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Original Article

Coronary Artery Disease in Patients with Type 2 Diabetes Mellitus: Correlating Ankle Brachial Pressure Index with Coronary Angiography

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ABSTRACT

Diabetes mellitus (DM) affects over 366 million people worldwide ; this figure is expected to rise to 522 million by the year 2030. The macrovascular complications of diabetes cause morbidity and mortality. Ankle brachial pressure index (ABPI) is a simple non-invasive tool which may indicate atherosclerotic changes in the blood vessels. It is useful in diagnosis of peripheral artery disease (PAD), and is also an indicator of increased cardiovascular morbidity and mortality. Previous studies have reported a correlation between ABPI and coronary artery disease (CAD). Despite the well-established association between diabetes and coronary artery disease, the role of ABPI in predicting the presence and severity of CAD in diabetics has not been proven. The study was done to find whether there was an association between ABPI and coronary angiogram in diabetics. **Materials and Methods:** This was a cross sectional study that included 100 patients of Diabetes Mellitus who had undergone a coronary angiogram during the current admission. All coronary angiograms were evaluated by a cardiologist. The ABPI was measured according to the standardized protocol before the patients underwent the coronary angiogram procedure. **Results:** Out of the patients, 4 patients (4.3%) had ABPI < 0.9 out of which 2 (50%) had double vessel disease and 2 (50%) had triple vessel disease. **Conclusion:** Though all patients with abnormal ABPI had CAD as assessed by CAG, not all patients with abnormal CAG had abnormal ABPI. Thus the utility of ABPI as a surrogate marker in screening of CAD is limited.

Key words: Ankle brachial pressure index, Coronary angiography, Diabetes mellitus.

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INTRODUCTION

Diabetes Mellitus [DM] affects over 422 million people worldwide in 2014; this figure is expected to rise further,[1] contributory factors being population growth , obesity and ageing of populations . The prevalence of DM in India is rising and predominantly affects the younger, economically productive age group. At present India has an estimated 62.4 million patients with diabetes.[2]

The complications of diabetes cause morbidity, mortality and disability; this is especially true for the macrovascular complications: coronary artery disease [CAD], cerebrovascular disease and peripheral vascular disease.[3] Macrovascular disease affects the entire arterial tree, therefore all the complications often occur simultaneously.

The number of persons afflicted attests to the impact of CAD on global health. CAD is the single most common cause of death in men and women.[4] The economic burden of CAD is tremendous because it affects young, economically productive members. It is expected that the prevalence of CAD will only increase in the next decade. The WHO estimates that by the year 2020 the global number of deaths from CAD will have risen from 7.1 million in 2002 to 11.1 million.[5] Various studies in India have revealed a CAD prevalence of approximately 11 % in the urban and 7% in the rural population across India.[6]

CAD is most commonly due to obstruction of the coronary arteries by an atheromatous plaque. The risk factors for atherothrombotic CAD are smoking, hypertension, DM, dyslipidemia and obesity. The diagnostic investigation for obstructing coronary lesions is the coronary angiogram.[7]

The coronary angiogram is an expensive, invasive test that requires the expertise of skilled and trained personnel. In India, the epidemic of DM and CAD far outweighs the number of trained personnel and centres equipped to do the coronary angiogram. Hence, to screen for CAD a non-invasive, inexpensive investigation that can be done at the secondary level hospital is the need of the hour.

Peripheral arterial disease [PAD] is a clinical manifestation of the atherosclerotic process. It is associated with greater cardiovascular risk and more rapid disease progression.[8] Diabetes markedly increases the risk of atherosclerosis and PAD.[9] Patients with PAD are at higher risk of CAD.[10] PAD, like CAD is asymptomatic in the majority of the patients and identifying patients with asymptomatic PAD and thus CAD is important.

