ORIGINAL ARTICLE

# A Study of Prevalence of Peripheral Arterial Disease in Type 2 Diabetes Mellitus Patients in a Teaching Hospital

**Vaibhav Shukla[1*], Jalees Fatima[1], Mohsin Ali[2], Abhinav Garg[2]**


## Abstract

**Introduction:** Diabetes mellitus is a major health problem in India as also the world. Peripheral arterial disease (PAD) is a known complication of diabetes which is relatively less commonly studied in comparison to other complications. The present study was undertaken to study the prevalence of PAD in diabetic patients in a teaching hospital.

**Materials and Methods:** 200 type 2 diabetic patients from indoor as well as outdoor of a teaching hospital were included in the study. Ankle brachial pressure index was used to assess PAD. ABPI values of 0.9 or less were taken as indicative of PAD.

**Results:** Out of 200 patients 72(36%) had evidence of PAD. There was a significant association between PAD and duration of diabetes, waist circumference, hypertension and microvascular complications.

**Conclusion:** The prevalence of PAD in Type 2 diabetics was found to be 36% in our study. Screening for PAD should be done in all diabetic patients to detect this complication early.


## Introduction

Diabetes is growing at an exponential rate all around the world and soon is to be an epidemic in many countries including India. According to predictions the global prevalence of diabetes is to double globally from 171 million in 2000 to 366 million in 2030 with a maximum increase in India.[1]

Peripheral arterial disease (PAD) is a known complication of type 2 diabetes mellitus. Studies have shown that prevalence of peripheral arterial disease in diabetic patients is affected by host factors including age, duration of diabetes, level of glycemic control and presence of peripheral neuropathy. PAD is associated with increased risk of lower extremity amputation, and is also a marker for atherothrombosis in cardiovascular, cerebrovascular and renovascular beds. Patients with PAD therefore have an increased risk of MI, stroke and death. Additionally, PAD causes significant long-term disability in diabetic patients.

Keeping these issues in consideration, the present study was carried out with an aim to study the prevalence of peripheral arterial disease in Type 2 diabetes mellitus patients in a teaching hospital and to see the correlation, if any, of peripheral arterial disease in type 2 diabetes mellitus with relevant factors such as disease duration, glycemic control and other complications of diabetes.

## Material and Methods

The study was a cross sectional study carried out on 200 Type 2 diabetes mellitus patients attending the medicine OPD and indoor departments of a tertiary care Hospital. Type 2 diabetes mellitus patients who gave written and informed consent were included in the study. Patients with leg ulcers, trauma or surgery of legs and ankle, lower limb filariasis, Deep venous thrombosis, smokers and ex smokers and those with renal impairment were excluded from the study.

A detailed history regarding age, sex, occupation, family history, personal habits, socio economic status, duration and treatment of diabetes was taken. Symptoms of intermittent claudication, exertional limb pain and rest pain in lower limbs were also enquired. A thorough clinical examination including examination of all peripheral pulses was done. Anthropometric measurements were recorded in all patients. Fundoscopy was done in all patients to look for retinopathy. All routine investigations were done.

Measurement of ankle brachial pressure index (ABPI) was made in supine position after 10 minutes of rest and in a quiet room. The index is ratio of systolic blood pressure measured at the ankle to the systolic blood pressure measured at the brachial artery. A pneumatic cuff placed around the ankle was inflated to suprasystolic pressure and subsequently deflated while the onset of flow was detected with a Doppler ultrasound probe (5-10 MHz) placed over the dorsalis pedis artery and posterior tibial artery, thus denoting ankle systolic blood pressure. Brachial artery systolic pressure was assessed by routine manner with use of stethoscope to listen for the first Korotkoff sound or a Doppler probe to listen for the onset of flow during cuff deflation.

