

## **Prevalence of Peripheral Arterial Disease among People Attending Diabetes Clinics at Primary Care Settings**

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**Objective:** The aim of this study is to use ankle-brachial index (ABI) to evaluate the prevalence of peripheral arterial disease (PAD) in diabetic patients and to identify the associated cardiovascular risk factors and their level of control.

**Design:** Cross-sectional Study.

**Setting:** Four primary healthcare centers.

**Method:** Four health centers were chosen randomly. People attending diabetes clinics were screened for PAD by measuring their ABI.  $ABI \leq 0.9$  was used to diagnose PAD. In addition, patients' medical records were reviewed for PAD risk factors including age, smoking, blood pressure, glycated hemoglobin, lipid profile, chronic kidney disease (CKD) and the use of guardian drugs. Further, self-reported data about presence of classical claudication symptoms were obtained.

**Result:** Three hundred thirty-one patients were included in the study. One hundred fifty-two (45.9%) patients were females. PAD was present in 67 (20.2%) patients. Classical claudication symptoms were present in 13 (19.4%) PAD patients. Clinical profile and the use of guardian drugs in the group was poor in general, but was worse among PAD patients. Statistically significant association was found between low ABI and stage  $\geq 3$  CKD ( $P=0.014$ ). Use of statins was lower in patients with PAD when compared with patients with normal ABI ( $P=0.00$ ).

**Conclusion:** The study revealed that PAD is highly prevalent among people with diabetes. Control of cardiovascular risk factors was poor in general, but was worse in patients with PAD. The use of guardian drugs was suboptimal.

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Diabetes is a common non-communicable disease worldwide. It has a significant impact on health because of its microvascular and macrovascular complications. Developing countries are facing the major impact of this disease<sup>1</sup>. Diabetes is prevalent in Bahrain; the estimated prevalence in 2010 was 15.4%, and it is expected to rise to 17.3% by the year 2030<sup>1</sup>.

Peripheral Arterial Disease (PAD) is defined as the group of disorders that affects any artery other than those which supply the heart<sup>2</sup>. It has been found to be very common in different cultural settings<sup>3-6</sup>.

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Screening for PAD is important for two main reasons. First, the majority of patients with PAD are asymptomatic, even in symptomatic patients atypical symptoms are common<sup>3,5,7,8</sup>. Moreover, asymptomatic disease can significantly increase the rate of progression to intermittent claudication, which could adversely affect the quality of life<sup>9,10</sup>. Second, PAD indicates generalized atherosclerosis and thus carries a very high risk for cardiovascular (CV) morbidity and mortality<sup>11,12</sup>. This is attributed to the fact that most of these patients have CV risk factors<sup>13</sup>. Therefore, diagnosing PAD would be helpful to identify and modify the risk factors to decrease the burden of CV morbidity and mortality.

Diabetes is a well-known risk factor for PAD<sup>4-6,14,15</sup>. PAD is usually extensive and severe when associated with diabetes<sup>16</sup>.

In Bahrain, a recent survey found that the prevalence of PAD among people with diabetes was around 12%<sup>17</sup>. However, the diagnosis was based on the absence of foot pulses and the presence of claudication, which could underestimate the prevalence considerably. A study in diabetic patients found that nearly one-third who gave no history of intermittent claudication were found to have PAD when tested by Ankle-Brachial Index (ABI) and one-fifth of patients with what were considered normal physical examination had PAD<sup>18</sup>. In another study, the use of pulses to diagnose PAD was found to have a very low sensitivity in a primary care setting<sup>19</sup>.

Measurement of ABI is a simple, non-invasive and reliable tool for PAD diagnosis and it is recommended to be used routinely in people with diabetes<sup>20,21</sup>. To the best of our knowledge, no studies were found, which use ABI for PAD screening in diabetic patients attending primary healthcare in Bahrain.

The aim of this study is to use ABI to evaluate the prevalence of PAD in diabetic patients and to identify the associated cardiovascular risk factors and their level of control.

## **METHOD**

The study was performed on diabetic patients aged 40 years and older who attended diabetes clinics from January 2010 to June 2010. The Epi info program version 3.5.3 was used to calculate the sample size according to the reported prevalence derived from a previous study<sup>17</sup>. Employing a precision of 0.05 and 99% confidence level, the calculated sample size was 277 persons. More subjects were included in the study to adjust for non-respondents.

A workshop to train diabetes nurses about theoretical and practical ABI measurements using Doppler device (Elite-200R, Nicolet Vascular Inc.) was arranged. A vascular radiologist conducted the workshop.