Ankle brachial pressure index [ABPI] is a simple, non-invasive, reproducible, quantitative measurement, which has a high sensitivity and specificity for the detection of PAD. It may also be an indicator of atherosclerotic disease in other vascular areas and of increased cardiovascular morbidity and mortality.[11] Data indicates that ABPI can be used as an indicator of future CAD.[12] However, despite the well-established association between diabetes and CAD, the role of ABPI in predicting the presence and severity of CAD in patients with diabetes has not been proven.

Our study aimed at finding whether ABPI in patients with Diabetes correlated with the presence and severity of CAD as assessed by Coronary Angiogram [CAG].

OBJECTIVES

1. To find if an association exists between ABPI and coronary angiogram results in patients with diabetes.
2. To correlate the degree of abnormality of ABPI with the extent of abnormality of coronary angiogram.

MATERIALS AND METHODS

A total of 100 patients with diabetes mellitus who were admitted to a medical college hospital and who had undergone coronary angiogram were included in the study.

Patients were considered diabetics if they were already diagnosed as having diabetes and were on insulin or oral antidiabetic drugs or if FPG was more than 126 mg/dl after 8 hours of fasting or HbA1C level more than 6.5 %. Each patient gave a written informed consent to participate in the study and the Institutions Ethics Review Board approved the study protocol.

Medical history was elicited and a directed physical examination was done.

The patients were subjected to the following investigations: Fasting plasma glucose [FPG], Post prandial plasma glucose [PPPG], Glycosylated hemoglobin [HbA1C], Serum creatinine, Haemoglobin [Hb], Lipid profile and Electrocardiogram.

All coronary angiograms were evaluated by an experienced cardiologist. Patients were then divided into 3 groups based on the number of coronary vessels with significant stenosis. i.e. more than 50 % block.

- Single vessel disease: only 1 vessel with more than 50% stenosis
- Double vessel disease: 2 vessels with more than 50% stenosis
- Triple vessel disease: all 3 vessels with more than 50% stenosis

Results were noted and classified according to the American Heart Association/American College of Cardiology classification into type A, type B and type C lesions.

The ABPI was measured according to the standardized protocol before the patients underwent the coronary angiogram. The patient would rest for a period of 5 minutes in supine position. Smoking and strenuous exercise prior to procedure were avoided. A sphygmomanometer cuff and a handheld Doppler [8 MHz Lifedop] were used to perform the measurement [Figure 1].

The posterior tibial artery was located using the Doppler wand and the cuff was placed just above the ankle and inflated 20 mm Hg above the last audible pulse and then deflated slowly until there was reappearance of the flow signal. The cuff pressure at reappearance of signal was the systolic blood pressure in the posterior tibial artery. Then the cuff was placed above the cubital fossa and the brachial artery systolic blood pressure was measured [Figure 2].

The higher of the two ankle pressures was divided by the higher brachial pressure to obtain the ABPI.

$$\text{ABPI} = \frac{\text{Highest ankle pressure [posterior tibial artery]}}{\text{Highest brachial pressure [brachial artery]}}$$

ABPI < 0.9 was considered abnormal and ABPI between 0.9 to 1.3 was normal [34]. ABPI > 1.3 was described as poorly compressible vessels and not included in the study.

Statistical analysis

Data was recorded and analyzed using SPSS software version number 20. Results on continuous measurements were presented on mean ± standard deviation [SD] and results on categorical measurements were presented in number [%] and analyzed using student *t*-test, Chi-square test,and one-way ANOVA test. Significance was assessed at 5 % level of significance.

RESULTS

Of the 100 patients, 39 [39%] were female and 61 [61%] were male. The majority of the patients fell between the ages of 51 to 70 years with a mean age of 60.76 ± 9.66 years. (Table 1) Only 93 patients were included in the analyses as in the remaining 7 patients, the ABPI was > 1.3. The mean ABPI of male and female patients were 1.11 and 1.05 respectively.