The higher of the two values (right and left) for the lower and upper limb were taken as the systolic pressure. ABPI was calculated using the formula:

ABPI = PLeg / PArm

Where $P_{Leg}$ is the systolic blood pressure of dorsalis pedis or posterior tibial arteries and $P_{Arm}$ is the brachial systolic blood pressure. ABPI of 0.9 or less was taken as indicative of peripheral arterial disease

## Results

A total of 200 type 2 diabetes mellitus

[1]Professor, [2]Junior Resident, Era Medical College, Lucknow, Uttar Pradesh; *Corresponding Author
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**Table 1: Comparison of demographic profile, duration of disease and anthropometric parameters**

| Parameter | PAD (n=72) | | No PAD (n=128) | | Statistical Significance 'p' value | |
|---|---|---|---|---|---|---|
| Male: Female | 32 (44.4%) / 40 (55.5%) | | 64 (50.0%) / 64 (50.0%) | | 0.450 | |
| | Mean | SD | Mean | SD | 't' | 'p' |
| Age (Yrs) | 57.01 | 11.79 | 54.65 | 9.68 | 1.531 | 0.127 |
| Duration (Yrs) | 11.11 | 5.84 | 7.33 | 4.31 | 5.227 | <0.001 |
| Height (cm) | 157.35 | 9.72 | 157.65 | 8.70 | -0.225 | 0.822 |
| Weight (kg) | 63.31 | 12.78 | 61.16 | 12.66 | 1.148 | 0.252 |
| Waist (cm) | 91.28 | 11.55 | 88.45 | 11.42 | 1.676 | 0.095 |
| Male | 91.10 | 11.57 | 87.57 | 11.51 | 1.414 | 0.161 |
| Female | 91.43 | 11.66 | 89.33 | 11.36 | 0.906 | 0.367 |
| Hip (cm) | 94.61 | 17.21 | 93.27 | 14.88 | 0.580 | 0.563 |
| Male | 94.59 | 23.40 | 91.55 | 17.27 | 0.722 | 0.472 |
| Female | 94.63 | 10.21 | 94.98 | 11.92 | 0.158 | 0.875 |

**Table 2: Comparison of fasting, post prandial blood sugar and HbA1c between the two groups**

| Parameter | PAD (n=72) | | No PAD (n=128) | | Statistical significance 'p' value | |
|---|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | 't' | 'p' |
| FBS (mg/dl) | 187.90 | 100.64 | 182.15 | 74.29 | 0.461 | 0.645 |
| PPBS (mg/dl) | 280.58 | 121.11 | 253.22 | 85.30 | 1.864 | 0.064 |
| HbA1c (%) | 7.48 | 1.16 | 7.47 | 1.23 | 0.036 | 0.971 |

**Table 3: Comparison of symptom status between the two groups**

| Symptom status | PAD (n=72) | | No PAD (n=128) | | Statistical significance 'p' value | |
|---|---|---|---|---|---|---|
| | No. | % | No. | % | $\chi^2$ | 'p' |
| Symptomatic | 26 | 36.1 | 0 | 0 | 54.13 | <0.001 |
| Asymptomatic | 46 | 63.8 | 128 | 73.6 | | |

**Table 4: Correlation of ABPI with other study parameters in PAD cases (n=72)**

| Parameter | "r" | "p" | Interpretation |
|---|---|---|---|
| Duration of DM | -0.52 | <0.001 | Inverse significant moderate correlation |
| Height | -0.03 | 0.797 | Weak non-significant correlation |
| Weight | -0.38 | 0.001 | Inverse significant mild correlation |
| Waist circumference | -0.35 | 0.003 | Inverse significant mild correlation |
| Males | -0.03 | 0.876 | Inverse non-significant weak correlation |
| Females | -0.55 | <0.001 | Inverse significant moderate correlation |
| Hip circumference | -0.20 | 0.099 | Inverse non-significant weak correlation |
| Males | -0.07 | 0.718 | Inverse non-significant weak correlation |
| Females | -0.45 | 0.003 | Inverse significant mild correlation |
| Fasting blood sugar | -0.26 | 0.028 | Inverse non-significant weak correlation |
| Blood Sugar (PP) | -0.38 | 0.001 | Inverse significant mild correlation |
| HbA1c | 0.11 | 0.351 | Weak non-significant correlation |
| S. Urea | -0.38 | 0.001 | Inverse significant mild correlation |
| S. Creatinine | 0.11 | 0.371 | Weak non-significant correlation |
| Total cholesterol | -0.25 | 0.036 | Inverse non-significant weak correlation |
| Triglyceride | -0.43 | <0.001 | Inverse statistically significant mild correlation |
| LDL | 0.01 | 0.940 | Weak non-significant correlation |
| Spot urine for microalbumin | 0.02 | 0.888 | Weak non-significant correlation |

