

Prevalence of peripheral arterial disease in type 2 diabetics in Pakistan

Javed Akram,¹ Aziz-ul-Hassan Aamir,² Abdul Basit,³ Mohammad Saleem Qureshi,⁴ Tariq Mehmood,⁵ Syed Khurram Shahid,⁶ Irshad Ahmed Khoso,⁷ Muhammad Ashraf Ebrahim,⁸ Aamir Omair⁹

Department of Medicine, Akram Medical Complex, Lahore,¹ Department of Diabetes and Endocrinology, Postgraduate Medical Institute, Hayatabad Medical Complex, Peshawar,² Department of Medicine, Baqai Institute of Diabetology and Endocrinology, Karachi,³ Department of Medicine, KRL Hospital, Islamabad,⁴ Medicare Hospital, Multan,⁵ Department of Endocrinology, Liaquat National Postgraduate Medical Centre, Karachi,⁶ Department of Endocrinology, Bolan Medical College and Complex Hospital, Quetta,⁷ Department of Endocrinology, Zubaida Medical Center, Karachi,⁸ Department of Community Health Sciences, Ziauddin University, Karachi.⁹

Abstract

Objectives: To observe the prevalence of peripheral arterial disease (PAD) and associated factors among people with type 2 diabetes in Pakistan.

Methods: A multicenter cross-sectional study was carried out at eight centers in all the provinces of Pakistan on people with type 2 diabetes. History of symptoms related to Peripheral arterial disease were noted and anthropometric measurements were recorded. Ankle brachial index (ABI) was measured using Doppler ultrasound; patients with ABI < 0.9 were classified as having low ABI.

Results: There were 830 patients in the study, (49% males and 51% females). Females were younger and had a higher body mass index (BMI) ($p < 0.001$). The prevalence of peripheral arterial disease was 31.6% with a 95% CI of 28.4% to 34.8%. There was no significant difference in the proportion of low ABI between males (30%) and females (33%) ($p = 0.29$). Patients with low ABI were found to have significantly higher BMI ($p = 0.02$) and waist circumference ($p = 0.001$).

The most common symptom in the patients with low ABI was pain on walking (84%), followed by numbness of the feet (64%). There was a significant difference in the reporting of all the symptoms ($p < 0.05$) except for numbness of the feet ($p = 0.57$) as compared to patients with normal ABI. No association was found between low ABI and duration of diabetes mellitus or cigarette smoking. There was no significant association between cardiovascular conditions and low ABI.

Conclusion: Peripheral arterial disease is common among people with type 2 diabetes in Pakistan and needs to be properly evaluated by the medical professionals as early diagnosis can help prevent future complications.

Keywords: Peripheral arterial disease, Type 2 diabetes, Ankle brachial index, Pakistan (JPMA 61:644; 2011).

Introduction

Peripheral arterial disease (PAD) is primarily the result of atherosclerotic changes in the vessels.¹ It is commonly manifested as intermittent claudication^{2,3} or critical limb ischaemia.³ A large majority of individuals, particularly elderly⁴ are asymptomatic and there is a slow and gradual progression of disease.⁵

Intermittent claudication only represents a small subset of the total population with PAD.³ Ankle Brachial Index (ABI), which is the ratio of ankle to brachial systolic blood pressure, is a simple, non-invasive and reliable bedside method for diagnosing the presence and severity of PAD. It is 95% sensitive and 100% specific against angiographically confirmed PAD and is the most widely used measurement for diagnosis of PAD.³ American College of Cardiology / American Heart Association (ACC/AHA) recommend measurement of ABI in symptomatic patients as a diagnostic criterion.⁶ The measurement of toe-brachial index is valuable

in patients with non-compressible vessels. Duplex ultrasound has the advantage of quantifying the severity of the lesion, but the imaging is limited by calcification.⁷

Diabetes mellitus is especially considered as an important risk factor for PAD.^{6,7} The number of people with diabetes is growing in Pakistan as a result of urbanization, physical inactivity and obesity. Pakistan is considered to be one of the countries with the largest population of people with diabetes and is ranked seventh globally by the International Diabetes Foundation.⁸ The prevalence of diabetes is high in Pakistan ranging from 7.6% to 11% among adults.⁹ It is important to diagnose diabetes early and offer treatment to avoid complications of the coronary and cerebral vasculature that are preventable.^{10,11} This study was designed to document the prevalence of peripheral arterial disease in the Pakistani population diagnosed with type 2 diabetes mellitus and to see the efficacy of cilostazol on them. We report here the prevalence of PAD in diabetics. The efficacy results are the subject of a separate paper.