Nonsmokers [43%] and reformed smokers [18%] had a mean ABPI of 1.06 and 1.13 respectively. (Table 2)

The patients with normal CAG had a mean ABPI of 1.13 and with triple vessel disease had a mean ABPI of 1.06. Coronary angiogram reports revealed 25% had normal coronaries, 27 % had single vessel disease, 16 % double vessel and 32 % triple vessel disease. (Figure 3)

We tested the hypothesis that abnormal ABPI could predict the presence of coronary artery disease as assessed by coronary angiogarm. Out of the 93 patients, 4 patients [4.3%] had ABPI < 0.9 . Of these 2 [50%] had

Figure 1: Handheld Doppler [8 MHz Lifedop].

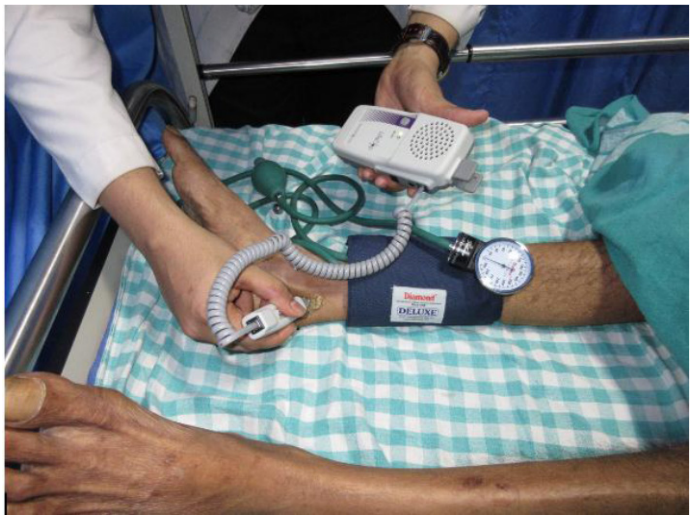

Figure 2: Method of Measurement of ankle and brachial pressures.

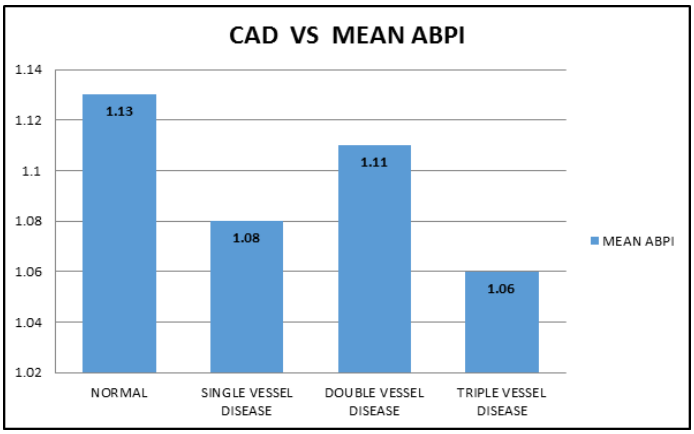

Figure 3: Vessels affected Vs mean ABPI.

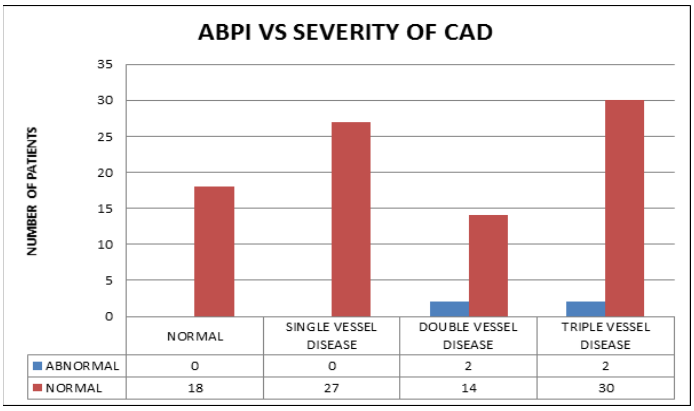

Figure 4: ABPI Vs severity of CAD.

