Angiographic Assessment of Coronary Artery Disease and its Correlation with Ankle-brachial Index in Patients with Diabetes Mellitus

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Abstract

Background: Coronary artery disease (CAD) due to atherosclerosis is like an epidemic in India. The role of diabetes mellitus (DM) with CAD is believed to be as important as CAD itself. Owing to the similar vascular involvement, patients with DM were frequently combined with peripheral artery disease (PAD). Although in outpatients, clinically suspected of having CAD, the relationship and interaction between DM and PAD remain unknown.

Aim and objective: The aim and objective of this study is to evaluate the relation of the ankle-brachial index (ABI) with the angiographic characteristics of CAD in patients with DM.

Materials and methods: This is a tertiary hospital study in which 50 adult patients were admitted and taken according to inclusion and exclusion criteria for the study. All patients in this study population underwent ABI measurement and coronary angiography was done. Patients were subdivided into two groups according to ABI, that is, patients with ABI >0.90 and ABI <0.90.

Results: There was a significant relationship between low ABI and severity of CAD. Low ABI group patients had a more severe form of CAD with a higher prevalence of triple vessel diseases, severe stenosis, and more involvement of the left anterior descending (LAD)artery. Risk factors like hypertension, diabetes mellitus, and low ABI were predictors of significant severe stenosis of coronary arteries.

Conclusion: Low ABI is a surrogate index of the severity of CAD. So it could be used in our everyday clinical cardiology practice as a noninvasive, easy, and cheap bedside test to assess and predict the severity of CAD.

Keywords: Ankle-brachial index, Atherosclerosis, Coronary Angiography, Coronary artery disease, Diabetes Mellitus, Peripheral Artery Disease.

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Introduction

Diabetes mellitus (DM) is a metabolic disorder of carbohydrate metabolism characterized by decreased ability of the body to synthesize or respond to insulin and thereby maintain proper levels of glucose in the blood.[1] Diabetes is a major cause of morbidity and mortality mostly related to the diseases that develop as a consequence of chronic diabetes mellitus.[2] These include diseases of large blood vessels (macrovascular disease, including coronary artery disease and peripheral artery disease), small blood vessels (microvascular disease, including retinal and renal vascular disease), and diseases of the nerves.[3]

One of the main macrovascular changes associated with diabetes include aggravated atherosclerosis and several vascular beds carry this atherosclerotic burden, that is., abdominal aorta, coronary arteries, carotid arteries, and popliteal arteries.[4,5] Estimation of arterial atherosclerotic burden is being investigated as a surrogate marker for evaluation of the risk of coronary artery disease (CAD) and also as a screening tool.[6] Atherosclerosis is a diffuse process, the central mechanism in peripheral arterial disease (PAD) and CAD being accelerated atherosclerosis is caused by endothelial dysfunction and dyslipidemia. PAD is associated with an increase in the incidence of multivessel and severe CAD and is a risk factor for major adverse cardiovascular events.[7]

Over two-thirds of the patients with evidence of PAD are asymptomatic and not diagnosed as having a systemic cardiovascular disease, resulting in inadequate treatment of the risk factors involved in the pathogenesis. The cardiovascular

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disease burden associated with PAD is the same, whether it is the asymptomatic or symptomatic form.[8] This, therefore, justifies the need to identify asymptomatic patients to intervene early and reduce the risk of cardiovascular-related mortality. Several studies have elucidated that subclinical atherosclerosis is associated with an increased risk of subsequent cardiovascular events, but there is currently no universally accepted method for detecting early atheroma in the general population.

Despite the importance of early detection, the diagnosis of PAD is usually overlooked in routine history and examination. PAD can be

reliably diagnosed using the ankle-brachial index (ABI). The ABI is an easy, noninvasive, and cheap method used in the diagnosis of PAD and can identify individuals at risk for cardiovascular disease in other arteries of the body, especially the coronary and carotid arteries.

Coronary angiography (CAG), the gold standard for the diagnosis and characterization of CAD, offers therapeutic options and determines prognosis. Heterogeneity of the composition, distribution, and location of atherosclerotic plaque within the coronary arteries also helps predict procedural outcome and complications after PCI.

