FREQUENCY OF PERIPHERAL ARTERIAL DISEASE IN HIGH RISK TYPE 2 DIABETES MELLITUS USING ANKLE-BRACHIAL INDEX AND ITS ASSOCIATION WITH THE RISK FACTORS AMONG PATIENTS PRESENTING IN JINNAH HOSPITAL, LAHORE

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ABSTRACT

Objective: To determine frequency of peripheral arterial disease (PAD) using ankle brachial index and its various risk factors in Pakistani patients.
Study Design: Cross-sectional study.
Place and Duration of Study: Allama Iqbal Medical College, Jinnah Hospital, Lahore, from Jan 2017 to Apr 2017.
Material and Methods: High risk type 2 diabetic patients were recruited for the study. After detailed history and clinical examination, fasting and 2-hours postprandial sugar levels and blood pressure were measured. Ankle brachial index (ABI) was used to measure PAD using portable smart dop instrument. Patients with ABI <0.9 were labeled as having PAD.
Results: There were 100 subjects in the study with mean age 54.9 ± 9.1 years. The mean duration of diabetes was 9.15 ± 2.3 years. The mean systolic and diastolic blood pressure was 144 ± 14 mm Hg and 91 ± 6 mm Hg respectively. The mean fasting and 2-hours post prandial blood sugar level of the study population were 171.5 ± 9.12 and 202.6 ± 11.3 mg/dl respectively. Based on abnormal ABI <0.9, the prevalence of PAD was 41.0% in our study population. Higher mean age, duration of diabetes mellitus, mean systolic blood pressure and smoking were found to be statistically significant risk factors for PAD (p-value<0.01).
Conclusion: PAD was highly prevalent in our population and was significantly associated with higher mean age of patients, longer duration of diabetes, higher systolic blood pressure and smoking.

Keywords: Ankle brachial index, Diabetes Mellitus, Peripheral arterial disease, Risk factors.

INTRODUCTION

Type 2 diabetes mellitus is highly prevalent in developing countries of Asia. Peripheral arterial disease (PAD) is one of the major complications of type II diabetes mellitus (DM)[1]. Atherosclerosis characteristically affects peripheral vessels of limbs and is an indicator for vascular compromise in other vascular beds of the body[2].

The prevalence of PAD in DM patients has been reported to range from 10% to 40.0%[3]. The presence of DM increases the risk of PAD more than four-fold[3]. For every 1% increase in hemoglobin A1c there has been a corresponding 26% increased risk of PAD[4]. Majority of the patients with PAD either present without any symptoms and about one third of the patients present with intermittent claudication[5]. Because of its asymptomatic silent progression, PAD in diabetics remains underdiagnosed and undertreated[6]. Symptomatic lower extremity PAD is associated with functional limitation and compromised quality of life, causing limb amputation and increased mortality[7].

The actual prevalence of PAD in type 2 diabetics has been difficult to determine owing to silent nature of the disease and non-uniform screening modalities for PAD. Ankle brachial index (ABI) has proven itself to be a reproducible, accurate and reliable method of estimation of PAD. In calculating ABI, systolic blood pressures are measured using a portable hand held doppler probe at ankle (dorsalis pedis and posterior tibial artery pressure) and at upper arm (brachial artery

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pressure). A ratio is calculated between these two readings. An ABI greater than 0.9 is considered normal whereas ABI less than 0.9 is abnormal and a strong indicator of PAD[8]. As compared to history and clinical signs, ABI has proven to be more accurate[8]. It has been shown to be 95% sensitive and 100% specific when compared with angiographically proven PAD[9].

Early detection of PAD with ABI in patients at high risk would allow early institution of preventive intervention. This can be optimized by identifying significant PAD risk factors in patients and carrying out ABI screening in those at high risk. In this study, we used ABI to quantify PAD burden in type 2 diabetic patients in our clinical setup and calculated the prevalence of various risk factors in the development of PAD. The study helped us identify modifiable risk factors that could be addressed prior to the onset of PAD in type 2 diabetics.

PATIENTS AND METHODS

This cross-sectional study was conducted following principles of good clinical practice as laid down in Declaration of Helsinki 2013. The study proposal was approved by Ethical Review Board of Allama Iqbal Medical College, Lahore, Pakistan. The sample size was calculated using World Health Organization (WHO) sample size calculator with 95% confidence interval, 5% margin of error, acceptable difference of 0.08 and assumed prevalence of peripheral arterial disease to be 20% in the study population. One hundred patients presenting at Jinnah Allama Iqbal Institute of Diabetes and Endocrinology (JAIIDE), Jinnah Hospital, Lahore were enrolled for the study using non-probability consecutive sampling. The study was conducted from January 2017 to April 2017. A written informed consent was obtained from all the participants of the study after explaining the study in detail.

