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'CORRELATION OF ANKLE BRACHIAL INDEX(ABI) WITH NUMEROUS EPIDEMIOLOGICAL AND LABORATORY PARAMETERS IN PATIENTS WITH PERIPHERAL ARTERY DISEASE(PAD)'

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INTRODUCTION

Peripheral arterial disease (PAD) is not an uncommon but a commonly neglected condition by many medical practitioners. It is a disease that threatens not only the limb but also life itself! Atherosclerosis is the commonest cause of PAD in the western nations. The cardinal symptom is intermittent claudication (IC) but majority of the patients are asymptomatic. Ankle-brachial pressure index (ABI) is an effective screening tool for PAD. A diminished ABI (< 0.9) is a definite sign of PAD. Its prevalence steadily increases with age. In Germany almost a fifth of the patients aged over 65 years suffer from it. With increasing life expectancy the prevalence of PAD is on the increase.[1] PAD is a manifestation of diffuse and severe atherosclerosis. It is a strong marker of cardiovascular disease; a very strong association exists between PAD and other atherosclerotic disorders such as coronary artery disease (CAD) and cerebrovascular disease (CVD). PAD is an independent predictor of high mortality in patients with CAD.

Smoking, diabetes mellitus and advancing age are the cardinal risk factors. A relatively small number of PAD patients lose limbs by amputation.[2,3] Most paitients with PAD die of either heart attacks or strokes and they die of the former conditions far earlier than controls. PAD still remains an esoteric disease and there is a significant lack of awareness of this condition by many physicians, and therefore under-diagnosed and underestimated. Measures to promote awareness of PAD among physicians and the society in general are needed. Since most patients are asymptomatic and carry potentially significant morbidity and mortality risks, screening for PAD should be made a routine practice at primary care level.[4]

Prevalence

In the western world atherosclerotic PAD is predominantly encountered in patients aged above 60 years and its prevalence increases steadily with age. Most of the earlier studies on PAD targeted either a male population or patients with CAD and therefore underestimated the actu-al prevalence of PAD in the community. The later studies included female patients and a greater cross-section of the general population and thereby yielded more realistic figures. In the younger age group men are more commonly C. Diehm et al. an ABI < 0.9 was 19.8% and16.8% respectively (distal arterial occlusions not included).[5]

Criqui's study estimated that there were approximately 4 000 000 claudicants and about 10 000 000 with asymptomatic PAD in USA.[10] With these figures one could say that for every claudicant there lurks 2–3 patients with asymptomatic PAD. Many studies have proven diminished ABI, especially in the subset of asymptomatic patients to be a useful marker of future cardiovascular events, especially in the asymptomatic patients. Many asymptomatic patients may succumb to heart attacks or strokes before they present with claudication.[4]

The prevalence of symptomatic PAD as manifest by IC in patients aged above 50 years varies from 2.7% to 4.6%. The prevalence of IC in patients aged 55–74 years in Ed inburgh Scotland was 4.6%. In Maastricht in the Netherlands in adults aged 45–74 years, it was 2.7%; it was 0.6% in the age group of 45–54 years, 2.5% in patients aged 55–64 years and 8.8% in the age group of 65–74 years. In the Swedish community for patients of the age group 50–89 years the prevalence of IC was 4.1%. In the study by Novo and co-workers in Palermo Italy comprising of 1558 patients of both sexes, there was a very high prevalence of IC; in patients aged 40–49 years the prevalence was 4.7% and in patients aged 50–59 years it was 9.2%.[41] In Germans aged > 65 the prevalence of IC was approximately 3%. The above figures clearly demonstrate that with advancing age the prevalence of PAD steadily increases. They also

convey the message that the vast majority of patients with PAD are asymptomatic and claudicants are only the tip of the iceberg.[3-6]

METHODS

This study was conducted on patients of type 2 diabetes mellitus at Department of medicine and Radiology in Vardhman Mahavir Medical College and Safdarjung Hospital, New Delhi a tertiary care hospital in northern India. Each patient gave written, informed consent to participate in the study. 70 consecutive patients, age between40-70 years, who satisfied the inclusion and exclusion criteria, were enrolled. Subjects were recruited from medicine OPD and wards. They Were subjected to detailed history and physical examination with investigation.