The ABI, calculated by dividing the highest systolic blood pressure of each lower limb artery by the highest systolic blood pressure of the upper limbs, is a simple, easy, and noninvasive tool with high specificity and sensitivity for the diagnosis of PAD.[9] Many studies have also reported its positive predictive value in CAD in patients suspected of having ischemic heart disease. Previous investigations revealed an inverse relationship between ABI and the severity of cardiovascular and cerebrovascular diseases and their risk factors.

An ABI <0.9 has 90% sensitivity and 98% specificity in detecting ≥50% stenosis in LL arteries and is considered as a worsening factor for cardiovascular risk, associated with an increased risk of myocardial infarction and cardiovascular accident. The primary objective of this study was to assess whether patients with an ABI <0.9 have more severe CAD detected on coronary angiography compared to patients with a normal ABI. The secondary objectives were to describe and compare the clinical characteristics of patients with normal and abnormal ABI and verify whether ABI is an independent predictor of CAD.

MATERIALS AND METHODS

Source of Data

This study was conducted in the Department of Medicine, Sri Guru Ram Das Institute of Medical Sciences and Research, Vallah, Amritsar, in close collaboration with the Department of Cardiology of the institution.

Study Design

This was a cross-sectional observational study performed in type 2 diabetes mellitus patients including both males and females. The study involved 50 patients who were presented to us with anginal chest pain and who had enzymatic and/or electrocardiographic changes compatible with the diagnosis of acute coronary syndrome (ACS) and were admitted to the EW/ICU/CCU.

Exclusion Criteria

- Lower limb surgery,
- Deep vein thrombosis,
- Limb deformities,
- Personal antecedent of revascularization to treat PAD,
- Known cases of chronic kidney disease were excluded.

Inclusion Criteria

1. Adult type-2 diabetic patients were diagnosed by the latest American Diabetes Association (ADA) criteria. According to American Diabetes Association Criteria (2016) patients were considered having diabetes mellitus if:
   - Fasting plasma glucose (FPG) >126 mg/dL (7.0 mmol/L), or
   - 2-h plasma glucose ≥200 mg/dL (11.1 mmol/L) during an oral glucose tolerance test (OGTT) (75 g anhydrous glucose dissolved in water), or
   - HbA1C ≥6.5% (48 mmol/mol), or

- In a patient with classic symptoms of hyperglycemia, a random plasma glucose ≥200 mg/dL (11.1 mmol/L).
2. Detailed history, clinical examination, anthropometric measurements, and biochemical indices were assessed for all the selected patients.

Measurements

The ABI was measured using a portable vascular Doppler scanning. All measurements were performed with the patient in a supine position after a 10-min rest. The systolic pressures of the posterior tibial and/or dorsalis pedis arteries were measured. The highest of these pressures was divided by the highest systolic pressure found in the brachial artery of the upper limbs to obtain the ABI.

Coronary Angiography

Coronary angiography was performed by the Judkins technique and coronary angiograms were visually analyzed by an experienced cardiologist. The degree of luminal narrowing was given in percentage from the prestenotic diameter. Artery is considered to be normal (0%), mild stenosis <50%, moderate stenosis 51–70%, and significant critical stenosis >70%.

OBSERVATIONS AND RESULTS

Among the 50 subjects enrolled, 30 were males and 20 were females. The mean age of the study sample was 58.50 ± 8.97 years; 61.20 ± 8.23 years in females and 56.70 ± 9.13 years in males. The average duration of diabetes was 9.9 ± 6.32 years and the mean HbA1c was 9.39 ± 1.87%. The study group had disease duration and deranged control of blood sugar sufficient to predict considerable atherogenesis. Demographics, characteristics, and frequency distribution of the study population have been described in Table 1.

A total of 35 patients (70%) of the studied population had ABI <0.9 (ABI+). The prevalence of ABI+ among men and women was 46 and 24%, respectively. Abnormal angiographic results were seen in 100% (35 persons) of the ABI+ group and 86.67% (13 persons of the ABI− group). The prevalence of atherosclerotic risk factors in ABI+ and ABI− patients are presented in Table 2. Poor glycemic control and hypertension were the most significant risk factors associated with CAD with a prevalence of around 78 and 64% among the study population. Peripheral artery disease as evidenced by the history of intermittent claudication was present in only 34% of patients while 70% of studied patients had ABI <0.9.