High risk type 2 diabetics were defined on the basis of following criteria:

- Age more than 40 years
- Type 2 diabetes mellitus for at least 5 years
- Presence of one or more risk factors for peripheral arterial disease (table-I)

Peripheral arterial disease (PAD), narrowing and occlusion of peripheral arteries of the body by atherosclerosis, was defined on the basis of ABI with a value less than 0.9 labeled as PAD.

ABI was measured using Hadeco smartdop 45 handheld vascular doppler, Marne Medical, Australia using the standard 8 MHz probe. Ankle brachial pressure index was calculated by dividing the higher reading of the ankle pressure at dorsalis pedis artery by brachial pressure of the same side. ABI ≥0.9 was considered as normal whereas ABI <0.9 was defined as PAD.

Type 2 diabetic patients fulfilling the inclusion criteria stated above were interviewed by the investigators using a pre-designed proforma. Patients with history of leg trauma, amputation of any limb, leg ulcers, limb swelling due to any cause, vasculitis and deep venous thrombosis were excluded from the study owing to their confounding effect on measurement of ABI. Demographic information (age, sex, marital status, residence, social status) were recorded. The recruited type 2 diabetics were assessed for well known risk factors of peripheral arterial disease.

Keeping patients in supine position, brachial and ankle blood pressures were measured in both arms and legs using palpatory methods. Then, smartdop instrument was used to see doppler blood flow and measure blood pressure at these sites. ABI was calculated by dividing ankle pressure readings with the brachial pressure. The lower values obtained were considered as true ABI and a reading less than 0.9 was labeled as indicator of peripheral arterial disease.

The collected information were entered in Statistical Package for Social Sciences (SPSS) version 20.0. Mean and standard deviation were calculated for quantitative variables like age, BMI, ABI etc. The qualitative variables like

presence or absence of diabetes, hypertension, smoking, dyslipidemia, ischemic heart disease, family history of atherosclerotic vascular events were analyzed in terms of frequencies and percentages. The differences between subjects with and without PAD in terms of risk factors were assessed using student's t-test for quantitative variables and chi-square test for qualitative variables. A *p*-value of less than 0.05 was considered statistically significant.

mean diastolic blood pressure was 91 ± 6 mm Hg. BMI ranged from 18.4-36.1 Kg/m^2 with mean BMI being 27.13 ± 4.1 Kg/m^2 (dempographic and clinical characteristics are given in table-I).

Diabetic control was checked using fasting and 2-hours post-prandial blood sugar levels. The mean fasting and 2-hours post prandial blood sugar level of the study population were 171.5 ± 9.12 and 202.6 ± 11.3 mg/dL respectively. Post-prandial glucose levels were better controlled in

Table-I: Demographic and clinical baseline characteristics of the study population.

	Men (n=45)	Women (n=55)	Total (n=100)	*p*-value
Age (years)	55.2 ± 7.2	52.1 ± 6.8	54.9 ± 9.1	0.0362
Duration of diabetes (years)	9.3 ± 2.9	9.1 ± 3.6	9.15 ± 2.3	0.76
History of Intermittent Claudication	15 (33.3)	23 (41.8)	38 (38.0)	0.38
History of Hypertension	30 (66.7)	33 (60.0)	63 (63.0)	1.012
History of Smoking	21 (46.7)	1 (1.8)	22 (22.0)	<0.001
History of Ischemic Heart Disease	8 (17.7)	10 (18.2)	18 (18.0)	1.000
Family History of Diabetes	24 (53.3)	29 (52.7)	53 (53.0)	1.000
Mean BMI (Kg/m^2)	26.95 ± 5.0	28.16 ± 4.7	27.13 ± 4.1	0.758
Mean Fasting Blood Sugar (mg/dL)	168.1 ± 8.2	174.6 ± 9.3	171.5 ± 9.12	<0.001
Mean 2-hours Post-prandial Glucose Level (mg/dL)	191.1 ± 7.4	206.5 ± 8.1	202.6 ± 11.3	<0.001
Mean Systolic Blood Pressure (mmHg)	146 ± 15	142 ± 14	144 ± 14	0.367
Mean Diastolic Blood Pressure (mmHg)	93 ± 7	90 ± 6	91 ± 6	0.984
Total risk factors (out of 10)	5.2 ± 1.4	4.8 ± 1.0	4.9 ± 1.3	0.415

Table-II: Prevalence of various risk factors for peripheral arterial disease.