Four diabetes clinics in four healthcare centers were chosen randomly. Informed consent was obtained. Patients were asked to rest for at least 5 minutes in supine position. The brachial pressure (BP) of both arms was measured. Then, the nurse measured systolic pressures for dorsalis pedis (DP) and posterior tibial arteries (PT) in both legs using a Doppler device (Elite-200R, Nicolet Vascular Inc.). The ABI was calculated by dividing the higher systolic pressure of DP or PT of each leg by the higher BP. The lowest ABI of each patient was included in the study.  $ABI \leq 0.9$  was considered diagnostic of PAD<sup>21</sup>. Patients with  $ABI \geq 1.4$  were excluded because these patients need other diagnostic tests to evaluate for PAD due to non-compressible tibial vessels resulting from vascular calcifications<sup>21</sup>. Patients were asked about the presence of

classic claudication symptoms, exertional fatigue, discomfort or frank pain localized to leg muscles that resolves with rest.

The medical records of these patients were reviewed for PAD risk factors by using a designed data collection sheet. These include age, sex, smoking, blood pressure, glycated hemoglobin (A1C), lipid profile: total cholesterol (TC), low density lipoprotein (LDL), high density lipoprotein (HDL), triglycerides (TG), evidence of chronic kidney disease (CKD) defined as kidney damage, albuminuria measured by albumin creatinine ratio (ACR) and/or estimated glomerular filtration rate (eGFR)  $< 60\text{ml}/\text{min}/1.73\text{m}^2$  [stage  $\geq 3$ ]<sup>15,22</sup>. Guardian drugs, such as, aspirin, statins and angiotensin-converting enzymes inhibitors (ACEI) were documented. Definition of control of hypertension, A1C and lipid profile was according to the seventh report of the Joint National Committee (JNC7), American Diabetes Association (ADA) and third report of the National Cholesterol Education Program recommendations<sup>23-25</sup>.

Data were analyzed by using SPSS software, version17. Chi-squared test was used to assess the association between ABI and each of the following factors: age, gender, level of control of PAD risk factors and the use of guardian drugs. Multiple logistic regression model that included all the studied risk factors and ABI status as the dependent variable was set to determine the independent predictors for low ABI. The model was estimated using the stepwise forward logistic FL method. P-value less than 0.05 was considered statistically significant. The central department of primary healthcare approved the study.

## RESULT

Three hundred forty-one type 2 diabetic patients were recruited for study, but ten patients had  $\text{ABI} \geq 1.4$  were excluded. Data of 331 patients were analyzed. One hundred fifty-two (45.9%) patients were females. The mean age was 54.2 with a standard deviation of  $\pm 8.3$  years.

Twenty-four patients (7.3%) of the total sample were smokers and 22 (6.6%) were ex-smokers. Symptoms of claudication were present in 88 (26.6%) patients. Clinical profile of patients and drugs used are presented in table 1 and 2.

**Table 1: Clinical Profile of Patients\***

Condition	Controlled (number and percentage)	Uncontrolled	No data*
Hypertension (target $<130/80$ )	85/328 = 26	243/328 = 74	3
A1C (target $<7\%$ )	78/325 = 24	247/325 = 76	6
Total cholesterol (target $<4\text{mmol}/\text{l}$ )	77/331 = 23.3	254/331 = 76.7	-
LDL (target $<2.6\text{mmol}/\text{l}$ )	156/323 = 48.3	167/323 = 51.7	8
Triglycerides (target $<1.7\text{mmol}/\text{l}$ )	219/327 = 67	108/327 = 33	4
HDL (target $>1\text{mmol}/\text{l}$ )	234/326 = 71.8	92/326 = 28.2	5

\*Missing data

**Table 2: Guardian Drugs Used\***

<b>Drugs Used</b>	<b>Yes (number and percentage)</b>	<b>No</b>
Statins	172 (52)	159 (48)
ACEI	141 (42.6)	190 (57.4)
Aspirin	195 (58.9)	136 (41.1)

\*331 patients

Fifty-two patients (15.7%) had ACR > 3.5 mg/mmol of creatinine and 11 (3.3%) had eGFR <60 ml/min/1.73m<sup>2</sup>.

Sixty-seven (20.2%) patients had low ABI ( $\leq 0.9$ ). The minimum measurement of ABI was 0.6 and the mean was 1.03 with a standard deviation of  $\pm 0.1$ . No significant association was found between the age and ABI. Distribution of patients by age group and ABI is presented in table 3. Twenty-eight patients (41.8%; 28/67) with low ABI were females. There was no significant association between sex and ABI, see table 4.

