

Prediction of Coronary Artery Disease using Ankle Brachial Pressure Index in Patients with Diabetes Mellitus: A Cross-sectional Study

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ABSTRACT

Introduction: Diabetes mellitus confers a tenfold risk of cardiovascular disease due to atherosclerosis. Screening a large number of patients for Coronary Artery Disease (CAD) in susceptible population groups are required. Ankle Brachial Pressure Index (ABPI) is a non invasive tool for identifying atherosclerosis and peripheral artery disease and can be used in large population studies. Hence the present study attempted to assess the applicability of ABPI as a tool for prediction of CAD in diabetic patients.

Aim: To calculate the ABPI in patients of diabetes mellitus and to assess the association of ABPI value with presence of CAD, duration of CAD and with the microvascular complications of diabetes mellitus.

Materials and Methods: This cross-sectional study was conducted at MMIMSR, Mullana, Haryana, India from December 2019 to July 2021. Total 100 patients suffering from type 2 diabetes mellitus for more than five years duration were included. Patients were divided into two groups based on the presence or absence of CAD. ABPI was calculated in each patients and its correlation was assessed with CAD and association with microvascular

complications of diabetes mellitus. The correlation assessed using Pearson correlation test. The mean was compared in with respect to Independent t-test (for two groups).

Results: Out of 100 patients, there were 78 males and 22 females of mean age 60.64 ± 10.97 years. Microvascular complications were present in 35% cases. Past history of CAD was present in 58%, stroke in 9%, hypertension in 15% and chronic kidney disease in 8% cases. Electrocardiogram (ECG) changes suggestive of CAD were observed in 62% while 2D-ECHO showed Regional Wall Motion Abnormality (RWMA) in 57 cases while 18 had angiographic evidence. Mean ABPI was 0.79 and 1.17 in the CAD and non CAD group respectively which was significant (p -value < 0.001). A negative correlation was observed with ABPI and duration of CAD in years with Pearson correlation value of -0.260 (p -value 0.049).

Conclusion: ABPI was also found to be negatively correlated with the duration of CAD and was significantly lower in diabetic patients with microvascular complications of diabetes. ABPI had a sensitivity of 84.5% and specificity of 90.5% in prediction of CAD in patients suffering from diabetes.

Keywords: Atherosclerosis, Hyperglycaemia, Microvascular complications, Peripheral artery disease

INTRODUCTION

Atherosclerotic cardiovascular disease is a leading cause of morbidity and mortality in India accounting for 272 deaths per 100000 population, standardised for age as compared to the global average of 235 with the highest CVD related deaths from Punjab and Tamil Nadu [1]. Diabetes Mellitus is an important modifiable risk factor for CAD as it causes accelerated atherosclerosis [2]. The reported prevalence of diabetes in Punjab and Haryana were found to be higher in rural areas as compared to urban areas with a low prevalence of patients who were having acceptable control of diabetes [2]. Thus, the burden of diabetes and concomitantly CAD is largely unrecognised in rural North India [2]. Hence, the need for a non invasive test for CAD in this group was recognised.

Peripheral artery disease is one of the manifestations of atherosclerosis. ABPI, originally described by Winsor in 1950 is a quick and useful tool for assessing and evaluating the presence of Peripheral Arterial Disease (PAD) of the lower extremities [3]. The usefulness of ABPI in CAD risk prediction was investigated by Chang ST et al., who found ABPI correlated well with coronary angiographic findings [4].

Li J et al., found more CVD related mortality in low ABPI as compared to normal ABPI in diabetic Chinese patients [5]. Espinola-Klein C et al., found that when a lower ABPI cut-off value was used in diabetic patients, more patients at risk of CAD events could be identified [6]. Wu CK et al., observed ABPI < 0.9 and > 1.4 correlate well with microvascular complications such as renal dysfunction and microalbuminuria in diabetic patients [7]. Hakeem F et al.,

could not establish a direct relationship between ABI and CAD on angiography but declared that a log linear relationship between ABPI and CAD risk was present in diabetic patients [8]. Consequently, there is increasing interest in ABPI as a non invasive tool capable of identifying subclinical atherosclerosis.