Inclusion criteria

1. Type 2 Diabetic diagnosed by American Diabetic Association (ADA) Criteria2011.
2. Duration- any duration.

Exclusion criteria

1.Patient with aortoiliac and ileofemoral obstruction.
2.Patient with aortoarteritis.
3.Buergers disease.
4.Smokers.
5.Collagen vascular disease.

A detailed clinical history of the patients was taken followed by a detailed clinical examination, which was recorded in a proforma sheet. The diagnosis of intermittent claudication (IC) was made based on the response to the questions in the proforma sheet.

RESULT

We studied 70 patients with type 2 diabetes (30 men and 40 women), who were evaluated using a detailed history, clinical examination and biochemical parameters. All these patients were subjected to Doppler ultrasound and accordingly grouped into PAD and non-PAD groups on the basis of their ABI.

The mean age of the patients was 54.96±8.804 years and the mean duration of diabetes was 5.357±4.634 years. Hypertension, either by history or by examination (SBP>140mmHg and/or DBP>90mmHg) was present in 35.7%of the patients. The mean BMI of the study

group was 25.44±25.21 Kg/m2. Obesity (BMI≥25Kg/m2) was present in 78.8% of patients The mean fasting and post prandial blood glucose values were 173.19 ± 80.901 mg% and 245.19 ± 100.511 mg% , respectively; while the mean HbA1c was 8.30.08 ± 1.70074%. Poor glycaemic control (HbA1C ≥ 6.5%) was seen in 64.23% of patients. The mean total cholesterol, serum LDL, serum HDL and serum triglyceride levels were, 167.67±29.217 mg%, 106.51 ± 35.049 mg%, 37.86 ± 6.75 mg% and 185.20 ± 91.578 mg%, respectively.

In the PAD group, mean systolic blood pressure, diastolic blood pressure, weight and HbA1c were higher as compared to the non-PAD group. High TG and cholesterol levels were more often seen in the PAD group.

The study found significant differences, like a higher prevalence of obesity (80% vs 64%), deranged HbA1C (100% vs 68%), peripheral pain(60% vs 30%), hypertension (50% vs 30%), and albuminuria (85% vs 32%) and fundus changes (50% vs 6%), ECG changes (75% vs 20%) in the PAD group.

PAD was found to be significantly correlated with age (p=.019), obesity (p=.062), HbA1C (p=.048), microalbuminuria (p=.012), ECG (p=.016) prevalence of CAD, fundus changes (p=.058)

These findings underline the importance of these factors in identifying type 2 diabetics at risk for developing PAD.

CAD was found in 15 out of 20 PAD patients (75%) as compared to 10 out of 50(20%) non-PAD patients.

We conclude that CAD, peripheral neuropathy, diabetic retinopathy, diabetic nephropathy is more prevalent in patients with PAD. However, this association needs to be confirmed in larger studies.

S.No	Parameter	Patients With Abi<0.9	Patients With Abi>0.9	Range	P-Value
		MEAN±SD	MEAN±SD		
1	AGE(YEARS)	56.40±8.85	53.52±8.74	40-70	0.019
2	BMI(KG/m2)	26.33±1.89	25.04±2.66	18-30.3	0.054
3	DURATION OF DIABETES(YEAR)	4.83±3.80	5.57±4.95	0-25	0.548
4	HEMOGLOBIN(gm%)	11.81±1.90	12.59±1.97	7-15.5	0.697
5	TLC(/cu mm)	9304±3222.45	8902±2981	4200-19800	0.81
6	PLATELETS(lacs)	2.10±1.27	2.14±1.31	0.75-8.4	0.652
7	ESR	26±15.13	28.02±15.92	4lacs-65lacs	0.621
8	BLOOD SUGAR[F](mg/dl	173.19±80.9	161.21±71.01	14-367	0.982
9	BLOOD SUGAR[PP](mg/dl	245.19±100.5	231.31±91.02	108-453	0.697
10	COLESTEROL(mg/dl)	167.67±29.22	156.21±26.29	106-239	0.711
11	HDL(mg/dl)	39.30±5.83	36.35±5.91	20-53.59	0.209
12	LDL(mg/dl)	106.75±38.5	106.98±35.1	46-164	0.403
13	TG(mg/dl)	180.25±109.2	188.47±86.55	59-440	0.817
14	ABI	1.16±0.98	3.56±1.02	0.18-6.6	—
15	BLOOD UREA(mg/dl)	49.14±29.95	44.01±25.02	15-164	1.25
16	CREATININE(mg/dl)	1.54±1.84	1.13±0.55	0.5-6.9	0.297
17	HBA1C(%)	8.10±1.22	8.73±1.77	6.1-14.3	0.048

Table 1: Distribution Of Male And Female In Our Study.