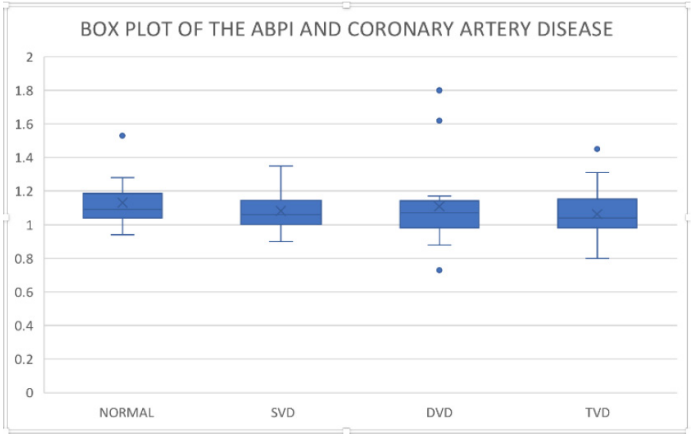

Figure 5: Boxplot illustrating ABPI Vs Vessels Affected.

double vessel disease and 2 [50%] had triple vessel disease. (p= 0.113) (Figure 4.) (Figure 5)

Out of the 75 patients who had abnormal CAG, the left anterior descending [LAD] vessel was most commonly involved followed by right coronary artery [RCA] and left circumflex artery [LCX].

DISCUSSION

This cross-sectional study aimed to correlate ABPI, a marker of PAD, with the severity of CAD as assessed by coronary angiogram.

Table 1: Clinical characteristics of subjects.

	Mean	Std. Deviation
AGE	60.76	9.661
BODY MASS INDEX	24.131	4.071
HB	13.011	1.711
FBS	160.66	67.001
PPBS	214.85	80.677
HbA1C	8.395	1.911
CREATININE	2.411	13.311
TOTAL CHOLESTEROL	172.16	58.681
TOTAL TRIGLYCERIDES	141.37	69.489
HDL	38.22	10.979
LDL	115.95	51.925
ANKLE SYSTOLIC PRESSURE	160.42	33.149
BRACHIAL SYSTOLIC PRESSURE	147.02	25.444
ABPI	1.090	0.158

Table 2: Clinical Characteristics of patients and mean ABPI.

	N = 100	MEAN ABPI
MALES	61	1.11
FEMALES	39	1.05
NON SMOKERS	43	1.06
REFORMED SMOKERS	18	1.13
HYPERTENSION – ABSENT	29	1.11
PRESENT	71	1.08
CORONARY ANGIOGRAM	N = 93	
NORMAL	18	1.13
SINGLE VESSEL DISEASE	27	1.08
DOUBLE VESSEL DISEASE	16	1.11
TRIPLE VESSEL DISEASE	32	1.06

We did not find a significant correlation between low ABPI and the presence or severity of coronary vascular disease.

All patients with an abnormal ABPI [< 0.9] had coronary artery disease, however, not all patients with coronary artery disease demonstrated angiographically had an abnormal ABPI. No significant correlation was found between the severity of ABPI impairment and extent of coronary artery disease. [p=0.202]

PAD is associated with a substantial increase in the risk of fatal and nonfatal cardiovascular events. Epidemiological studies have confirmed an association between diabetes and an increased prevalence of PAD, however, many patients are asymptomatic and this condition often remains undiagnosed.

Asymptomatic PAD is defined as resting ABPI < 0.90 with an absence of prior lower extremity peripheral vascular event or clinical symptoms indicative of intermittent claudication. Symptomatic PAD is defined as intermittent claudication, history of lower extremity peripheral vascular

revascularization and/or limb amputation because of PAD regardless of ABPI value.