In patients with diabetes mellitus there is accelerated and more widespread atherosclerosis which confers a high risk of CVD and leads to 50-70% of all deaths in this group [5]. Timely diagnosis and treatment of CAD in patients with Type 2 DM are therefore essential. The ABPI is the ratio of ankle systolic blood pressure and brachial systolic blood pressure and is a non invasive test widely used for confirmation and quantification of peripheral artery disease. Factors that affect the prevalence of peripheral artery disease in diabetes mellitus are age, duration of diabetes, HbA1c level and presence of microvascular complications such as renal disease, dyslipidemia, microalbuminuria etc., [9-13].

In normal individuals ABPI is 1.00-1.40. Ankle brachial index > 1.40 signifies vascular calcification and consequent non compressible arteries. With the development of haemodynamically significant stenosis, the systolic pressure in the leg is decreased and hence the ankle brachial index starts to decrease. Values between 0.91-0.99 are considered borderline while values less than < 0.90 are deemed to be diagnostic of PAD [4].

In India, the diabetes capital of the world, studies by Pednekar S et al., Dsouza NV and Bhat S and Sarangi S et al., concluded that ABPI ≤ 0.9 was a useful predictor of future CVD risk [14-16]. However, inspite of a high prevalence of diabetes and CAD in

Punjab and Haryana, studies on screening tools for the same are sparse from these areas. Therefore, the need to assess non invasive screening tools like ABPI for subclinical CAD was felt.

Hence, the present study was conducted to calculate ABPI in patients of diabetes mellitus, to correlate ABPI values with CAD and microvascular complications of diabetes mellitus and thus assess the applicability of ABPI in prediction of CAD in diabetic patients.

MATERIALS AND METHODS

This cross-sectional study was conducted in Inpatient Department (IPD) and Intensive Care Unit (ICU) of MMIMSR, Mullana Medical College Hospital, Haryana, India, over for period of 18 months between December 2019 to July 2021. Institutional Ethical committee approval (IEC no 1626) was taken prior to conduct the study.

Inclusion criteria: Patients aged >18 years, with Type 2 Diabetes Mellitus according to the World Health Organisation (WHO) criteria 1997 [17], fasting blood glucose >125 mg/dL and postprandial >200 mg/dL and with the duration of diabetes ≥5 years duration were included.

Exclusion criteria: Patients with limb amputations or local injuries, filariasis, ulcers, deep vein thrombosis, gross oedema, critically ill or in shock, active smokers and type 1 diabetes mellitus were excluded.

Sample size: The sample size was calculated to be 250 initially using the formula:

$$(Z)^2pq/l^2 = Z^2 \times 21.4 \times 78.6 / 5^2 = 258.4$$

where, Z=1.96

p=21.4% prevalence of CAD in diabetic patients in India [18].

q=(1-p) and l=absolute error. The confidence interval of 95%

The power of study with this sample size would be 80%.

However, due to the constraints posed on hospital services and type of admissions during COVID-19 pandemic during 2020-2021 the sample size obtained was 100.

Data collection: After taking informed consent, data regarding history, physical examination and investigations were collected for the diagnosis as per Performa. CAD was diagnosed by a history of angina or any past history or any treatment for CAD/ECG changes and 2-D ECHO. Study subjects were divided into two groups. Group A included cases of CAD and group B included cases with no evidence of CAD.

Measurement of ABPI was made after five minutes of rest. Using a pneumatic cuff size 12 placed around the ankle 3 cm above medial malleolus, the pressure was measured at both the dorsalis pedis and posterior tibial arteries using hand-held continuous sine wave Doppler probe (5-10 mhz) (Philips affinity-50G). Pneumatic cuff size 12 cm for arm circumference 32 cm, cuff size 17 cm for arm circumference 32-42 cm and cuff size 20 cm for arm circumference ≥43 cm was used in both arms for measuring brachial artery pressure. ABPI was calculated by dividing the higher systolic blood pressure value of the lower limb with that of the upper limb.

