycerides,

low HDL, LDL and urine ACR. In patients with  $ABI > 1.3$ , the predictors of PAD were IHD, elevated diastolic BP, lost superficial sensations, lost deep sensations and triglycerides. Li and his colleagues reported that albuminuria and peripheral neuropathy were independent risk factors for PAD in patients with DM. But they also found that advancing age, retinopathy and HbA1c were other independent risk factors for PAD [16].

We conclude that the risk of micro- and macrovascular disease is high in Egyptian patients with diabetes and PAD. There is a strong correlation between PAD and microvascular disease in Egyptian population with diabetes mellitus. Early diagnosis and good control of risk factors could reduce PAD progression and complications. Screening for PAD is recommended in all patients with diabetes and microangiopathy. This could be done through detailed history and clinical examination as well as the necessary laboratory investigation. Non-invasive imaging would be needed in suspected cases.

### Disclosure statement

The authors declare no conflict of interest.

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