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Prevalence and risk factors of Peripheral Arterial Disease in Type 2 Diabetes Mellitus

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Abstract

Introduction: *Type 2 diabetes mellitus is generally associated with vascular complication like nephropathy, retinopathy, neuropathy, coronary artery disease and peripheral vascular disease. Microalbuminuria has a strong correlation with microvascular as well as macrovascular complications of type 2 diabetes mellitus. Establishment of peripheral vascular complications leads to early diagnosis, prevention, and treatment of renal and cardiovascular complications. This study investigated the value of ankle-brachial index (ABI) for prediction of microalbuminuria in type 2 diabetic patients.*

Materials and Methods: *Measurement of ABI with colour Doppler ultrasonography was carried out for 100 patients with type 2 diabetes mellitus. An ABI Index less than 0.9 were defined as a predictive marker for atherosclerosis. Microalbuminuria and risk factors of atherosclerosis were compared between the patients categorized based on the ABI values.*

Results: *The mean ABI was 1.1 ± 0.2 (range 0.52 to 1.6) and 20 (20%) had an abnormal ABI (< 0.9). The correlations were significant between abnormal ABI and duration of disease ($p<0.001$), cardiovascular event and cardiac care unit admission ($p<0.001$), hypertension ($p<0.01$), and dyslipidemia ($p<0.001$). There was a significant correlation between ABI and microalbuminuria (odds ratio 0.05; 95% confidence interval, 0.038 to 0.630; $P<0.01$).*

Conclusions: *The ABI is a noninvasive and reliable assay for detection of peripheral and cardiovascular complications, and also early stage of nephropathy in diabetic patients. In patients with an abnormal ABI, long-term follow-up for earlier detection and prevention of complications is helpful.*

INTRODUCTION

Diabetes mellitus (DM) is a multifactorial disease characterized by hyperglycaemia resulting from defects in insulin secretion, insulin action or both. The complication of diabetes include microvascular disease due to damage to small blood vessels that affect eyes, nerves and kidney and macrovascular diseases due to damage to the arteries that affect brain, heart and extremities. Diabetes mellitus is the most common cause of end-stage renal disease, blindness, and nontraumatic lower extremity amputation in adults. This is caused by progressive atherosclerosis.[1] As a result there is increase in cerebrovascular accidents by 2-fold and cardiovascular accident by 3-fold in these patients. Hypertension, lipid metabolism disturbance and obesity accompany this metabolic syndrome and aggravate complications.[2]

Peripheral arterial disease (PAD) is characterized by atherosclerotic occlusive disease of the lower extremities and is a marker for atherothrombotic disease in other vascular beds.1 The prevalence of peripheral arterial disease (PAD) in diabetic patients was found to be 3.2% in a study from South lndia.[3] and as high as 15.9% in a western population.[4]This reportedly low prevalence of PAD in South India is in marked contrast to the high prevalence rate of coronary artery disease (CAD).[5,6]

A reliable diagnosis of PAD can be made using the ankle-brachial index (ABI). This simple, painless and highly reproducible test can be performed in a physician's office and requires only a blood pressure apparatus and a hand-held, continuous-wave doppler probe. The focus of the vascular complications of diabetes has been on coronary artery disease and nephropathy while peripheral vascular disease has largely been ignored, especially in India.

The normal range of ABI is between 0.9 and 1.4. Values below 0.9 show peripheral vessel disease and an occlusion more than 50% in one or more important body vessels, with a sensitivity of 95% and specificity of 100%. More severe coronary vessel involvement is considered as the value of the index decreases, and the value below 0.4 shows advanced ischemia. An ABI more than 1.4 is characteristic of calcified and nonsqueezable vessels.[7] In these cases toe brachial index could be used for definite establishment of peripheral vessel involvement.[8,9]

We aimed to investigate the value of ABI for prediction of microalbuminuria (an early marker of renal involvement) in type 2 diabetic patients. Regarding the importance of early diagnosis of coronary disease in diabetic patients and the predictive value of ABI in identifying cardiovascular complications, this study could inform the screening approach for vessel involvement in patients with type 2 DM to prevent serious complication of DM relevant with other risk factors.

MATERIALS AND METHODS

We randomly selected 100 patients with type 2 diabetes (30–70 years of age) from the outpatient unit of Indira Gandhi Institute of Medical Science, Patna. Type 2 diabetes mellitus was defined using 1985 World Health Organization criteria.[10]

Patients with malignancies, intermittent claudication or nephropathy was excluded. After explaining aim and objective, informed consent was taken from all the patients. Data on age, gender, duration of DM, history of smoking, history of cardiovascular or cerebral accidents (including history of admission to intensive unit care), hypertension (blood pressure equal to or more than 125/75 mm of Hg), dyslipidemia (low-density lipoprotein level > 140 mg/dL), microalbuminuria (urine albumin between 30-300 mg per 24 hours), and body mass index were studied.