On angiography, there was a higher prevalence of double vessel and triple vessel disease among the study population, that is, 32 and

Table 1: Demographic profile of the patients admitted for study

Characteristics	N (%)
Male sex	30 (60)
Age in years (mean ± SD)	58.50 ± 8.97 years
Smokers	9 (18.0)
Nonsmokers	41 (82.0)
Alcoholics	19 (38)
Dyslipidemia	27 (54)
Systemic arterial hypertension	32 (64)
Family history of coronary artery disease	7 (14)
Obesity (BMI > 25 kg/m^2)	12 (24)
H/O Claudication	17 (34)

Table 2: Correlation of various risk factors and ABI

Variables	Ankle-brachial index (Abnormal <0.9)	Ankle-brachial index (Normal >0.9)	p-value
Hypertension	27	5	0.095
Smoking	8	1	0.172
Dyslipidemia	16	11	0.073
Family history of CAD	6	1	0.929
Alcohol	16	3	0.086
BMI >25	9	3	0.665
HbA1c (>8.0)	28	11	0.713

Table 3: Correlation between number of coronary vessels affected and ankle-brachial index

	Variables	ABI <0.9	ABI >0.9	Total
CAG	DVD	13	3	16
		26.0%	6.0%	32.0%
	Noncritical CAD	0	2	2
		0%	4.0%	4.0%
	SVD	5	10	15
		10.0%	20.0%	30.0%
	TVD	17	0	17
		34.0%	.0%	34.0%
Total		35	15	50
		70.0%	30.0%	100.0%
p-value		0.001 (sig.)		

ABI, ankle-brachial index; CAG, coronary angiography; DVD, double vessel disease; SVD, single vessel disease; TVD, triple vessel disease

Table 4: Correlation of vessel involved with ABI

Coronary artery	ABI <0.9	ABI >0.9
Left main coronary artery (LMCA)	1	1
Left anterior descending (LAD)	35	8
First diagonal (D1)	2	1
Left circumflex artery (LCX)	19	3
First obtuse marginal (OM1)	1	1
Second obtuse marginal (OM2)	1	1
Right coronary artery (RCA)	21	5
Posterior descending artery (PDA)	1	0
p-value	0.001 (sig.)	

34%, respectively as shown in Table 3. Among the vessels involved, the left anterior descending artery was involved more than the right coronary artery and left circumflex artery as shown in Tables 4. There was a higher prevalence of lesions in the proximal segments and the degree of stenosis was severe in our study population.

Lower ABI <0.9 was found to have a significant correlation with the number of vessels involved with a p-value of 0.001 as shown in Table 3. ABI <0.9 was also related to vessel involved and a higher degree of stenosis (>70% stenosis) as shown in Tables 4 and 5.

Table 5: Correlation between severity of coronary artery lesions and ankle-brachial index

	Variables	ABI <0.9	ABI >0.9	Total
Degree of lesion	No lesion	0	2	2
		0%	1.6%	1.6%
	Mild <50% stenosis	6	3	9
		4.8%	2.4%	7.2%
	Moderate 50–70% stenosis	13	5	18
		10.4%	4%	14.4%
	Severe >70% stenosis	84	12	96
		67.2%	9.6%	76.8%
Total		103	22	125
		82.4%	17.6%	100.0%
p-value		0.001 (sig.)		

Discussion

The atherosclerotic disease is multifactorial. Peripheral artery disease, an expression of peripheral atherosclerotic disease, is a more severe form, defined as a worsening factor in the cardiovascular risk stratification of patients at intermediate risk.

The age of all patients included in our study varied between 40 years and 80 years. The most common age group studied was between 50 years and 70 years with a mean age of 58.50 ± 8.97 years. Among all the patients, 60% of patients were male and 40% of patients were female. The mean age in male patients was 61.20 ± 8.23 years and in female patients was 56.70 ± 9.13 years. Similar trends were observed in a study done by Oliveira et al. who included registry data of 163 patients in which there were 101 men (62%) and 62 women (38%) with a mean age of 62.5 ± 9.71 years.[9]

Out of 50 patients, 32 patients (64%) were hypertensive while the rest 18 patients (36%) were normotensive. In a similar study by Lin et al., a total of 1234 patients were studied, in which 315 patients (64%) had both DM and hypertension.[10] Combination of HTN and diabetes is associated with increased severity of coronary artery disease.