Group	No. of Patients	Percent
MALE	30	42.9
FEMALE	40	57.1
TOTAL	70	100

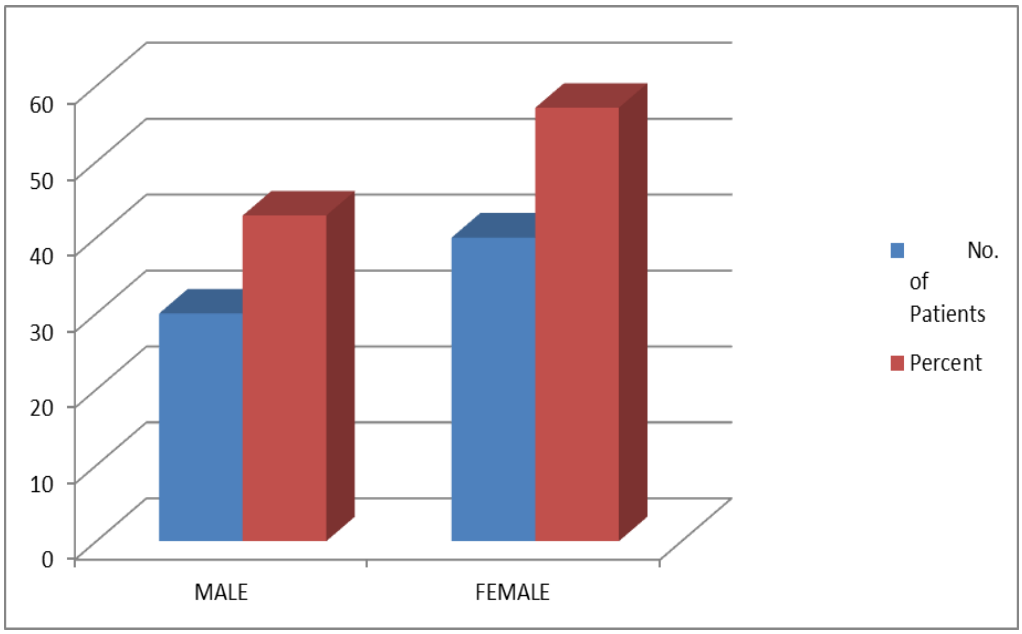

Figure 1: Sex Distribution.

Total number of 70 patients of type-2 DM were included in the study. Out of 70 patients, 40 were female and 30 were male. And respective percentage of male were 42.9 and female were 57.1

RELATIONSHIP BETWEEN PAD WITH AGE

Table 2: Table showing relation between PAD with mean age.