Interpretation of ABPI-for peripheral artery disease diagnosis [19]:

Resting ABPI measurement-severity of peripheral artery disease;

- >1.4 Calcification may be present;
- >1.0-Probably no PAD;
- 0.90-0.99-Equivocal or borderline PAD;
- 0.41-0.90-Mild to Moderate PAD;
- <0.4-Severe PAD;
- <0.3-Critical Limb Ischemia-CLI

The parameters assessed included the duration of diabetes, HbA1c level, co-morbidities like hypertension, baseline biochemical investigations to assess the microvascular complications. Urine microalbuminuria >30 mg/g by dipstick and eGFR<60 mL/minute

for diabetic nephropathy and lipid profile for diabetic dyslipidemia denoted by total cholesterol >250 mg/dL, Low Density Lipoprotein (LDL) >100 mg/dL and High Density Lipoprotein <40 mg/dL and Triglyceride >150 mg/dL after a 12 hour overnight fasting were evaluated [20]. Clinical evidence of diabetic retinopathy and neuropathy was evaluated in form of fundus examination and decreased vibration sense, touch and pain sensation or loss of ankle jerks, respectively.

All data was noted in pretested datasheets. Appropriate statistical analysis was done at the end of the study to compare ABPI values between the two groups and correlated with CAD and other microvascular complications.

STATISTICAL ANALYSIS

Statistical analysis was carried out using IBM Statistical Package for Social Sciences (SPSS) statistical version 20.0. All quantitative variables were estimated using measures of central location. Mean was compared with respect to Independent t-test (for two groups). Pearson's correlation test was used for relationship and using ROC Curve for cut-off value with 95% confidence interval, sensitivity and specificity. All statistical tests were seen at two-tailed level of significance (p-value <0.01 and p-value <0.001).

RESULTS

Out of 100 cases of diabetes, there were 78 males and 22 females with mean age of 60.64±10.97 years and a range of 34-80 years. Majority 32% of patients were in 61-70 year age group. Among them 38% were obese, 38% were overweight with Mean BMI 28.07±4.02. Microvascular complications of diabetes were observed in 35% with 31 having neuropathy, 18 having retinopathy and 15 having nephropathy. Among these 58% had history of CAD while 9% had history of stroke, 41% had history of alcohol consumption, 15% were hypertensive and 8% had CKD [Table/Fig-1].

Patient characteristics		Number	Percent	Total	
Gender	Male	78	78	100	
	Female	22	22		
Age (years)	<40	4	4	100	
	40-50	18	18		
	50-60	26	26		
	>60	32	32		
Body mass index (kg/m ²)	18.5-24.5	24	24	100	
	24.6-29.9	38	38		
	30+	38	38		
Microvascular complications	Absent	Total	35	35	100
	Present	Neuropathy	31	88.6	
		Nephropathy	15	42.9	
		Retinopathy	18	51.4	
History of CAD	Present	58	58	100	
	Absent	42	42		
Duration of CAD (years)	5.78±2.27	-	-	-	
History of stroke	Present	09	09	100	
	Absent	91	91		
History of alcohol consumption	Present	41	41	100	
	Absent	59	59		
Hypertension	Present	15	15	100	
	Absent	85	85		
CKD	Present	08	08	100	

[Table/Fig-1]: Demographic and clinical characteristics of patients.

In 62% ECG had changes suggestive of CAD while 57% had RWMA on 2D-Echo and in 18% who had undergone CAG all had

evidence of CAD in variable severity. Fatty liver was observed in 7% with hepatomegaly in 2%. Lipid profile was deranged in 15% and albuminuria was seen in 12%.

Patients were divided into two groups with group A with 58 patients having CAD and group B with 42 patients not having history of CAD. Mean ABPI in group A having CAD (0.79 ± 0.20) was less than non CAD group (1.17 ± 0.21) and this difference was statistically significant (p -value < 0.001). Association between ABPI and symptoms of CAD was observed which was statistically significant (p -value < 0.001) as also between ABPI and RWMA on 2D-echocardiography in diabetic patients (p -value = 0.004) [Table/Fig-2].