patients were included in the study. Out of these 72 patients were found to have an ankle brachial pressure index of less than 0.9 and hence diagnosed to be having peripheral arterial disease. The remaining 128 patients did not have peripheral arterial disease.

A multivariate linear regression model was proposed in which ABPI was proposed to be a dependent variable on independent variables – age, sex, duration, waist circumference, hip circumference, post-prandial blood sugar, triglyceride, LDL, spot urine for microalbumin, hypertension, CAD, retinopathy and neuropathy respectively. The model showed a significant negative correlation of duration, waist circumference and hypertensive status with ABPI whereas a significant positive correlation of retinopathy and neuropathy was observed with ABPI. The model had a reasonable explanatory power ($r^2$=0.614), thus inferring that variations in dependent variables correlated with variations in dependent variables to an estimated precision of 61.4%.

## Discussion

Peripheral arterial disease is considered to be a complication of diabetes mellitus, especially among those with prolonged duration of diabetes. It affects the quality of life of patients and is a major source of disability among diabetic patients. Patients of peripheral arterial disease are at a higher risk of coronary artery disease and stroke. In the present study we made an attempt to evaluate the prevalence of PAD among patients with diabetes mellitus.

For this purpose a total of 200 patients of type 2 diabetes mellitus attending the outdoor or indoor wards of the hospital, fulfilling the inclusion criteria for the study were included in the study after obtaining their written and informed consent. PAD was classified on the basis of ankle brachial pressure (ABPI). ABPI is a widely acknowledged criteria for classification of peripheral arterial disease and has quite frequently been used for assessment of peripheral arterial disease among diabetic patients.[2,3] ABPI is an objective criteria which is reliable and widely accepted and validated criteria and in many studies symptom profile has validated the usefulness of this criteria.[4,5]

In the present study, prevalence of PAD was 36% in T2DM patients. The prevalence of PAD among diabetic patients as observed in different studies varies substantially. Using ABPI as criteria its prevalence varies from as low as 3.5% in newly diagnosed diabetics [2] to as high as 42.6%[6] in a study population with median age 52.5 years whereas based on a combination of ABPI and symptomatic criteria, its prevalence could be as high as 87.2%.[7] There are studies that show a variability in ethnicity to be responsible for prevalence of PAD,[3] while some studies indicate that diabetic status itself is responsible for the higher prevalence of PAD.[8,9] The prevalence rates seem to increase with increasing duration of diabetes. In the present study, the prevalence of PAD was found to be 36% using ABPI<0.9 as the criteria. Using similar criteria, findings close to present study were also obtained by Solanki *et al.* (2012)[10] (35%), Mwebaze and Kibirige (2014)[11] (39%) and Ali *et al.* (2012)[12] (39.28%). Other studies reporting prevalence of PAD close