	Mean Age±SD	P-Value
ABI(<0.9)	56.4±8.846	0.019
ABI(>0.9)	53.52±8.739	0.28

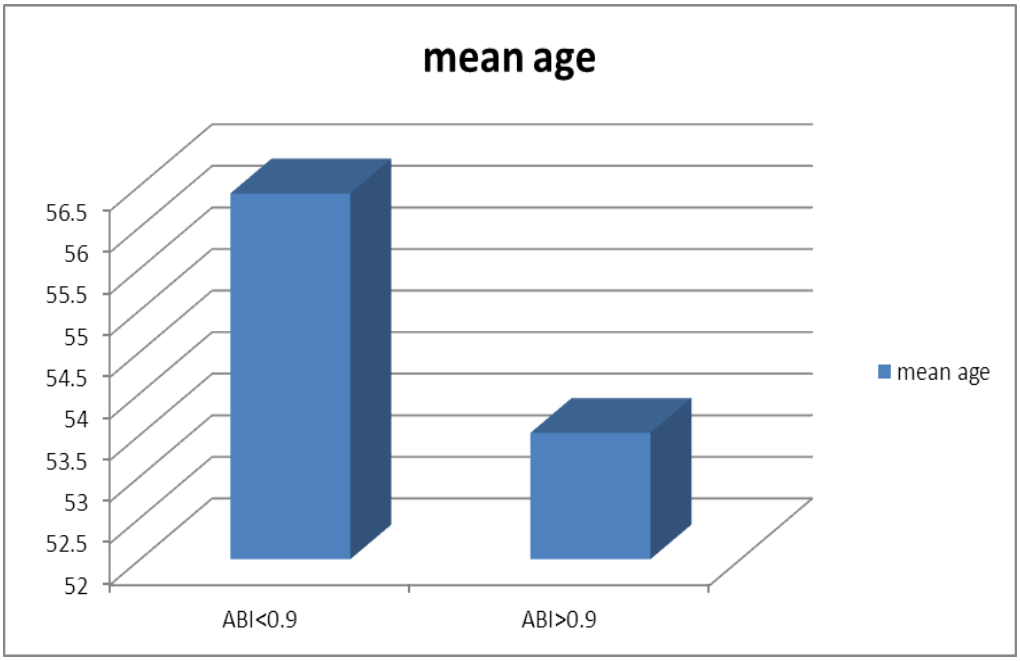

Figure 2: Correlation between AGE and PAD.

PAD-Group(ABI<0.9) mean age is 56.4±8.846 while in Non-PAD group(ABI>0.9) mean age is53.52±8

RELATIONSHIP OF ABI WITH HBA1C

Table 3: Correlation of ABI with HBA1C.

Group	HBA1C<6.5(%)	HBA1C>6.5(%)	Total	P-Value
ABI<0.9	0(0)	20(100)	20(100%)	0.048
ABI>0.9	16(32)	34(68)	50(100%)	0.122

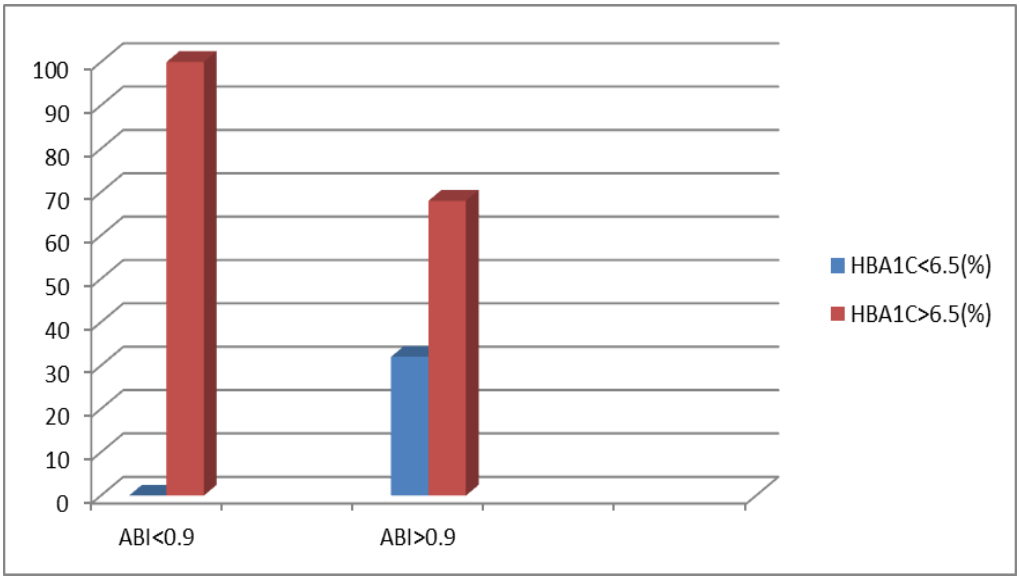

Figure 3: Correlation Between Hba1c And Abi.

Among ABI<0.9 patients 100% have HBA1C>6.5 while only 68% have HBA1C> 6.5 in ABI>0.9 groupOf patients and P-Value is 0.048 which is significant.

RELATIONSHIP BETWEEN ABI<0.9 AND MICROALBUMINURIA

Table 4: Correlation Of Abi<0.9 Patients With Microalbuminuria.

Group	Microalbuminuria Present	Microalbuminuria Absent	Total	P-Value
ABI<0.9	17(85)	3(15)	20(100%)	0.012
ABI>0.9	16(32)	34(68)	50(100%)	0.297

