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An Observational Study of Prevalence and Risk Factors Associated with Peripheral Vascular Disease

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Abstract
Peripheral vascular disease (PVD) is stenosis of arteries supplying other than those in brain and heart. The prevalence of PVD is very high in general practice and it is under-diagnosed most of the times. Simple investigation tool like Ankle Brachial Index (ABI) can be used to screen patients with high risk factors and diagnose the disease in the early phase itself, so that morbidity associated with the disease can be reduced.
Keywords: *Peripheral vacslar disease, ABI, Risk factors, Prevalence, Screening.*

Introduction

This Peripheral vascular disease (PVD) or peripheral artery occlusive disease is defined as obstruction or deterioration of arteries other than those supplying the heart and those within the brain. It also refers to signs, symptoms or abnormal non invasive tests in one or both legs attributable to obstructive atherosclerotic disease or some other aetiology[1]. There are various risk factors associated with the incidence of PVD and it varies from region to region based on population, lifestyle and environmental changes. The major factors associated are gender, age, smoking, hypertension, diabetes mellitus, renal insufficiency, dyslipidemia, morbid obesity etc,. The underlying pathology is the impairment of circulation and resultant ischemia to the end organ involved[2]. The prevalence of PVD in primary care practices is high, yet physician awareness of the PVD diagnosis is relatively low. A simple ABI measurement identified a large number of patients with previously unrecognised PVD. Atherosclerosis risk factors were very prevalent in PVD patients, but these patients received less intensive treatment for lipid disorders and hypertension and were prescribed anti-platelet therapy less frequently than were patients with CVD. These results showed that under-diagnosis of PVD in primary care practice may be a barrier to effective secondary prevention of the high ischemic cardiovascular risk associated with PVD.[3]

Increased mean levels of low density cholesterol, triglycerides and systolic blood pressure may help to explain the higher prevalence of PVD in diabetic subjects compared with that in normal glucose tolerance subjects.[4] PVD is an important predisposing factor for atherosclerosis, which in

2010 was estimated to affect more than 202 million people worldwide[5]. It affects about 4.3% of Americans aged 40 years and older, reaching 12.29% and 29% in those over 60 and 70 years of age, respectively[6] . Mohan et al have reported the prevalence of PVD in South Indian diabetics to be 3.9%[7]; in Western series the prevalence ranges between 22 – 45%[8]. The prevalence of PVD in diabetics also increases with the duration of diabetes from 15% to 45% at 10 to 20 years respectively after the diagnosis of diabetes[9]. Hyperglycaemia seems to be a stronger risk factor for PVD[10]. Smokingis also a stronger risk factor for PVD[11]. Increased risk of PVD is also associated with the number and duration of smoking[12]. Older age is an important risk factor for PVD in patients with diabetes[13]. Novel risk factors like hyper-homocystineamia have also been proposed in the development of PVD[14]. However a majority of PVD patients reports no symptoms.[15].

Hence it is essential to study the risk factors which are commonly associated with PVD in our region and to identify the severity and outcome of these factors. It has become important to identify the disease in its initial stage and to prevent the adverse outcome of the disease by prior screening and proper history eliciting. Encouraging vulnerable patients to avoid the modifiable risk factors which cause adverse outcomes and to lead a disease free survival is our main goal.

Material and Methods

This was a Cross sectional study with duration from December 2017 to June 2019. Two approaches to sample size was made. One to detect a 45%[1] prevalence of PVD among adults aged >40 years of age, and another to detect an odds ratio of 2.0 with the prevalence of PVD and associated factors. A choice will be made based on clinic attendance, patient and consent given by them during the study period. In order to detect a hospital based prevalence of 45% with 5% absolute precision (40% to 50%) and 95% confidence interval, Sample size n = $[N*p(1-p)]/ [(d^2/Z^2_{1-\alpha/2}*((N-1)+p*(1-p))]$