Evidence of CAD		N	ABPI Mean \pm SD	t-value	p-value
History of CAD	Present	58	0.79 ± 0.20	9.168	< 0.001
	Absent	42	1.17 ± 0.21		
Symptoms suggestive of CAD	Present	62	0.798 ± 0.197	10.222	< 0.001
	Absent	38	1.2 ± 0.181		
RWMA on 2D echocardiography	Present	57	0.787 ± 0.193	3.012	0.004
	Absent	5	1.068 ± 0.279		

[Table/Fig-2]: Table showing comparison of ABPI in diabetic patients with CAD and those without CAD.

CAD: Coronary artery disease; RWMA: Regional wall motion abnormality
p-value < 0.05 considered significant

In present study, mean HbA1C value was 8.66 ± 0.04 and mean serum creatinine was 1.23 ± 0.41 , mean values of all the biochemical parameters are shown in [Table/Fig-3]. ABPI was also found to be negatively correlated with duration of CAD with an r -value of -0.260 [Table/Fig-4]. A non significant association of ABPI with alcohol consumption was observed. ABPI was also compared between patients with microvascular complications and those with none and was significantly lower in patients who had diabetic neuropathy, nephropathy and retinopathy as compared with those who had none. ABPI was compared between patients who had hypertension and those who were normotensive and found to be significantly lower in hypertensive patients (p -value = 0.003). A significant difference was observed in subjects with CKD and without CKD [Table/Fig-5].

Parameters	Mean values \pm SD
Serum creatinine (mg/dL)	1.23 ± 0.41
eGFR (mL/min/1.73 bsa)	67 ± 6.87
HbA1c (%)	8.66 ± 0.04
Lipid profile (mg/dL)	
HDL	44.7 ± 0.63
LDL	118.04 ± 6.07
TG	163.45 ± 0.07
TC	196.5 ± 0.09
Microalbuminuria	57 ± 0.86

[Table/Fig-3]: Mean values of biochemical parameters.

		ABPI	Duration of CAD in years
ABPI	r-value	1	-0.260^*
	p-value		0.049
Duration of CAD (years)	r-value	-0.260^*	1
	p-value	0.049	

[Table/Fig-4]: Correlation of mean ABPI with duration of CAD in years.

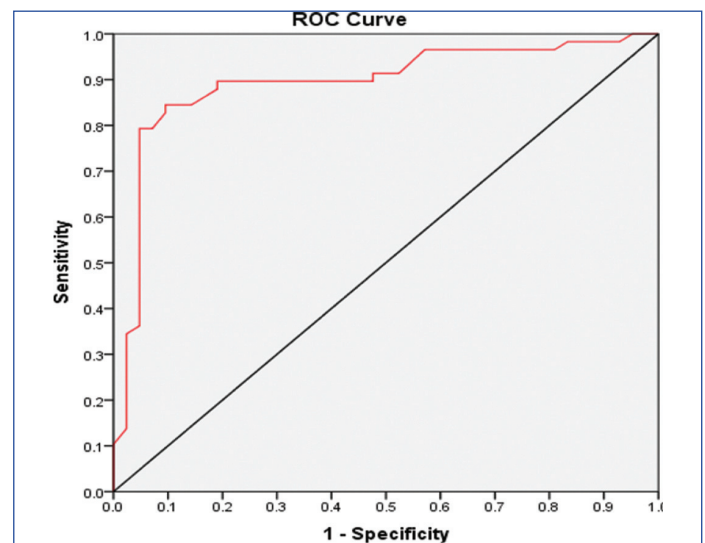
*Correlation is significant at the 0.05 level (2-tailed); Correlation assessed using Pearson correlation test

Variables		N	ABPI	t-value	p-value
Microvascular complications	Neuropathy	31	0.777 ± 0.214	4.589	0.0001
	Nephropathy	15	0.783 ± 0.228	3.290	0.002
	Retinopathy	18	0.808 ± 0.248	3.139	0.002
	None	65	1.026 ± 0.264	Ref	

Dyslipidemia	Yes	15	0.768 ± 0.17	1.69	0.001	
	No	85	1.080 ± 0.70	Ref		
Co-morbidity	Hypertension	Yes	15	0.762 ± 1.66	3.013	0.003
		No	85	0.974 ± 0.286		
	CKD	Yes	08	0.676 ± 0.84	3.083	0.003
		No	92	0.974 ± 0.271		
Stroke	Yes	09	0.840 ± 0.29	0.917	0.093	
	No	91	1.052 ± 0.68			
Personal habits	Alcohol consumption	Yes	41	0.880 ± 0.287	2.185	0.31
	No	59	0.999 ± 0.255			