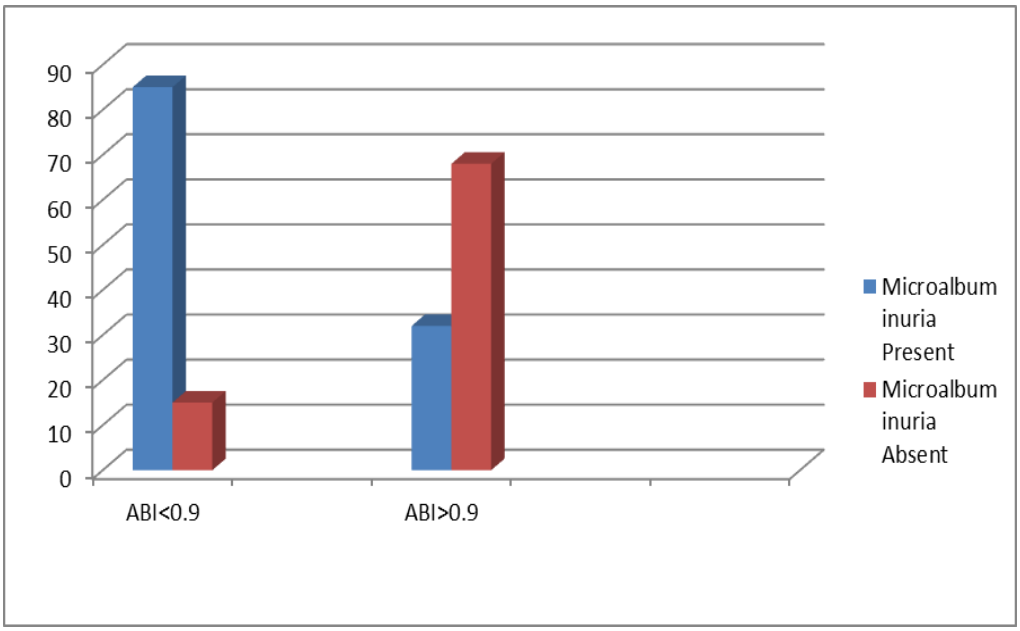

Figure 4: Correlation Of Abi With Microalbuminuria.

Among ABI<0.9patients 85% have microalbuminuria while only 32% have microalbuminuria in ABI>0.9 group of patients and P-Value is 0.012 and this is significant.

RELATIONSHIP BETWEEN PAD AND LIPID PROFILE

Table 5: Correlation Between Lipid Profile And Pad.

Group	For Abi<0.9 Patients (Mean±Sd)	For Abi>0.9 Patients (Mean±Sd)	P-Value
S CHOLESTROL	174.50±25.30	164.90±30.45	0.711
HDL	36.30±5.83	37.29±7.07	0.49
LDL	106.75±38.50	106.42±33.99	0.403
TG	180.25±109.18	187.18±84.7	0.817

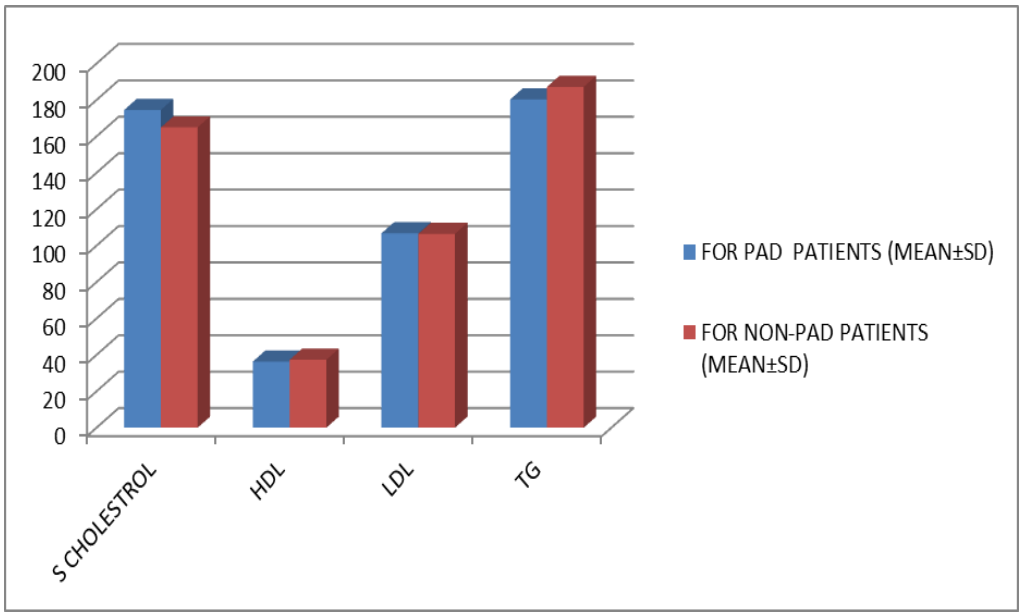

Figure 5: Correlation Of Abi With Lipid Profile.