**Table 3: Distribution of Patients by Age and ABI**

<b>Age Group (years)</b>	<b>Low ABI (%)</b>	<b>Normal ABI (%)</b>	<b>Total</b>
40-49	13 (19.4)	86 (32.6)	99 (29.9)
50-59	36 (53.7)	114 (43.2)	150 (45.3)
$\geq 60$	18 (26.9)	64 (24.2)	82 (24.8)
<b>Total</b>	<b>67 (100)</b>	<b>264 (100)</b>	<b>331 (100)</b>

P=0.1

**Table 4: Distribution of Patients by ABI and Sex**

<b>Sex</b>	<b>Low ABI</b>	<b>Normal ABI</b>	<b>Total</b>
	<b>(number and percentage)</b>		
Males	39 (58.2)	140 (53)	179 (54.1)
Females	28 (41.8)	124 (47)	152 (45.9)
<b>Total</b>	<b>67 (100)</b>	<b>264 (100)</b>	<b>331 (100)</b>

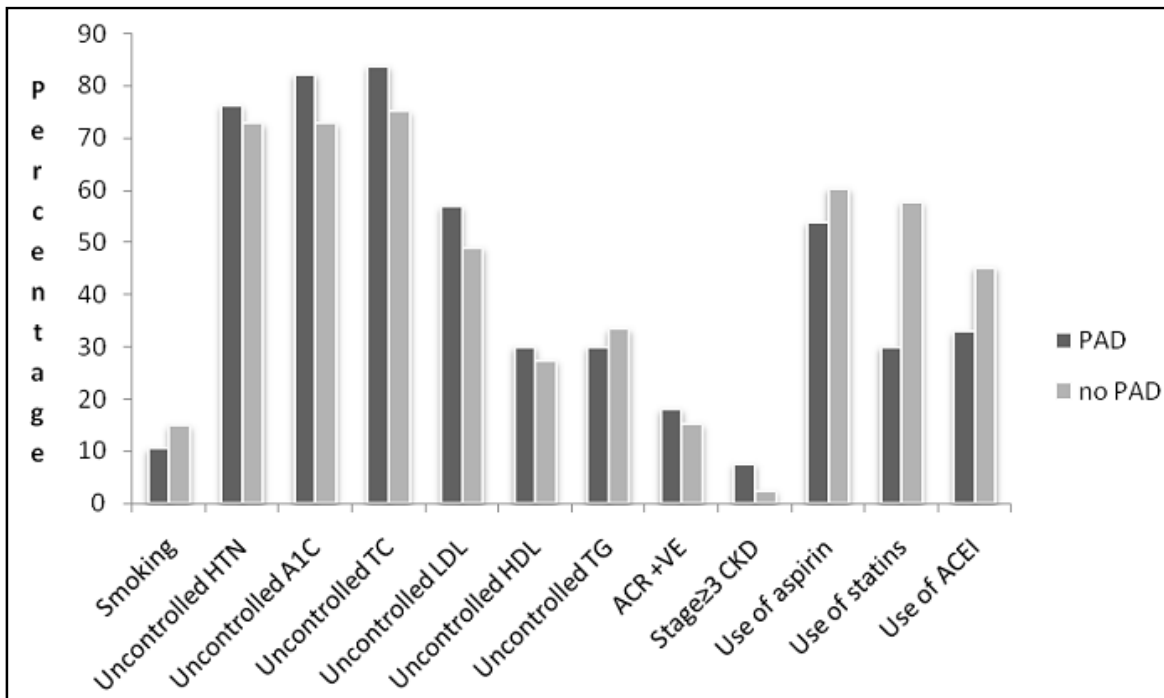
P=0.49

No significant association between symptoms of claudication and low ABI (P=0.286). Relationship between the level of control of risk factors, use of guardian drugs and ABI is presented in table 5 and figure 1.

**Table 5: Relationship between Level of Control of Risk Factors, Use of Guardian Drugs and ABI**

Risk Factor	Low ABI ( $\leq 0.9$ )	Normal ABI	P value
	Number (%), N=67	Number (%), N=264	
Smoking	7 (10.4)	39 (14.8)	0.587
Uncontrolled hypertension (HTN)	51 (76.1)	192 (72.7)	0.622
Uncontrolled A1C	55 (82.1)	192 (72.7)	0.193
Uncontrolled total cholesterol (TC)	56 (83.6)	198 (75)	.09
Uncontrolled LDL	38 (56.7)	129 (48.9)	0.229
Uncontrolled HDL	20 (29.9)	72 (27.3)	0.497
Uncontrolled triglycerides (TG)	20 (29.9)	88 (33.3)	0.493
+VE ACR*	12 (18)	40 (15.1)	0.1
Stage $\geq 3$ CKD	5 (7.5)	6 (2.3)	0.014
Use of aspirin	36 (53.7)	159 (60.2)	0.204
Use of statins	20 (29.9)	152 (57.6)	0.00
Use of ACEI	22 (32.8)	119 (45.1)	0.163