Cigarette smoking is a major risk factor for coronary heart disease, stroke, and peripheral vascular disease. In the present study, out of 50 patients, 9 patients (18%) were smokers while 41 patients (82%) were nonsmokers. As the study was done mainly in a Sikh predominant population, therefore the numbers of smokers were less. Smoking was nonexistent in women as all of 20 female (100%) diabetics were nonsmokers due to cultural and religious beliefs. In a similar study by Calton et al., 9 patients (12%) out of 75 were found to be smokers.[11] Pajunen et al. found 30 patients (54.55%) to be ex-smokers and 8 patients (14.55%) to be current smokers.[12]

Obesity was defined by BMI >25 kg/m^2 according to South Asian guidelines. Out of 50 patients, 12 patients (24%) were obese (BMI >25 kg/m^2) and 14 patients (28%) were normal having BMI between 18.5 kg/m^2 and 22.9 kg/m^2 and 24 patients (48%) were overweight having BMI between 23 kg/m^2 and 24.9 kg/m^2. In a similar study, on 470 patients, they observed that among diabetic patients, 70 (76%) patients were normal/overweight and obesity was found in 22 (24%) of patients. They also found that despite the increased risk of developing CAD, in recent years an "obesity paradox" has been described in which moderately obese individuals being referred for coronary angiography have a paradoxically lower CAD burden compared to their nonobese comparators.

In our study, HbA1c levels >8% were considered as poor glycemic control. Out of 50 patients, 39 patients (78%) had poor glycemic control. Rest 11patients (22%) had good glycemic control. The majority of patients had HbA1c >9% with a mean HbA1c level of 9.39 ± 1.87%. Saleem et al. conducted a study on 703 diabetics who underwent coronary angiography and stenting. Among them, 291 (41.4%) diabetics had good glycemic control and 412 (58.6%) diabetics had poor glycemic control. The adjusted risk of major adverse cardiovascular events (MACE) in diabetic patients with poor glycemic control was 2.1 times the risk in nondiabetics.[13] Similar result was seen in a study also.

In our study, 28 patients (56%) had hypertriglyceridemia and 22 patients (44%) had normal triglyceride levels with a mean of 194.36 ± 61.64 mg/dL. The mean HDL level was 38.06 ± 12.48 and 37.00 ± 11.13 mg/dL in male and female diabetics, respectively. In a similar study by Bittencourt et al., they observed that lower HDL (39.2 + 13.2 vs 44.4 + 15.9 mg/dL, $p = 0.003$), and higher triglycerides (140 [106–204] vs 121 [78.5–184.25] mg/dL, $p = 0.002$) were associated with a progressively higher number of significant coronary lesions and multivessel involvement.[14]

Diabetics have an increased predisposition to develop multivessel and multisession disease. In our study, 2 patients (4%) had noncritical CAD, 15 patients (30%) had single vessel disease (SVD), 16 patients (32%) had double vessel disease (DVD), and 17 patients (34%) had triple vessel disease (TVD). A maximum number of patients (34%) in our study had TVD. Thus, the prevalence of TVD was more common in our study. In a study by Calton et al., among 75 patients, 12 patients (16%) had SVD, 20 patients (26.6%) had DVD, and 43patients (57.3%) had TVD.[11] Similar studies by Hamby et al. found TVD to be significantly common in diabetic patients than in nondiabetics.[15]

There was a high prevalence of undiagnosed PAD in the population, the majority of patients were asymptomatic. Although a history of intermittent claudication was present in 34% of patients, 70% of patients were found to have ABI <0.9 suggestive of PAD.

The association between smoking and the risk of PAD has been established in the literature. In our study, there was a higher prevalence of smoking in those with PAD (16 vs 2%) than in those without PAD. However, the overall prevalence of smoking was low (18%) in our study. The majority of our study group belonged to the Sikh population and there was a low prevalence of smoking in them, the association of smoking and PAD (ABI <0.9) was not significant statistically ($p = 0.172$; >0.05).