Methods

A multicenter, cross-sectional study was carried out between December 2004 and December 2005 in eight centers in all the provinces of Pakistan. The centers were situated in the following cities of Pakistan: Karachi (3 centers), Multan, Lahore, Islamabad, Peshawer, Quetta, one centre each. Type 2 diabetic patients, 40 years or older were enrolled in the study.

The sample size was determined as 100 subjects from each center based on a 95% confidence level with an accuracy of $\pm 10\%$ for the prevalence of PAD from each center. The overall accuracy for the complete study was determined to be $\pm 3\%$ for an expected prevalence of 25% for the PAD with a total sample size of 800 for all the centers. Each center was required to recruit 130 subjects presenting with Type 2 diabetes mellitus to account for a 15% non-response / dropout. The subjects were selected consecutively from the population coming to the Outpatient Department till the required number was collected from each center. The study population was representative of the people with known diabetes mellitus as most of the centers were tertiary care centers in the major cities of Pakistan.

Patients were asked about history of cigarette smoking. Blood pressure, height, weight and waist circumference were noted. The weight was measured in indoor clothing and without shoes. The height was measured in an upright position and without shoes. The waist circumference was measured by applying the measuring tape directly to the skin, in a standing position. The midpoint between the lowest rib and the iliac crest was taken as the waist measurement.¹²

ABI was determined in both legs by Doppler Ultrasound using Super Dopplex II Bi-directional Doppler Model SD-II (Huntleigh/UK) by measuring systolic brachial pressure in both the arms and in the dorsalis pedis and posterior tibial artery in both the legs. ABI was calculated by using the higher of the two brachial pressures as the denominator and higher of the two ankle pressures (either the dorsalis pedis or the posterior tibial) as the numerator (separate for each leg). Tea / coffee was not consumed for 30 minutes prior to Doppler ultrasound. The ABI was classified as non-compressible, calcified vessel (ABI >1.3), normal (ABI 0.91-1.3), mild to moderate peripheral arterial disease

(ABI 0.41-0.9), and critical leg ischaemia (ABI <0.4).¹

The exclusion criteria were, people with Type 1 diabetes, those with amputation of both lower limbs and patients taking vasodilators or anti-platelet therapy. Only aspirin (on ethical grounds) was allowed, depending upon the physicians' decision. All the participants were screened for signs and symptoms of peripheral arterial disease. History was elicited for exertional pain and/or rest pain, nocturnal pain and numbness or tingling sensations. Any trophic changes and description of ulcers, if present were noted.

The data was double-entered using Epi-Info v6.04b to minimize data entry errors. The frequencies of all the variables were generated to check the validity of the responses. Any outliers or responses outside the acceptable ranges were checked manually against the case record forms and corrected where possible. The results are presented as prevalence (in %) with 95 percent confidence intervals. Students t-test was used for comparison of the numerical variables and Chi-Square test / test of proportions were used to compare the categorical variables. Test of Median was applied to compare the duration of diabetes between the two groups because the data was positively skewed due to some high values. All statistical tests were conducted at a confidence level of 95% and a p-value <0.05 was considered statistically significant.

The study was conducted in accordance with Helsinki Declaration and an approval of ethical committee/review board was obtained from each center. All patients were briefed about the study and an informed consent was taken.

Results

There were a total of 830 subjects whose Ankle Brachial Index (ABI) values were available, these consisted of 409 (49.3%) males and 421 (50.7%) females. The average number of participants from each center was 104 ± 11 ; seven of the centers contributed a sample of 94 to 107 subjects, one center from Karachi contributed 129 people with diabetes.

Table-1 provides the details for the physical parameters of the subjects. Females were younger and had a higher body mass index ($p<0.001$) although the waist circumference did not show any significant difference ($p=0.18$) between males and females.

Table-1: Age and Physical parameters of Subjects (Mean \pm sd).

	Total*	Males	Females	p-value
Age (years)	54.2 \pm 8.9 (n=830)	55.6 \pm 9.2 (n=409)	52.8 \pm 8.4 (n=421)	<0.001
Weight (kg)	70.5 \pm 12.7 (n=817)	72.2 \pm 12.7 (n=403)	69 \pm 12.4 (n=414)	<0.001
Height (cm)	159.4 \pm 10.5 (n=800)	165.3 \pm 9.3 (n=396)	153.6 \pm 8.2 (n=404)	<0.001
Body Mass Index (kg/m ²)	27.9 \pm 5.7 (n=800)	26.5 \pm 4.9 (n=396)	29.3 \pm 6.1 (n=404)	<0.001
Waist circumference (cm)	97.7 \pm 12.7 (n=572)	97 \pm 13.1 (n=292)	98.4 \pm 12.4 (n=280)	0.18

*Total 'n' is different for the different variables because of missing / incomplete observations for some patients.