[Table/Fig-5]: Comparison of mean ABPI with microvascular complications, dyslipidemia, co-morbidities and alcohol consumption in study subjects. p-value < 0.05 considered significant

In all 100 study subjects ABPI was calculated and a cut-off value of 0.970 was calculated. An ROC curve was plotted to calculate the sensitivity and specificity of ABPI in prediction of CAD in diabetic patients. The curve plotting true positivity against false positive rate at different cut-off points occupied close to the upper left corner reflecting a high degree of accuracy in prediction of CAD risk in subject population. Area under curve was calculated to be 0.893 with a standard error of 0.035 and a 95% confidence interval lower bound and upper bound lying between 0.824 and 0.963. As cut-off value is close to 1 ABPI was found to be an accurate predictor of CAD in patients of diabetes mellitus with a sensitivity of 84.5% and specificity of 90.5% in prediction of risk of CAD which was significant (p -value = 0.0001) [Table/Fig-6,7].



[Table/Fig-6]: A ROC curve was plotted after calculating ABPI in all study subjects. It plots the true positivity of ABPI in prediction of CAD in diabetes patients against false positive rate. As the curve lies in the upper left part of the graph reflecting a high accuracy in prediction of CAD in diabetic patients

Area	Std. Error	p-value	95% Confidence interval		Cut-value	Sensitivity	Specificity
			Lower bound	Upper bound			
0.893	0.035	0.0001**	0.824	0.963	0.970	84.5%	90.5%

[Table/Fig-7]: Area under the curve showing sensitivity and specificity of ABPI in prediction of CAD in diabetic patients. p-value < 0.05 considered significant

DISCUSSION

The present study was conducted to assess the usefulness of ABPI as a tool for predicting CAD in diabetic patients. ABPI is a quick and non invasive tool used for assessing and evaluating the presence of PAD of the lower extremities.

This was a hospital-based observational study that included 100 patients with diabetes. ABPI of all study subjects was calculated and correlated with the presence of CAD and microvascular

complications in type 2 diabetes mellitus. The subjects were divided into 2 groups-Group A which had a history of CAD in which there were 58 patients and Group B with no history of CAD in which there were 42 patients. No significant differences were found between the two groups when age was taken into consideration (p -value >0.05). This was similar to the findings of Yerra S et al., and Reda AA et al., [21,22]; but Chang ST et al., reported that ABPI <0.9 was observed in younger diabetic patients than those with ABPI >0.9 [4].

In the present study, Group A (CAD) there were 44 (75.9%) males and 14 (24.1%) females while in Group B (non CAD) there were 34 (81.0%) males and 8 (19.0%) females. No significant difference was found between the two groups in terms of gender, similar to the findings of Yerra S et al., and Reda AA et al., [21,22].

ABPI was found to be negatively correlated with the duration of CAD with Pearson correlation value -0.260 which was significant with (p -value= 0.049). No studies were found to have analysed ABPI with duration of CAD. In Group A (CAD), 86.2% were obese or overweight and normal BMI was seen in 13.8%. In Group-B (non CAD) 61% were obese or overweight while normal BMI was seen in 38.1%. BMI was significantly more in CAD group.

The mean value of HbA1c in Group A (CAD) was 9.21 and was 7.77 in Group B (non CAD). Mean HbA1c levels were significantly higher in cases with history of CAD. Higher HbA1c was also associated with lower values of ABPI (ABPI <0.9) and this relation was statistically significant (p -value= 0.039). It was consistent with that of Liu H et al., who reported that HbA1c was independently associated with lower ABI [23].