In all patients, blood pressure was measured, cardiovascular examination was done, and brachial, radial, ulnar, femoral, popliteal, dorsalis pedis, and posterior tibialis pulses were measured by one same examiner. Then the highest systolic pressure in the lower and upper extremities was measured by one radiologist by means of a Doppler ultrasonography device (Toshiba Nemio-30, Osaka, Japan) using an AT probe. Systolic blood pressure was measured by wrapping sphygmomanometer cuff around each of the two ankles and wrists, respectively, after a 10-minute rest and the ABI was calculated as the highest ankle systolic pressure divided by highest brachial systolic pressure in each patient. An ABI < 0.9 was defined as a low ABI indicative of peripheral arterial disease. Albumin in the urine was estimated by turbidimetric immunoassay in terms of mg/g of creatinine. First voided early morning mid-stream urine was taken. Only one sample was obtained from each patient for measurement of albumin and this was one of the limitations in this study.

The patients were categorized into 3 groups based on their ABI (< 0.9, 0.9 to 1.4, and > 1.4). The three groups were compared using the chi-square test and the 1-way analysis of variance, where appropriate. The SPSS software (Statistical Package for the Social Sciences, version 17.0) was used for analyses. A p value less than 0.05 were considered significant.

RESULTS

This study was performed on 100 patients with type 2 DM, including 43 men (43%) and 57 women (57%). The mean age was 53.93 ± 7.65 years. The mean duration of DM was 114 months with the shortest duration of 6 months and the longest duration of 300 months. Body mass index was greater than 25 in 69 participants (69%) and less than 25 in 31 participants (31%). There were 17 (17%) smokers. Dyslipidemia was present in 67 patients (67%), high blood pressure in 50 patients (50%), cardiovascular events and admission to cardiac care unit in 7 (7%), and diabetic foot ulcer in 19 (19%). (Table 1)

Table: 1 Demographic data.

Characteristic	Percentage (%)
Gender	
Male	43
Female	57
Body mass index	
>25	69
≤25	31
Hypertension	50
Dyslipidemia	67
Microalbuminuria	29
Smoking	17
Mean duration of diabetes (months)	114
Cardiovascular disease	7
Foot ulcer	19
No dorsalis pedis pulse	9
No tibialis posterior pulse	10

Table: 2 Correlation between Atherosclerosis Risk Factors and Ankle-Brachial Index

Characteristics	Ankle – brachial index		
	<0.9	0.9-1.4	>1.4
Mean age (years)	51.75	54.32	56.14
Gender			
Male	8(40)	30(41.10)	5(71.43)
Female	12(60)	43(58.90)	2(28.57)
Body mass index (kg/m²)			
>25	11(55)	53(72.60)	5(71.43)
≤25	9(45)	20(27.40)	2(28.57)
Hypertension (mm of Hg)	13(65)	33(45.21)	4(57.14)
Dyslipidemia (mg/dL)	16(80)	46(63.01)	5(71.43)
Microalbuminuria (mg/g)	11(55)	13(17.81)	5(71.43)
Smoking	6(30)	9(12.33)	2(28.57)
Mean duration of diabetes (months)	132.24	105.24	169.68
Cardiovascular disease	4(20)	2(2.74)	1(14.29)
Foot ulcer	7(35)	10(13.70)	2(28.57)
No dorsalis pedis pulse	4(20)	4(5.48)	1(14.29)
No tibialis posterior pulse	5(25)	4(5.48)	1(14.29)

Table: 3 Correlation between ABI<0.9 and various variable.

Variables	Regression coefficient	p-value
Age (years)	0.77	<0.001
BMI (kg/m²)	0.12	>0.05
Duration (years)	0.87	<0.001
Systolic BP (mm of Hg)	0.76	<0.01
LDL-Cholesterol (mg/dL)	0.77	<0.001
Microalbuminuria (mg/g)	0.80	<0.01

The mean ABI measured by Doppler ultrasonography was 1.07 ± 0.24 (range 0.52 to 1.6). The patients were stratified into 3 groups: the first group were 8 men (8%) and 12 women (12%) with an ABI between 0.52 and 089 (mean 0.72 ± 0.16); the second group were 30 men (30%) and 43 women (43%) with an ABI between 0.9 and 1.4 (mean 1.13 ± 0.15); and the third group were 5 men (5%) and 2 women (2%) with an ABI between 1.41 and 1.6 (mean of 1.5 ± 0.06). There was no significant relationship between sex and ABI groups (p = 0.50). The mean age was 51.75 ± 6.59 years in the first group, 54.32 ± 7.9 years in the second group, and 56.14 ± 6.49 years in the third group (p = 0.31). The mean duration of DM was higher in those with high ABIs (p = 0.04) (Table 2). A history of cardiovascular events was higher in the first group. In addition, there was a significant correlation between high blood pressure and an ABI less than 0.9 (p = 0.02) (Table 2). There was also a significant correlation between dyslipidemia and an ABI less than 0.9 (p < 0.001) (Table 2).