Table-2: Comparison of Low Ankle Brachial Index with Duration of Diabetes Mellitus, Gender and Smoking status.

	Low ABI (≤ 0.9)	Normal ABI (> 0.9)	p-value
Duration since Diagnosis of Diabetes Mellitus (in years)	N=262	N=568	
Mean ± Sd	8.5 ± 6.2	9.4 ± 6.4	0.052a
Median (IQR*)	8 (5,13)	7 (4,12)	0.26b
Gender			
Male (n = 409)	122 (29.8%)	287 (70.8%)	0.29c
Female (n = 421)	140 (33.3%)	281 (66.7%)	
Smoking Status**			
(Males)	N=122	N=287	
Smoker	30 (24.6%)	64 (22.3%)	0.61c
(Females)	N=140	N=281	
Smoker	4 (2.9%)	4 (1.4%)	0.31c
Waist circumference**			
(Males)	N=59	N=233	
Mean ± Sd	100.6 ± 14.4	96.1 ± 12.6	0.02a
(Females)	N=53	N=227	
Mean ± Sd	102.1 ± 11.7	97.6 ± 12.4	0.02a

*IQR = Interquartile range

**The smoking status and waist circumference were available for 409 and 292 subjects respectively

a: Student's t-test for independent samples

b: Median test

c: Chi-Square test.

A low ABI (≤ 0.90) was present in both legs of 179 (21.6%) patients and one leg of 83 (10%) patients. Thus the total prevalence of peripheral arterial disease (one or both legs) was 31.6% (95% CI of 28.4%, 34.8%). Only six (0.7%) of these patients suffered from critical limb ischaemia (ABI ≤ 0.40), while all others had mild to moderate PAD (ABI 0.4 - 0.9). There were 568 (68.4%) people who had normal ABI of

more than 0.9. There was no significant difference in the proportion of low ABI between males and females with 122 (29.8%) out of 409 males having low ABI as compared to 140 (33.3%) out of 421 females with low ABI (p=0.29).

The presence of various symptoms is presented in Figure. Information about symptoms in the legs regarding pain on walking, pain at rest, nocturnal pain and numbness was available for 261 (99.6%) patients with low ABI and 559 (98.4%) patients with normal ABI. There were 20 (7.7%) patients who were asymptomatic despite having a low ABI, while at least one symptom was present in 241 (92.3%) patients with a low ABI. In the patients with normal ABI there were 100 (17.9%) patients who had no symptoms (p<0.001). The most common symptom in patients with low ABI was pain on walking in 220 (84.3%) patients, followed by numbness in 167 (64%) patients. The most common symptom in the group with normal ABI was numbness in the feet in 369 (66%) patients followed by pain on walking in 343 (61.4%) patients. The comparison of the different symptoms in the two groups is shown in figure 1. There was a significant difference in the reporting of all the symptoms except for numbness in the feet (p = 0.57).

Table-2 shows the comparison of different factors between the patients with low ABI as compared to those with normal ABI. The duration of diabetes since diagnosis in the subjects ranged from 1 to 35 years with a mean of 9.1 ± 6.3 years. There was no significant difference (p=0.052) between the duration of being diagnosed as having diabetes mellitus and the presence of a low ABI.

The association between other cardiovascular

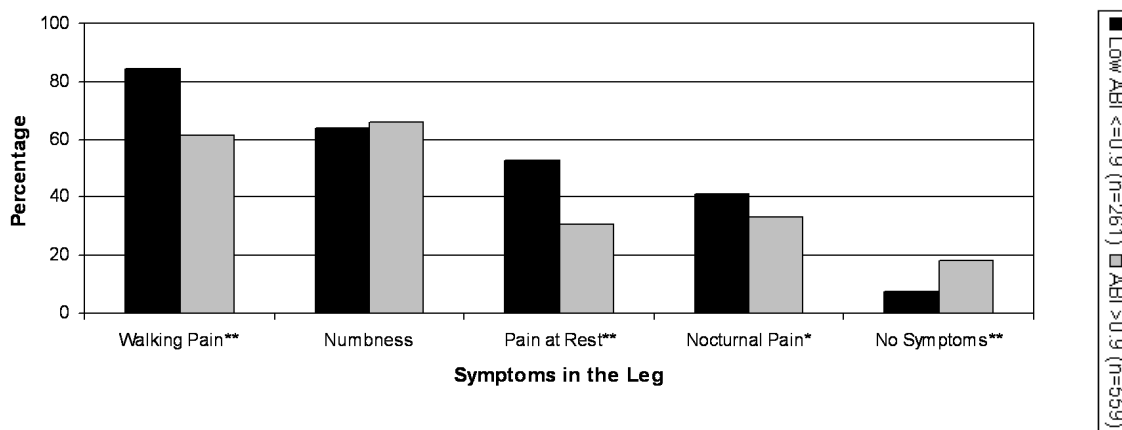


Figure: Comparison of symptoms in patients with low and normal ABI.