**Table 5: Multivariate analysis – linear regression (n=200)**

| Independent variables | Unstandardized coefficients | | Standardized coefficients | t | Sig. |
|---|---|---|---|---|---|
| | B | Std. error | Beta | | |
| (Constant) | .942 | .081 | | 11.632 | <0.001 |
| Age | .000 | .001 | -.016 | -.235 | 0.814 |
| Sex (Male=1, Female=2) | .007 | .010 | .044 | .711 | 0.478 |
| Duration | -.004 | .001 | -.283 | -3.211 | 0.002 |
| Waist circumference | -.001 | .001 | -.206 | -2.153 | 0.033 |
| Hip circumference | .000 | .000 | .052 | .545 | 0.586 |
| PP blood sugar | $-8.41x10^{-5}$ | .000 | -.103 | -1.603 | 0.111 |
| Triglyceride | $-7.16x10^{-5}$ | .000 | -.102 | -1.640 | 0.103 |
| LDL | $-2.25x10^{-5}$ | .000 | .009 | .135 | 0.892 |
| Spot urine for microalbumin | $-1.99x10^{-5}$ | .000 | -.044 | -.683 | 0.495 |
| Hypertension (Yes=1, No=2) | -.031 | .012 | -.188 | -2.553 | 0.011 |
| TropI (Yes=1, No=2) | -.005 | .013 | -.027 | -.406 | 0.685 |
| Retinopathy (Yes=1, No=2) | .076 | .015 | .332 | 5.000 | <0.001 |
| Neuropathy (Yes=1, No=2) | .027 | .013 | .138 | 2.099 | 0.037 |

$r^2$=0.614

to ours were Akram *et al.* (2011)[13]and Khurana *et al.* (2013)[14] who reported this prevalence to be 31.6% and 33.3% respectively. Among different studies carried out in Indian subcontinent the prevalence of PAD in diabetes ranged from 4.47% to 39.28%[12-14,20] depending upon patient characteristic, geographical differences and other study specific correlates.

In the present study, no significant association of gender was observed with prevalence of PAD though a higher percentage of females (55.5%) had PAD. Female gender has been indicated to be associated with a higher risk of developing PAD in a study,[15] however, this was a complex relationship that showed that progression of disease was just reverse with males who showed a swifter progression towards declining ABPI once the PAD is diagnosed. Some other studies from Indian subcontinent have reported females to be at a higher risk (Premanatha and Raghunath, 2010; Solanki *et al.*, 2012; Ali *et al.*, 2012).[10,12] However, in a study conducted outside the continent, Zitton *et al.* (2012) found males to be at a higher risk. The ethnic differences in determining the gender differences has been highlighted by Eschol *et al.* (2014)[16] who also showed that in Asian Indians, the risk of PAD was higher in females as compared to males. Altogether, the risk of PAD has been cited to be higher in females, especially in Asian Indian population. In the present study we also found females to have a higher relative risk of PAD (RR=1.11) yet we could not establish it statistically.

In the present study, age of patients did not emerge as a significant predictor of PAD. However, several studies have shown age to have a significant association with PAD.[2,5,14,17,19,20]

In the present study, we did not find a significant association of PAD with any of the glycemic control markers studied (fasting blood sugar, PP blood sugar and $HbA_{1c}$ levels). In our opinion, current poor glycemic control adjudged as a risk factor for PAD that has occurred retrospectively is not a justified option unless the current glycemic control is proven to be a reflection of a long-term glycemic status of patient. However, contrary to our view point, a study has shown the current glycemic status to have a significant association with PAD.[20] However, this relationship is not an empirical relationship and most of the studies reviewed by us do not support it as a predictor of PAD.

In the present study duration of diabetes was found to be significantly higher in PAD patients as compared to those not having PAD. This finding is in accordance with the pathogenesis model of microvascular and macrovascular complications as proposed by Fowler[23] who held sustained hyperglycemia to be responsible for both microvascular and macrovascular complications in diabetics. Association between duration of diabetes and PAD has been highlighted by a several studies reviewed by us.[14,18,20,24] Thus duration of disease seems to be an empirical risk factor supported by a large body of previous research and revalidated in the present study too.