The ABPI is the ratio of the ankle and brachial systolic blood pressure and is used to assess individuals with PAD. It is a simple, noninvasive, reproducible, quantitative measurement which has a high sensitivity and specificity for the detection of PAD and has been validated against angiographically proven disease and found to have a sensitivity of 95% and specificity of 100%.

The American Diabetes Association paper quotes the normal range of ABPI as 0.91–1.3. An ABPI index of 0.90 or less suggests the presence of PAD and is a marker of cardiovascular risk.[13] A low index indicates the presence of flow resistance in a peripheral artery and reflects the presence of generalized atherosclerosis. Among population-based cohorts, the ABPI is highly specific but not sensitive for predicting cardiovascular disease. The American Heart Association [AHA] Prevention Conference V described the ABPI as a strong and independent risk factor for cardiovascular mortality.[14] Given that it is simple to perform, noninvasive and inexpensive, the ABPI is a useful vascular risk prediction tool.

Factors affecting ABPI

1. Age – Cross-sectional studies has shown that ABPI decreases with age probably because of the increased prevalence and progression of PAD.

2. Height – taller people have higher ABPI due to the greater distance from the heart.

3. Gender –ABPI was found to 0.02 lower in women than in men in a subset of MESA [Multi Ethnic Study of Atherosclerosis] study.

4. Post Exercise – There was a mild decrease in ABPI in healthy patients when measured immediately after exercise, perhaps owing to the vasodilation of the exercising muscle in the ankle region.

5. Calcification – conditions like medial calcinosis and end-stage renal disease leads to calcification of the vessels and hence ABPI is found to be more than the normal range.

In our study, we found that though not all patients with abnormal CAG had abnormal ABPI, patients with normal CAG tended to have a higher ABPI.

Sadeghi M *et al*. have shown a relation between ABPI and severity of CAD and concluded that ABPI could be a useful noninvasive tool to assess coronary vascular disease.[15] However, this study differed from ours, in that it included all patients with suspected cardiovascular disease and not only patients with diabetes. PAD in patients with diabetes differs both in pathophysiological mechanism and clinical manifestation from those with PAD due to other causes. The genesis of PAD in diabetics is multifactorial. Inflammation, enhanced coagulation and inhibition of fibrinolysis all play a role. PAD in diabetics tends to be more diffuse,[9] is more severe in the lower limbs and is asymptomatic longer, therefore presenting at a more advanced stage.[14]

In a prospective cohort study of elderly unselected patients, the presence of PAD increased the risk of major vascular events and mortality.[17] However, there was no difference in cardiovascular risk between symptomatic and asymptomatic PAD. This study, again, unlike our study, was not restricted to patients with diabetes.

A Chinese study on patients with type 2 DM did find a correlation between PAD and coronary vascular disease. In Chinese patients with type 2 diabetes, all-cause and CVD mortality in patients with low ABPI were 12.4%, as compared to patients with normal ABPI, with an all-cause mortality rate of 5%.[18] However, this study included symptomatic PAD also, unlike our study where patients with symptomatic PAD were excluded. Shih-Tai Chang *et al.* found in their study that ABPI could predict CAD in diavetics. Different ethnicities might play a role in these varying results.[19] It is also interesting to ponder whether ethnic differences might play a role in varying normal ranges of ABPI in different populations, thus explaining the differences between results from studies conducted in various ethnic groups. The MESA study showed that small differences existed between ABPI in different groups, even amongst normal individuals.[20]

Bhavana Sosale *et al.* found that even asymptomatic PAD detected by abnormal ABPI correlated with the presence of CAD. In this study, one out of six asymptomatic patients with diabetes had PAD and one in four patients with PAD had CAD.[21]

In a cross-sectional study done in Lahore , only 3 patients [13.6%] out of the 22 patients who had triple vessel disease had ABPI < 0.9 [p = 0.07].[22] The results of this study, similar to ours, where abnormalities in coronary angiogram are counterintuitively, not reflected in ABPI, raises the question of whether ABPI ranges used in the West are actually applicable to patients in the subcontinent. That ethnicity plays a role in the value of ABPI is known and has been shown in several studies.[23,20]

PAD associated with diabetes differs from that caused by other factors such as smoking. The distal vasculature is more involved and there is a strong association with medial artery calcification. (MAC). MAC increases arterial stiffness, thus causing an increase in the ABPI. This may be a factor which obviates applying the general population criteria of normal and abnormal ABPI to patients with diabetes.