	Walking Pain	Numbness	Pain at Rest	Nocturnal Pain	No Symptoms
Sensitivity	84%	64%	53%	41%	-
Specificity	39%	34%	69%	67%	-

*Statistically significant difference at p<0.05

**Statistically significant difference at p<0.001.

conditions and low ABI was also determined. It was found that the history of having hypertension, myocardial infarction / angina or stroke / TIA was not significantly higher in patients with low ABI as compared to those with normal ABI. The Odds Ratios were found to be insignificant for hypertension (OR=0.83, 95% CI: 0.63, 1.13) and stroke / TIA (OR=0.89, 95% CI: 0.35, 2.18). The Odds Ratio was found to be lower for patients with low ABI regarding the history of myocardial infarction / angina (OR=0.46, 95% CI: 0.24, 0.87).

Discussion

This study reports the prevalence of peripheral arterial disease among diagnosed people with type 2 diabetics in Pakistan. To our knowledge this is the first large scale study in Pakistan to see the prevalence of peripheral arterial disease in this population. There is a widespread belief amongst the medical professionals that PAD is a disease of the West and is infrequent in Pakistan. The estimated prevalence of PAD greatly varies among the population studied and the diagnostic criteria applied. Basit et al reported a prevalence of 5.5% peripheral vascular disease among 2199 type 2 diabetic patients surveyed based on the absence of dorsalis pedis or posterior tibial pulses.¹³ The prevalence may vary with the type of diagnostic approach. In our study, although the number of subjects was less as compared to Basit et al, we had employed Doppler for the diagnosis of peripheral arterial disease, which is a more reliable method for the diagnosis.³ The prevalence of PAD among the general population in the United States has been estimated to be 4.3% (corresponding to more than 5 million adults) in adults aged > 40 years on the basis of mean ankle-brachial index < 0.9 in either leg.¹⁴ Mohan et al reported a prevalence of only 3.9% in a large population of 4941 patients in South India¹⁵ on the basis of ankle-brachial index determined by Doppler.

In this study, ABI was used as the diagnostic criteria as it is a simple test that can be used with accuracy with little practice. Contrary to the general belief, and earlier reports,¹³ the study showed a prevalence of PAD in 31.5% of patients. This may be higher than in the general population as the study was focused on diagnosed type 2 diabetics.

Most individuals with peripheral arterial disease are asymptomatic and less than 20% patients report classical symptoms of PAD.⁷ In PARTNERS study¹⁶ conducted across 350 primary care centers across the United States, only 8.7% patients in the PAD-only group had classical symptoms of PAD. In the present study 68% patients had walking pain. This high percentage of pain may be attributable to old age, arthritis or other unrelated conditions.

There is a strong association of PAD with diabetes. Studies of glycosylated haemoglobin have shown that the relative risk of PAD in people with type 2 diabetes is 1.28.¹⁷ Diabetes is a rapidly growing public health problem in

Pakistan. There were an estimated 6.9 million diabetics in 2007 and the number is expected to rise to 11.5 million by 2025.⁸ PAD progresses more rapidly in diabetics and its prevalence also increases with age and the duration of diabetes.² This is evident from the 31.5% prevalence observed in our study. However, there was no significant association between duration of diabetes and a low ABI in our study.

A recent study¹⁸ in USA reported that only half of those who had some awareness of PAD had no knowledge that diabetes and smoking increased the risk for PAD, 25% knew that PAD poses increased risk for heart attack and stroke and only 14% knew that PAD was associated with increased risk for amputation. Keeping in view the low overall literacy rate (57%) of Pakistan,⁹ it is anticipated that very few patients would be aware of PAD and its associated complications. The situation is compounded by the fact that awareness among the medical professionals is also low. There is a dire need for creating awareness of the disease and its complications so that the disease can be managed in its early stages.

A limitation of the study was the self-reporting of duration of diabetes. There were no medical records to verify the duration of diabetes. Another limitation was lack of data on glycaemic control. Glycaemic control, as judged by HbA1c levels, would have been helpful in relating the prevalence of PAD with the level of control.

Conclusion

The study demonstrates a high prevalence of PAD among people with type 2 diabetes in Pakistan which needs to be appropriately evaluated by the medical professionals. Measurement of ABI, correlates with the clinical condition, is a simple and effective method for diagnosing the disease early which can help in reducing the risk of complications associated with PAD.

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Delay in publication of this study is regretted. It was a multicentre study involving 10 centres from different cities of Pakistan. The processing, analysis and writing of the manuscript was delayed due to unavoidable reasons.

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