Lipid profile in our study have no any significant correlation (P>0.05) in both ABI<0.9 and ABI>0.9 group.

DISCUSSION

ABI is a non-invasive test has sensitivity of about 90% and specificity of about 98% for detecting PAD before any clinical presentation of diabetic patients. The ABI is measured by placing the patient in a supine position for 5 minutes. Sphygmomanometer cuff is positioned above the elbow and above the ankle for respective measurement. The cuff is inflated around 20 mm of Hg above the value of BP is noted, when flow just begins to be picked up with colour Doppler pulse wave. Systolic pressure is measured in both arms, and the higher value is used as the denominator of ABI. Systolic blood pressure of the dorsalis pedis or the

posterior tibial artery is then measured by placing the cuff just above the ankle. The higher value is the numerator of the ABI in each limb.[9,11]

Prevalence of Peripheral Arterial Disease(PAD)

The prevalence of PAD as detected by Doppler ultrasound (ABI) was 28.6 % (men-40% and women- 60%) comparable with the prevalence found in previous studies in India and abroad. Marinelli et al 152 in 1979 studied 458 patients and found PAD in 33% of the cases by history,clinical examination and Doppler ultrasound. In another study conducted by Janka et al 18 in 1980 PAD was found in 15.9% out of 623 patients. This was a hospital outpatient based study with a study design.[12]

Other studies by Walters et al. in 1992 153, Migdalis et al. in 1992 154 and The Fremantle diabetes study in 2005 by Paul et al158 showed a PAD prevalence of 23.5%,44% and 13.6%, respectively.

Few Indian studies have assessed PAD. Two large studies from South India, namely by Mohan et al. in 1995156 (n=4941) and CUPS in 200017 (n=1262) found a prevalence of PAD in diabetics of 3.9% and 6.3% respectively. CUPS was a community based study unlike ours which was hospital based. This could also the higher age of selected patient could. account for the higher prevalence of PAD in our patients compared to those in CUPS.

Recently Agrawal et al191 in 2000 (n=4400) and Madhu et al159 in 2006 (n=364) found prevalence of PAD in diabetics to be18.1% and 13.73% respectively. These two studies were performed in North India. The study by Agarwal et al191 was performed on outpatients with a study design similar to ours.[12]

Demographic parameters

In the current study, the mean age was 56.4 ± 8.846 years in PAD group and 53.52 ± 8.739 years in non PAD group and mean duration of diabetes was 5.357 ± 4.6369 years. In PAD group mean duration of diabetes were 4.825±3.801 years and in non PAD group 4.572±4.950. Both age and duration of diabetes were significant predictions of PAD, a finding similar to that of previous studies.(P value=0.019) significant for age in PAD group. The Fremantle diabetes study158, a community based study, included subjects with a mean age of 63.4 ± 10.9 years and a mean duration of diabetes as of 4 years in subjects without PAD, Subjects with PAD had a mean age of 70.7 ± 13.2 years with a mean duration of

diabetes of 5 years. Both variables, age and duration of diabetes, attained statistical significance (p< .05) as predictors of PAD. In the study by Agrawal et al191 a significant correlation was found between age, duration of diabetes and prevalence of PAD. In CUPS17, a significant correlation was shown between age and PAD. Age has also been shown to be a significant predictors of PAD in studies by Walters et al. in 1992 153 and by Mohan et al.156 in 1995.[13]

Anthropometric parameters

The correlation of obesity with diabetes is well known. In India, the prevalence of obesity among type 2 diabetics is reportedly lower than in Western studies. Normal BMI, for Indian population is considered to be less than 23 kg/m2.In the present study, mean BMI were 26.333 ± 1.89 kg/m2. for patients with PAD and in without PAD. were 25.048 ± 2.66 kg/m2.(P=0.08) is non significant.The prevalence of obesity (BMI > 25 kg/m2) in PAD patients was 80% as compared to 64% in non-PAD patients.