Population size (for finite population correction factor or fpc) (N): 100000

Hypothesised % frequency of outcome factor in the population (p): 45%+/-5

Confidence limits as % of 100(absolute +/- %)(d): 5%

Sample size n = $[100000*0.45(0.55)]/ [(0.05)^2/1.96^2*(100000-1)+0.45*(0.55)]$ = 379

For association between prevalence and predisposing factors, with an odds ratio of 2.0 the samples size[2] required is

The standard normal deviate for $\alpha = Z_\alpha = 1.960$

The standard normal deviate for $\beta = Z_\beta = 0.842$

Pooled proportion = $P = (q_1*P_1) + (q_0*P_0) = 0.373$

$A = Z_\alpha\sqrt{P(1-P)(1/q^1 + 1/q_0)} = 1.905$

$B = Z_\beta\sqrt{P_1(1-P_1)(1/q_1) + P_0(1-P_0)(1/q_0)} = 0.813$

$C = (P_1-P_0)^2 = 0.026$

Total group size = $(A+B)^2/C = 283$

Inclusion Criteria

All Patients of age >40 years who are diagnosed as peripheral vascular disease by ABI

Exclusion Criteria

- Patients with venous insufficiency and venous ulcers.
- Patient with previous history of autoimmune disease.
- Those who refuse to be a part of the study.

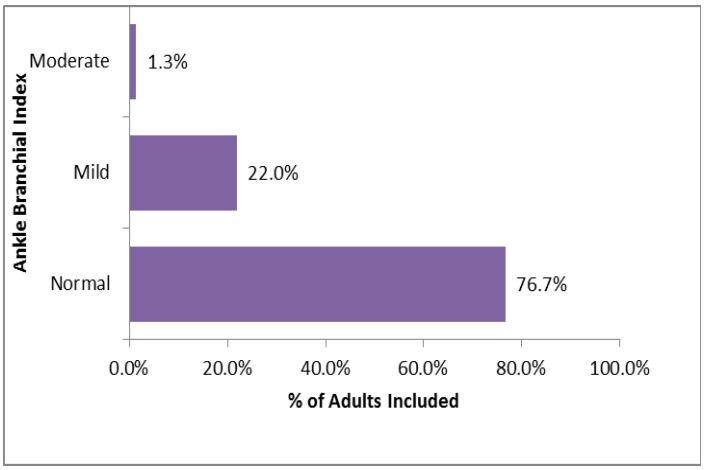
Methodology

After getting consent, all patients of age >40 years will be screened by ankle brachial index. Those who are diagnosed to have peripheral vascular disease will be examined clinically after taking a detailed history. A questionnaire will be asked to the patient. Finally a master chart will be made by which various risk will be assessed statistically.

A total of 537 were screened during December 2017 to June 2019, for PVD using ankle branchial index. Prevalence with 95% confidence interval (with normal approximation) was calculated. All positive cases (n-130) and 282 negative for PVD, where history and complete laboratory tests were available was included for risk factor analysis.