By convention, low ABPI is defined as < 0.9. However, an ABPI of < 1.1 is not normal.[24] It has been shown that an ABPI of less than 1.1 in men and less than 1 in women may indicate an increased risk of carotid and coronary atherosclerosis. Moreover, the MAC associated with diabetes decreases the sensitivity of ABPI as a screening tool. Increasing the threshold to 1 or 1.1 might improve solve this issue. When we analyzed data defining low ABPI as < 1.1, we found that a larger number of cases of abnormal CAG had abnormal ABPI. Our study, therefore, raises the question of whether the cut-off of normal ABPI must be revised, at least for patients with diabetes. (Figure 6)

The getABI study concludes that the screening and treatment of PAD may improve cardiovascular and cerebrovascular outcomes.[25] Our study, however, indicates that CAD in DM can antedate even asymptomatic PAD. Therefore regardless of the presence or absence of PAD as assessed by clinical screening, all patients with diabetes need aggressive risk factor modification since CAD can very well occur with normal peripheral arteries.

Limitations of the study: The study was limited by a low sample size and by the fact that we excluded patients with symptomatic PAD. Additionally, the study did not include a control study group of non- diabetics. In spite of these limitations, the study highlights the importance of screening for CAD in all diabetics, regardless of the presence or absence of

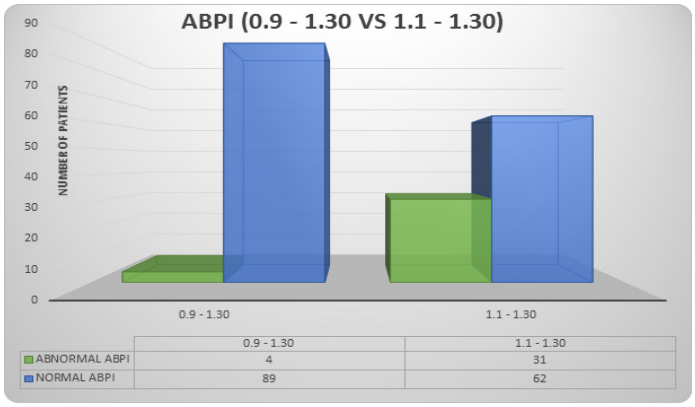

Figure 6: Comparison OF ABPI 0.9 – 1.30 VS 1.1 – 1.30.

peripheral vascular disease. We also raise the question of redefining the normal limits of ABPI.

CONCLUSION

In our study, though all patients with abnormal ABPI had CAD as assessed by CAG, not all patients with abnormal CAG had abnormal ABPI. Thus the utility of ABPI as a surrogate marker in screening of CAD is limited. Redefining the parameters of normal ABPI to a new lower limit of 1.1 (as compared to previous value of 0.9) might improve the efficacy of ABPI as a screening tool and help build the correlation between ABPI and CAD in diabetes.

Additionally, absence of PAD in patients with diabetes does not obviate the need for aggressive screening and management of cardiovascular risk factors and disease.

CONFLICT OF INTEREST

The author declare that there is no conflict of interest.

ABBREVIATIONS

DM: Diabetes Mellitus; **ABPI:** Ankle Brachial Pressure Index; **PAD:** Peripheral Arterial Disease; **CAD:** Coronary Artery Disease; **CAG:** Coronary angiography.

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