Of all the participants 19 (19%) had a history of diabetic foot ulcer, of whom 7 patients (7%) had an ABI less than 0.9 (the first group). In addition, 9 patients (9%) had no pulse in the dorsalis pedis, of whom 4 patients (4%) were in the group with abnormal ABI. No tibialis posterior pulsation was found in 10 patients (10%), of whom 5 patients (5%) were in the group with abnormal ABI.

Out of 100 patients of known type 2 diabetes mellitus, who participated in the urine microalbuminuria assay, 20 patients were in the first group, 73 in the second group, and 7 in the third group. Among these microalbuminuria was found in 11 patients (55%) of the first group, in 13 patients (17.81%) of the second group, and in 5 patients (71.43%) of the third group. There was a significant correlation between an ABI less than 0.9 and microalbuminuria (p < 0.01).

DISCUSSION

Diabetes mellitus is an extending metabolic disorder in the world with microvascular and macrovascular complications that if not being diagnosed and properly treated leads to debility, increased mortality, and morbidity. Diabetes mellitus leads to acceleration of atherosclerotic changes in vessels and thus involvement of different organs. In this study, we evaluated identifying and screening of atherosclerosis in diabetic patients by the use of the ABI and found that 19.9% had an ABI less than 0.9 while 72.3% of the diabetic patients had normal ABI (between 0.9 and 1.4) and 7.8% had an ABI greater than 1.4.

Few Indian studies have assessed PAD in diabetes mellitus patients. Two large studies from South India, namely, by Mohan et al (n=4941) and CUPS (n=1262) found a prevalence of PAD in diabetics to be 3.9% and 6.3% respectively.[11,3] Two recent studies from North India, one by Agarwal et al (n=4400) and the other by Madhu et al (n=364) found the prevalence of PAD in diabetics to be 18.1% and 13.73% respectively.[12,13]

In the Fremantle diabetes study, age, duration of diabetes, higher systolic blood pressure and higher BMI were found to be significant predictors of

PAD.[14] In the study by Agrawal et al a significant correlation was found between age,duration of diabetes and prevalence of PAD.[12] In both CUPS[5] and in the study by Mohan et al[11] age and higher systolic blood pressure predicted PAD.2 Systolic blood pressure was also shown to be a predictor of PAD in the study by Janka et al.[6] In our study, age and duration was significant predictor of PAD. The prevalence of hypertension was 50% but prevalence was 65% among PAD group (ABI<0.9). Mean systolic blood pressure was 152 ± 18.99 mm of Hg in this study (p<0.01). There was significant correlation between systolic blood pressure and ABI<0.9. This was in accordance with the above studies.

There was no significant relationship between BMI and ABI <0.9 in the current study, which was in line with some studies.[3,12] This shows that obesity is not a risk factor for atherosclerosis.

There was a high prevalence of smoking in those with PAD (30%). In study done by Norman PE et al similar result was observed that smoking was found to be more prevalentin the PAD group than in the non-PAD group (24% vs 12.6%) and it was found to be significantly associated with PAD.[14]

The rate of dyslipidemia was 67% in this study. It was more (80%) in the group with an ABI less than 0.9 and there was a significant correlation between dyslipidemia and an ABI less than 0.9. This was in accordance with similar studies.[15,16] This shows the effect of dyslipidemia in progression of atherosclerosis.

Microalbuminuria was found in 29% of our patients and in 55% of those with an ABI less than 0.9. There was a significant correlation between an ABI less than 0.9 and microalbuminuria (P < 0.001). Tseng and colleagues[17] also demonstrated that albumin-creatinine ratio significantly correlated with abnormal ABI (less than 0.9) and peripheral arterial disease, but the mean age of patients was 65 years old, and thus, coexistence of peripheral arterial disease and abnormal ABI may be due to physiologic atherosclerotic changes in this range of age.

In our study, cardiovascular events were more frequent in the patients with abnormal ABI and a significant relationship was found between ABI less than 0.9 and cardiovascular events; there was a strong correlation even after omitting the bias-inducing variants. In the Rafii and colleagues[18] study, a significant correlation was found between abnormal ABI and positive exercise test. Nematipur and colleagues[19] measured ABI and performed coronary angiography and showed that all the patients with an ABI less than 0.9 had coronary vessel disease and ABI decreased with increasing number of vessels involved.

CONCLUSIONS

Considering cardiovascular complications as the most important factor in the mortality of Diabetic patients, the use of simple, easily available, noninvasive, and reliable methods as screening test for these complications is recommended. The use of the criterion of an ABI less than 0.9 in diabetic patients declines the necessity of monitoring cardiovascular complications and related risk factors. The abnormality of this index also warrants evaluating the other asymptomatic vascular complications such as carotid artery and

coronary vessels involvement in order to prevent severe vascular complications in organs such as the heart and brain. However, impossibility of a fully evaluation of cardiac complications was the limitation of the current study.

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