Risk Factor	Prevalence (%)
Hypertension	63 (63)
Hyperlipidemia	24 (24)
Smoking	22 (22)
Ischemic heart disease based on history and ECG	18 (18)
Family history of diabetes	53 (53)
Age >52 years	73 (73)
Male gender	45 (45)
Fasting blood sugar (FBS) >150 mg/dL	68 (68)
Body mass index (BMI) >25 Kg/m^2	58 (58)

RESULTS

There were 100 subjects enrolled in the study with mean age 54.9 ± 9.1 years (range: 39-74 years) and male to female ratio 1 : 1.2. Mean duration of the diabetes was 9.15 ± 2.3 years (range: 5-16 years). Sixty three percent of the patients were hypertensive whereas 22% were smokers. Fifty nine percent of the patients had positive family history of diabetes. The mean systolic blood pressure was 144 ± 14 mm Hg and

men than in women, 191.1 ± 7.4 and 206.5 ± 8.1 mg/dL respectively (*p*-value<0.001).

On the basis of ABI<0.9, the prevalence of peripheral arterial disease came out to be 41.0% in our study population. Women were more affected than men with ABI <0.9 in 24 out of 55 (43.6%) female patients and in 17 out of 45 (37.7%) male patients (*p*-value=0.615). Intermittent claudication was reported in 38 out of 41 (92.7%) patients with PAD. On clinical

examination, 10 out 41 (24.4%) patients with abnormal ABI had decreased peripheral pulses. The prevalence of various risk factors for PAD is shown in table-II.

The study population was stratified into two groups: Those suffering from peripheral arterial disease and those that did not suffer from PAD. The effects of various risk factors on these groups were assessed using student's t-test for quantitative variables and chi-square test for qualitative variables. These results are summarized in table-III. Higher mean age, duration of diabetes mellitus, mean systolic blood pressure and smoking were found to be statistically significant risk factors for PAD. The differences of PAD in different studies are given in table IV.

DISCUSSION

The primary objectives of the study to find the prevalence of peripheral arterial disease and its various well known risk factors in high risk type 2 diabetes mellitus were successfully met. Ankle brachial index was used to measure peripheral arterial disease which had proven to be very sensitive and specific in detecting peripheral arterial disease by many investigators earlier[10,11].

Table-III: Differences in the prevalence of risk factors for PAD group and non-PAD group.

Risk Factor	Peripheral Arterial Disease (ABI<0.9) (N=41) n(%)	Non-Peripheral Arterial Disease (ABI>0.9) (N=59) n(%)	*p*-value
Mean age (years) Mean ± SD	68.1 ± 6.2	54.2 ± 5.8	<0.001
Duration of Diabetes (years) Mean ± SD	13.5 ± 5.1	7.9 ± 4.7	<0.001
Hypertension	28 (68.3)	31 (52.5)	0.315
Mean systolic blood pressure (mmHg)	151 ± 12	141 ± 14	0.0015
Hyperlipidemia	11 (26.8)	14 (23.87)	0.496
Smoking	10 (24.4)	6 (10.2)	<0.05
Ischemic heart disease based on history and ECG	7 (17.1)	11 (18.6)	0.325
Family history of diabetes	21 (56.1)	30 (50.1)	1.003
Age >52 years	24 (58.5)	28 (47.5)	>0.05
Male gender	20 (48.8)	26 (44.1)	0.865
Mean fasting blood sugar level (mg/dl)	180.2 ± 8.1	164.9 ± 7.6	<0.05
Fasting blood sugar (FBS) >150 mg/dl	30 (73.2)	39 (66.1)	0.325
Mean BMI (Kg/m^2)	27.35 ± 3.95	27.0 ± 4.1	0.982
BMI >25 Kg/m^2	23 (56.1)	32 (54.2)	0.862

Table-IV: Prevalence of PAD as assessed by abnormal ABI in different studies.