In our study, the majority of patients were using oral antidiabetics (OAD) and had poorly controlled diabetes. The mean HbA1c was 9.39 ± 1.87%. Using a cut-off level of >8% for poor control, 22% had poor glycemic control in the non-PAD (ABI >0.9) group compared to 56% in the PAD group (ABI <0.9). The correlation of poor control of diabetes with ABI was found to be nonsignificant with a p-value of 0.743. Although studies by Walter et al. and Janka et al. found inferior glycemic control to be a predictor of PAD.[16,17]

Studies have shown that patients with an ABI <0.9 had a higher prevalence of multi-vessel CAD than those with a normal index. In our study, TVD was present in 17 (34%) patients having ABI <0.9. The correlation between the number of coronary vessels affected and ankle-brachial index (ABI <0.9) was found to be highly significant with a p-value of 0.001. Data from the Framingham Offspring Study (3,113 patients) revealed that the prevalence of CAD in patients with an ABI <0.9 was three times higher than that in patients with a normal index (30 vs 10%, p <0.01).[9]

Out of 50 patients enrolled in our study, the maximum number of patients, that is, 43 (86%) had left anterior descending artery involvement, followed by 26 patients (52%) who had right coronary artery involvement, 22 patients (44%) had left circumflex artery involvement, 2 patients (4%) had left main coronary artery disease. First obtuse marginal, second obtuse marginal, first diagonal, and posterior descending artery involvement were found in 2 (4%), 2 (4%), 3 (6%), and 1 (2%) patients, respectively. In a similar study, found that 315 patients (84%) had LAD lesions, 249 patients (66.4%) had RCA lesions, 197 patients (52.5%) had LCX lesions, and 35 patients (9.3%) had LMCA lesion.

Among patients with ABI <0.9, the number of lesions with mild stenosis <50% was 6 (4.8%), with moderate stenosis 50–70% was 13 (10.4%), and with severe stenosis >70% in 84 (67.2%), whereas in patients with ABI >0.9, the number of lesions with mild stenosis <50% was 3 (2.4%), with moderate stenosis 50–70% was 5 (4%), and with severe stenosis >70% in 12 (9.6%). The correlation of degree of the lesion and ankle-brachial index (ABI <0.9) was found to be highly significant ($p = 0.001$; <0.05). In a study in Iraq, it was observed that low ABI patients had the presence of multiple coronary lesions in multiple vessels; p-value 0.0001. They also showed that in low ABI index patients coronary lesions tend to be in a severe category according to angiographic interpretation standards. Similar results were seen by Oliveira et al. in their study.

In our study; among patients with ABI <0.9, 50 lesions (44.42%) of 113 lesions were in the proximal segment, 45 lesions (39.82%) were in the mid segment, 13 lesions (11.50%) were in the distal segment, and 5 were diffuse, thus proximal segment was most commonly involved followed by mid and distal segments. Chang et al. in his study reported a greater proportion of lesions at the ostial level and in proximal segments in patients with an ABI of <0.9 than in those with an ABI of ≥0.9.[18] Similar results were observed by Papamichael et al. in another study.[19]

The sensitivity and specificity of ABI to diagnose CAD in diabetics were found to be 72.92% (95% CI: 58.5–84.72) and 100% (95% CI: 15.81–100) in our study. Therefore, ABI was found to be more specific for CAD. Otah et al. demonstrated that three vessel arterial disease or left main coronary artery disease can be predicted by the ABI, with sensitivity and specificity of 85 and 77%, respectively.[20] Hatmi et al. in their study concluded that a low ABI has almost perfect specificity (99.7%) and a positive predictive value of 95.8% but low sensitivity (64%).[21]

In conclusion, the findings of this research have indicated that ABI could be a useful method in assessing both the atherosclerotic risk factors and the degree of coronary involvement in suspected patients. However, making more accurate decisions for using this method in diagnosing and preventing CAD needs further studies with large sample sizes of the general population. It is recommended to evaluate the relationship between different levels of ABI, especially ABI >1.4, which was not included in our study. To conclude we can use ABI as a useful tool for out-patient determination of the risk of CAD, the severity of atherosclerosis in patients with diabetes mellitus in a noninvasive, easy, and cost-effective manner.

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