Sixteen of the total 20 patients with (BMI >25 kg/m2) 80% had PAD and 32 of 50 patients with BMI > 25 kg/m2 (64%) in non-PAD. This suggests that factors other than obesity also play a significant role in the occurrence of PAD in type 2 diabetic patients.. (P=0.08).In the Fremantle diabetes study158, mean BMI in the non-PAD group was 28.2 ± 4.5 kg/m2 whereas in the PAD group it was 29.7 ± 5.2 kg/m2 (p<.0001). Obesity was found to correlate significantly in the study. Walters et al. in 1992153 also found obesity to be a significant predicator of PAD. Indian studies (CUPS17, Agrawal et al191) did not find any correlation of PAD with obesity.[14]

In our study there was no correlation found between obesity and PAD. Our results along with those of other Indian studies like CUPS17 and the study by Agrawal et al191, suggest that unlike in Western populations, obesity does not appear to be a significant risk factor for PAD in Indian diabetics.

Blood glucose control parameters

The majority of study patients had uncontrolled diabetes. The mean HbA1c was 8.308 ± 1.70074%. On comparing the two groups, mean HbA1c was 7.01 ± 0.86 mg% in the non-PAD group as compared to 7.92 ± 0.86 in the PAD group. Using a cut off level of >6.5 mg% for poor control, 76% had poor glycaemic control in the non-PAD group compared to 95% in the PAD group. The mean fasting and post-prandial blood glucose levels in our study were

173.19 ± 80.901 mg% and 245.19 ± 100.511 mg% Blood glucose levels were comparable in the PAD and the non-PADgroups. HbA1C level was found to significantly high in patients with PAD (P<0.05). as compared to those without PAD.

Walters et al. 153 and Janka et al.156 also found such an association as blood sugar values were found to be significant predictors of PAD.These studies suggest a relationship between inferior glycaemic control and PAD.Our findings, statistically significant similar to previous study. This suggest that HbA1c and poorer glycemic control plays a significant role in occurance of PAD in type 2 DM.[15]

Lipid parameters

The important lipoprotein abnormalities in Indian diabetics are described as elevated levels of triglycerides, VLDL, small dense LDL and decreased levels of HDL. Since fatty acid accumulation and oxidation play a key role in the pathogenesis of PAD, deranged lipid levels must play an important part in the prevalence of PAD.

In our study, differences were found between serum triglyceride levels, HDL levels, total cholesterol and serum LDL levels between the PAD and the non-PAD subgroups.

In our study shows, a mean serum cholesterol 174.50±25.30 mg/dl in PAD group compared to 164.90±30.45 in non PAD group nonsignificant (P=0.711). Mean HDL level (low HDL defined as<40 mg%) was seen in PAD group 36.30±5.83 mg/dl and patients in the non- PAD as compared to 37.29±7.07mg/dl. High total cholesterol levels (defined as cholesterol level > 200 mg %) were found more often in the PAD than the non-PAD group, but not statistically significant. P value is 0.711.

Walters et al153 and Mohan et al.156 found serum total cholesterol levels to be one of the predictive factors for PAD. Although the comparison in our study was not found to be statistically significant.[16]

Microalbuminuria

In our study there was significant difference in the prevalence of microalbuminuria between group of patients with and without PAD. Out of 20 PAD patient 17(85%) had microalbubinuria but in 50 non PAD patient only 16(32%) had microalbuminuria. (P value-0.012) significant In our patients mean blood urea was 49.143 ± 29.9541(p value-0.171) and mean serum creatinine was 1.545 ± 0.28(p value-0.297). These parameters were comparable

in the two groups. Our study showing that microalbuminuria is predictor of PAD. K. Wattanakit.et.al Among the 6,760 subjects, aged 45-84 years, 326 (4.8%) had prevalent PAD. 813 (12.0%) subjects had microalbuminuria and 100 (1.5%) had macroalbuminuria. Among diabetic subjects, those with albuminuria (micro and macroalbuminuria combined) were 1.90 times more likely to have PAD (95% CI: 1.19-3.04) than those with no albuminuria. However, the role of albuminuria as a risk factor for PAD has been evaluated in mostly small studies. These studies suggest that albuminuria may be an important risk factor for PAD in the general population and in high risk populations of diabetic subjects 195.[17]

CAD and PAD Association[18,19]

The prevalence of CAD (ECG changes based on Minnesota codes) like MI was 75% in PAD patients and 20% in non-PAD patients. Our study shoes higher prevalence of CAD statistically significant (p= 0.016) may be due to higher age of selection and other comorbid association with PAD in Type 2 diabetes mellitus and less number of subject in study. However this association needs to be confirm in larger studies.

The Fremantle diabetes study158 was a prospective study to assess the association between PAD and CAD. This study found that a low ABI was associated with a 67% increase in the risk of cardiac death.