\*  $>3.5$ mg/mmol of creatinine; N=number



**Figure 1: Relationship between Control of Risk factors, Use of Guardian Drugs and Presence of PAD**

The presence of stage  $\geq 3$  CKD ( $P = 0.014$ ) and not being on a statin ( $P = 0.00$ ) were the most important independent risk factors and predictors for low ABI in this study.

## DISCUSSION

The study showed that one-fifth of the patients had PAD. There was no statistically significant age or gender difference among the identified patients. Less than 20% of PAD patients gave history of claudication. Risk factors control level was poor among the total group, it was worse among PAD patients.

The study revealed that the prevalence of PAD is around 20%. Other studies reported similar or higher prevalence<sup>3,4,6,7,26</sup>. The prevalence in this study is higher than that found by Al Mahroos et al<sup>17</sup>. Because of younger age group (mean age 54 years), the finding of this study indicates that PAD is highly prevalent. Indeed, the prevalence is likely to be under estimated because the patients were not evaluated for the presence of concomitant neuropathy, which lowers the sensitivity of ABI. In a study, one-third of the patients with PAD had false negative ABI results because of concomitant neuropathy<sup>27</sup>. The clinical profile of the patients showed that about 75% have uncontrolled A1C, which increases the risk for microvascular complications including neuropathy<sup>28</sup>. Therefore, one would expect high prevalence of neuropathy as well.

While the association between PAD and gender is inconsistent, increasing age is a well-known risk factor for PAD as found in several studies<sup>9,15</sup>. This study showed insignificant association between age and PAD, which is probably due to the relatively younger age group included in the study, more than 75% of the patients were less than 60 years.

The study showed that less than one-fifth (19.4%) of PAD had classical caudication symptoms which is consistent with several other studies<sup>8,19,29,30</sup>. Diabetic patients could have advanced disease without symptoms when accompanied by neuropathy. This highlights the importance of screening and rationalizes the recommendation of ADA to screen people with diabetes who are above 50 years and those less than 50 in the presence of other risk factors<sup>20</sup>. However, it should be mentioned that the data about claudication in this study were self-reported and may not be accurate.

PAD shares similar risk factors with coronary heart disease [CHD]; it is considered as CHD equivalent<sup>15,25</sup>. Therefore, risk factors should be treated with the same degree of aggressiveness. However, several studies have shown that PAD patients are treated less aggressively and risk factors are managed suboptimally<sup>3,31</sup>. In this study, patients with PAD had worse profile than those without PAD, although the differences did not reach statistical significance; except for those who use statins. The risk for intermittent claudication, hospitalization, amputation and revascularization was found to increase linearly with the increase in A1C<sup>32</sup>.

The study indicated that CKD is more likely to be prevalent among patients with PAD and the difference was statistically significant. This is an expected finding as CKD is a predictor of cardiovascular disease (CVD); the prevalence of PAD was found to be inversely related to eGFR<sup>33</sup>. Furthermore, the mere presence of microalbuminuria was found to double the risk of PAD prevalence when compared to normo-albuminuria<sup>34</sup>. However, due to the small number of patients who had positive test for albuminuria, the difference did not reach statistical significance in this study.

In this study, the use of guardian drugs is suboptimal; 48% were not on statins, which is inconsistent with ADA recommendations. ADA recommends that statins therapy should be added regardless of baseline lipid levels for diabetic patients without CVD who are over the age of 40 years and have one or more other CVD risk factors<sup>24</sup>.

In addition to their proven efficacy to lower CV risk as shown in several trials, statins have been found to improve leg function in PAD patients independent of their cholesterol level [i.e. pleiotropic effect]<sup>35,36</sup>. Similarly, ACEI have beneficial effect independent of their anti-hypertensive properties<sup>37</sup>. As a primary prevention strategy, guidelines recommend aspirin use in these patients<sup>21,24</sup>. However, based on data from recent trials, the evidence that supports its use is scarce and needs to be confirmed<sup>38</sup>.

## CONCLUSION

**The study revealed that PAD is highly prevalent among people with diabetes. Risk factors were poorly controlled in general but were worse in patients with PAD. In addition, the use of guardian drugs was suboptimal.**

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