Symptoms of CAD like angina and exertional dyspnoea were present in 62 cases and no symptoms of CAD were seen in 38 cases. Mean ABPI was 0.798 in cases with symptoms of CAD and it was 1.2 in cases with no symptoms of CAD which was statistically significant. In the Framingham offspring study by Murabito JM et al., CAD prevalence was 30% in patients with ABPI <0.9 compared with 10% with ABPI >1.0 with a significant p -value [24]. The study by Xu L et al., demonstrated that the risk of CAD doubled with ABPI <0.9 in patients with type 2 diabetes [25]. The American Heart Association Prevention Conference V described the ABPI as a strong and independent risk factor for cardiovascular mortality and recommended it to be used to detect subclinical disease in the prevention of cardiovascular mortality and stroke.

Out of 100 subjects in the present study, 35 diabetics had microvascular complications like diabetic neuropathy (31), nephropathy (15) and retinopathy (18). Mean ABPI was found to be 0.777 in those with diabetic neuropathy (p -value= 0.0001), 0.783 in cases with diabetic nephropathy (p -value= 0.002) and 0.808 in cases with diabetic retinopathy (p -value= 0.002) while in cases with no microvascular complications mean ABPI was 1.026. Thus mean ABPI was significantly lower in cases with microvascular complications as compared to cases with none. Potier L et al., also reported a significant association between diabetic neuropathy and retinopathy with lower values of ABPI [26]. Abouhamda A et al., also reported lower ABPI <0.9 to be associated with diabetic nephropathy and neuropathy [27].

A 2D-ECHO was done in 62 cases and showed RWMA in 57 cases which had a mean ABPI of 0.787 and no evidence CAD was seen in 5 cases which had a mean ABPI of 1.068. The difference between mean ABPI in these two was significant (p -value= 0.004). Many studies were not found that showed relationship between ABPI and RWMA/LV dysfunction on 2D-ECHO but Ward [28] found that LVEF is less than 55% among patients with low ABI is more common than normal ABI. Santo Signorelli S et al., reported LVEF $<50\%$ had higher prevalence with ABI ≤ 0.9 while Thatipelli MR et al., found no relation between ABPI and positive stress echocardiography [29,30].

History of alcohol intake was seen in 41 cases and was absent in 59 cases. Mean ABPI was 0.88 in cases with history of alcohol and 0.99 in cases with no history of alcohol which was statistically significant. Xie X et al., also reported a significant association between ABPI and alcohol consumption in men [31]. Yang S et al., reported a significant association between alcohol consumption and lower extremity arterial disease (ABPI <0.9) and opined that patients with T2DM should be advised to stop drinking, to prevent the onset of LEAD [32].

In the present study, hypertension was seen in 15 cases with mean ABPI 0.76 while 85 subjects who were normotensive had mean ABPI of 0.984. Chronic kidney disease was seen in eight cases with mean ABPI 0.676. In 98 subjects with no CKD mean ABPI was 0.974. Mean ABPI was significantly lower in diabetics with CKD and hypertension (p -value= 0.003). Ontenddu S et al., and Wu CK et al., also demonstrated that PAD (defined as an ABPI <0.9) is significantly associated with CKD [7,33]. Chen FA et al., showed that patients with stage 3-5 CKD who have a lower ABI have a rapid decline in renal function and a high incidence of cardiovascular events and Chen FA et al., indicate that ABPI <1.0 and ≥ 1.4 are significantly associated with future clinical PAD among CKD patients [34]. Korhonen PE et al., found that almost one third of the hypertensive patients had asymptomatic PAD or borderline PAD (ABPI <0.9) [35].

Limitation(s)

The study was limited by a small sample size which was due to unavoidable circumstances of COVID-19 pandemic. Also, all patients could not be screened for CAD by coronary angiography due to affordability issues.

CONCLUSION(S)

Mean ABPI was significantly lower in diabetic patients with microvascular complications of diabetes, co-morbidities like hypertension, obesity and CKD and those with symptoms, ECG or echocardiographic evidence of CAD. There was a negative correlation between ABPI and duration of CAD. Thus, ABPI a cost-effective and non invasive investigation that can predict the presence of CAD in type 2 diabetes mellitus. In developing countries where economic constraints preclude other invasive and costly modalities of screening for asymptomatic patients. The potential benefit of early detection of the asymptomatic disease and its treatment has not been established and needs to be studied in large populations but holds promise in countries with a large burdens of diseases.

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