Year of Study	First Author	Country	Prevalence of PAD as Assesed by ABI <0.9
2017	Umer et al (current study)	Pakistan	41.0
2013	Solanki et al[12]	India	35.0
2012	Agarwal et al[1]	India	14.4
2012	Ali et al[13]	Pakistan	39.3
2011	Akram et al[14]	Pakistan	31.6
2007	Sodhi[15]	India	18.5
2006	Norman et al[16]	Australia	13.6
2004	Selvin[17]	USA	14.5
2000	Premalatha et al[18]	India	6.3
1995	Mohan et al[19]	India	3.9
1997	Al-Zahrani	Saudia Arabia	42.5
1992	Walters et al[20]	UK	23.5

The prevalence of PAD came out to be 41% in our study population which matches with an earlier study conducted by Solanki *et al* who reported an abnormal ABI in 35% of hospital based Indian population[12]. Our results closely match with earlier reports from Pakistan in which Akram *et al*[14] and Ali *et al*[13] reported prevalence of PAD to be 31.6% and 39.3% respectively. The higher prevalence in our population can be explained by the fact that we only included high risk diabetic patients in our study with diabetes for at least 5 years and presence of at least one or more risk factors for PAD. This can also be attributed to higher mean age, higher BMI and more female population in our sample. It may also be postulated here that PAD development varies in various ethnicities that needs further research to establish a definitive association.

An earlier study by Norman *et al* reported age, higher duration of diabetes, higher systolic blood pressure and higher BMI to be significant predictors of PAD[16]. Ali *et al* described female gender, higher duration of diabetes and hypertension to be significantly associated with PAD[13]. Various studies have shown higher systolic blood pressure to be a strong risk factor for PAD[1,14,15,17-20].

Our results are in agreement with the aforementioned reports. The group with PAD had higher mean age (68.1 ± 6.2 years) than the non-PAD group (54.2 ± 5.8 years), *p*-value=0.0002. Similarly, patients with PAD had higher mean duration of diabetes (13.5 ± 5.1 years) as compared to the non-PAD group (7.9 ± 4.7 years), *p*-value=0.0041.

In our study, 68.3% patients had hypertension in PAD group while 52.5% in non-PAD group. The mean systolic blood pressure was 151 ± 12 mmHg in PAD group while 141 ± 14 mmHg in non-PAD group. The difference in the mean systolic blood pressure between the two groups was statistically significant, *p*-value=0.0015. Similar results have been reported earlier by Solanki *et al* and Agarwal *et al* who reported higher systolic blood pressures in patients with peripheral arterial disease[1,12].

Smoking is considered to be one of the important risk factors for PAD[21,22]. We defined smoking as cigarette smoke >1 cigarette per day. According to our definition, 24.4% patients with smoking had PAD as compared to only 10.2% in the non-PAD group, *p*-value=0.0216. Many studies have established strong association of smoking with PAD[23]. However, our results differed here from Ali *et al* who could not establish a significant relationship between smoking and PAD in their study[13].

We checked glycemic control in our study using fasting and 2-hours post-prandial sugar levels as opposed to HbA1c as the former are more quick and cost-effective. Some investigators have shown fasting blood sugar levels to be more reliable than HbA1c in correlating with ABI[24]. We found normal fasting blood sugar level in 31% of our population which demonstrates the urgent need to create more awareness amongst patients to control this parameter to halt or slow the progression of their disease.

Moreover, higher BMI, hyperlipidemia, family history of diabetes and male gender are all well documented risk factors for PAD which we were not significantly related to PAD in our study population.

With the growing age of the diabetic population of Pakistan, the prevalence of its complications is bound to increase simultaneously. As depicted by this study, a very high prevalence of abnormal ABI warrants urgent interventions to reduce morbidity and mortality associated with PAD. By creating more public awareness about PAD among patients and use of ABI as a reliable tool for assessment of PAD among practitioners, we can impart better quality of life years to diabetic patients. Effective treatment of diabetes, control of hypertension and dyslipidemia, regular exercise, smoking cessation are some of the very effective counter strategies.

Limitations of our study include small sample size. Studies based on more extensive multicenter study populations are needed to establish a definitive opinion on Pakistani population on the topic. It should also be noted that aging causes arteriosclerosis of vessels that raises ABI value despite a decline in ABI due to PAD in diabetes. An ABI ≥1.3 indicates stiff non-compressible or partially non-compressible vessels which may give false negative results of PAD. Our study did not have any provision to address this issue as well.

CONCLUSION

The prevalence of PAD (41.0%) and its risk factors is very high in Pakistani population. Mean age of the patients (p=0.0002), duration of diabetes mellitus (p=0.0041), mean systolic blood pressure (p=0.0015) and smoking status (p=0.0216) were significantly different between patients with PAD and those with normal ABI.

Disclaimer

The abstract or any other findings of this research paper have not earlier been presented or submitted at any forum, conference.

CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

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