In the present study increased lipid levels (total cholesterol and LDL) were found to be significantly associated with PAD. Dyslipidemia has been reported to be significantly associated with PAD in several previous studies too however component of lipid profile showing this association was not same in all the studies.[3,15,20,24] For example, present study did not show triglyceride as a predictor of PAD, however, Rhee *et al.*[15] in their study found triglyceride to be a significant predictor of PAD. On the contrary, another study[24] found three lipid parameters, *viz.*, total cholesterol, HDL and triglyceride to be significantly associated with PAD.

Mean spot urine for microalbumin levels of PAD and non PAD groups too did not show a significant difference in the present study. A relationship between urine albumin levels and PAD among diabetic patients has been shown by Agarwal *et al.* (2012).[24] Similar association was also reported by another study too.[11] However, this finding in general is not empirical in nature and the findings of present study also do not support such relationship.

In the present study, comorbidities like hypertension and CAD did not show a significant association with PAD, however, presence of complications like retinopathy and neuropathy were found to be significantly higher in PAD cases as compared to those not having PAD. Hypertension is a known risk factor for PAD,[21] some of the studies reviewed by us have also shown it to be significantly associated with PAD.[2,3,12,15,19] The inability to find a significant association of hypertension as a risk factor for PAD as observed in the present study could probably be due to a high prevalence of hypertension irrespective of PAD status. In the present study 61.1% of PAD and 52.3% of non PAD patients had hypertension. This widespread prevalence of hypertension in both the groups seems to have taken over the independent effect of hypertension which failed to emerge as a specific characteristic and remained a feature of generalized characteristic of study population.

On the other hand, absence to find a significant association of CAD with PAD could mainly be attributed to the lower prevalence of disease in both the groups or presence of some other factors other than PAD in the non PAD group, contributing towards CAD risk might influence this relationship.

Association of diabetic complications such as retinopathy and neuropathy with PAD has already been documented in some studies[3] and findings of present study substantiated these. Fowler[23] in their study suggested sustained hyperglycemia as the common etiological factor for different micro and macrovascular complications of diabetes, the findings of present study underscored this fact.

In the present study, PAD was categorically defined as ABPI<0.9, however, some of the variables being analyzed, *viz.* duration of diabetes, anthropometric and biochemical measurements were continuous in nature and how does the interplay of these continuous variables with ABPI work among PAD patients, was evaluated by us by studying a linear correlation between ABP and these parameters.

On performing a linear correlation analysis, an inverse mild and significant correlation of ABPI was observed with weight, waist circumference, PP blood sugar, S. Urea and Triglyceride. ABPI also showed an inverse, moderate and significant correlation with duration of diabetes. All these are known risk factors of PAD as illustrated above and the findings of present study show that gradual changes in these parameters also affect the severity of PAD.

In the present study, evaluation of gender-specific correlation of waist and hip circumference with ABPI, revealed that for males the correlation was found to be inverse, weak and non-significant. However, among females, an inverse, moderate and significant correlation with waist circumference and an inverse mild and significant correlation with hip circumference was observed. These findings in turn indicate as to why females are at a higher risk of PAD as proposed by several previous studies.[10,12]

In the present study, on multivariate analysis, duration of diabetes, waist circumference, hypertensive status, presence of diabetic complications, *viz.* retinopathy and neuropathy were significantly associated with ABPI. Several other workers have also illustrated the multivariable model of PAD and findings of present study in consonance with the literature also underscores the multidimensional and multivariable status of PAD.[2,21]

The findings in the present study thus provided an overview of prevalence of PAD among diabetics and various risk factors associated with it. The findings were interesting and useful for preparation of a prevention and management strategy. However, despite being useful the information provided by the present study is not adequate to understand the problem clearly. Further long-term longitudinal study to assess the role of different risk factors and multi-centric studies and systemic reviews/meta analysis are recommended to understand the problem and unravel other unexplored dimensions.

### Conclusions

The results of our study show the prevalence of peripheral arterial disease to be 36% in a teaching hospital. There was a significant correlation between PAD and duration of diabetes, waist circumference, hypertension and microvascular complications A larger study is required to confirm these findings and screening for PAD should be done in all diabetic patients to detect this complication early.

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