Similarly, the Cardiovascular Health study 164, a prospective study to evaluate the association of PAD and CAD, enrolled 5,888 participants above 65 years of age. ABI was measured at the baseline. All participants had a detailed assessment of prevalent CVD and were contacted every 6 months to assess total mortality and CVD events (including CVD mortality, fatal and nonfatal myocardial infarction, congestive heart failure and angina.)

The crude mortality rate at 6 years was highest (32.3%) in those with prevalent CVD and a low ABI, and lowest in those with neither of these findings (8.7%). The risk for incident congestive heart failure (relative risk [RR]=1.61) and for total mortality (RR=1.62) in those without CVD at baseline but with a low ABI remained significantly elevated even after adjustment for cardiovascular risk factors.

For each 0.1 decrement in the ABI below 1.0, event rates increased .Even within this group, a low ABI was associated with increased age- and gender-adjusted risk of total and CVD mortality and remained independently associated with CVD mortality.

In the CUPS study17, the prevalence of CAD was not found to be significantly higher in the PAD group as compared to the non-PAD group. However, a similar study from South India by Krishaswamy et al192 showed that PAD was common in elderly people with coronary artery disease. All patients were in study were admitted to geriatric word and a cross sectional evaluation was done. They recruited 80 people aged 60 years or above with coronary artery disease. PAD was found to be present in 19 patients (23.7 %).

In another study done by Leng et al 193 1,592 subjects aged 55-74 years were selected randomly and the presence of peripheral arterial disease was determined and and classified into claudicants, major and minor asymptomatic patients. This cohort was followed prospectively over 5 years for subsequent cardiovascular events and death.

Claudicants had a significantly increased risk of developing angina compared with normals (RR : 2.31,95% Cl : 1.04-5.10), and asymptomatic subjects had a slightly increased risk of myocardial infarction and stroke. Deaths from cardiovascular disease were more likely in both claudicants (RR : 2.67, 95% Cl :1.34-5.29) and subjects with major (RR : 2.08, 95% Cl : 1.13-3.83) or minor asymptomatic disease (RR : 1.74, 95% Cl : 1.09-2.76).

At baseline 288 subjects (18.2%) had an ABI index ≤ 0.9. After five years, subjects with an index ≤ 0.9 at baseline had an increased risk of non-fatal myocardial infarction (RR 1.38, 95% CI 0.88 to 2.16), stroke (RR 1.98,95% CI 1.05 to 3.77), cardiovascular death (RR 1.85,95% CI 1.15 to 2.97), and all cause mortality (RR 1.58,95% CI 1.14 to 2.18) after adjustment for age, sex, coronary disease, and diabetes at baseline.

In a study by Mckenna et al 194, a cohort of 744 patients underwent noninvasive testing for lower extremity peripheral arterial disease (PAD). Using a ratio of the ankle and brachial blood pressures (ABI) of less than 0.85 as the criterion, the relative risk (RR) for total mortality associated with PAD was 2.36 (95% CI 1.60- 3.48) after adjusting for baseline covariates in a proportional hazards model. There was a strong trend for increasing risk with decreasing ABI ($P < 0.0001$). The specific cause of death for which survival was directly related to the magnitude of ABI was myocardial infarctions.

Recently Sodhi et al 188 performed ultrasonic evaluation of ABI in 195 individuals aged 40 years and above. After logistic regression analysis it was found that abnormal ABI (i.e. ≤ 0.9)

was significantly associated with established cardiovascular risk factors, such as smoking and hypertension. This study excluded patients with established CAD.

A higher incidence of CAD has been shown in patients with PAD by several studies. However CUPS study17, a cross-sectional study from South India, failed to find a correlation between CAD and PAD

CONCLUSIONS

According to our results, PAD was present in 14.3% of type 2 diabetics, with comparable prevalence of 13.9% and 14.9% in men and women, respectively.

Risk factors significantly associated with PAD were age, duration of diabetes, systolic and diastolic blood pressure, smoking, HbA1C and CAD.

The present study also compared risk factors between PAD and non-PAD patients in subjects already diagnosed to have CAD. A significant correlation was found for age, waist hip ratio, smoking, HbA1C, total cholesterol, low HDL, triglyceride levels and microalbuminuria.

However, further studies, with a larger sample size, are needed to investigate the possible mechanisms linking PAD and CAD and to determine whether PAD predicts the development and progression of CAD.

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