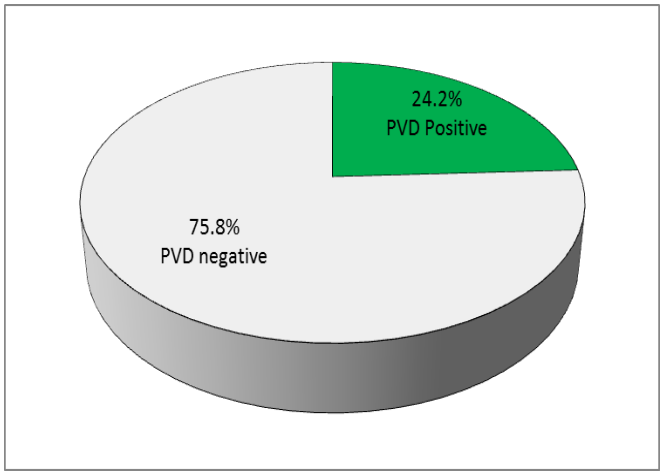
Results

Figure 1 Ankle Brachial Index values among those Screened



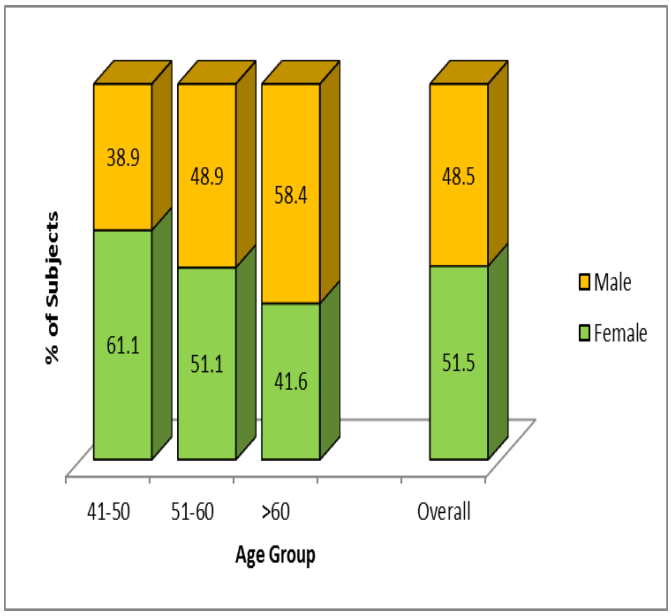
ABI was done for all of the 537 adults screened. Classification of an adults as having PVD was done based on ABI <0.9. Based on this definition, the number of adults classified as positive for PVD was 130. Out of this, about one-fifth (22.0%, n-121) were categorised as having mild and 9(1.3%) as moderate.

Figure 2 Prevalence of Peripheral Vascular Disease



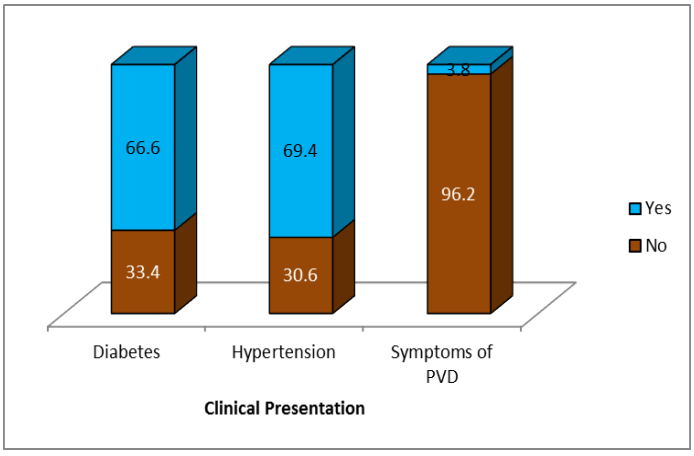
Prevalence of PVD among adults >40 years of age attending a general surgery department is 24.2% [95% CI: 20.6, 27.8].

Figure 3 Age and Sex Distribution



The subjects were aged 56.2±8.8 years ranging from 41 to 94 years. There were more number of adults in the 51-60 (45.5%) years age group compared to 41-50 (28.8%) and those aged >60 years (25.8%). The graph depicts that- about 58.4% of male over 60 years of age were having PVD (Figure3).

Figure 4 Presentation of Systemic illness & Symptoms of the Adults in the Study



Two-thirds (66.6%, n-261) of the adults reported of having diabetes during the time of screening. Similarly, a significant (69.4%) proportion reported hypertension during history taking. Almost all (96.2%) were asymptomatic to PVD (Figure4).

Table 1 Smoking and PVD

Smoking	PVD		p value	OR[95% CI]
	Absent	Present		
No	83.5%	16.5%	<0.0001	11.2 [6.8,18.4]
Yes	31.2%	68.8%		

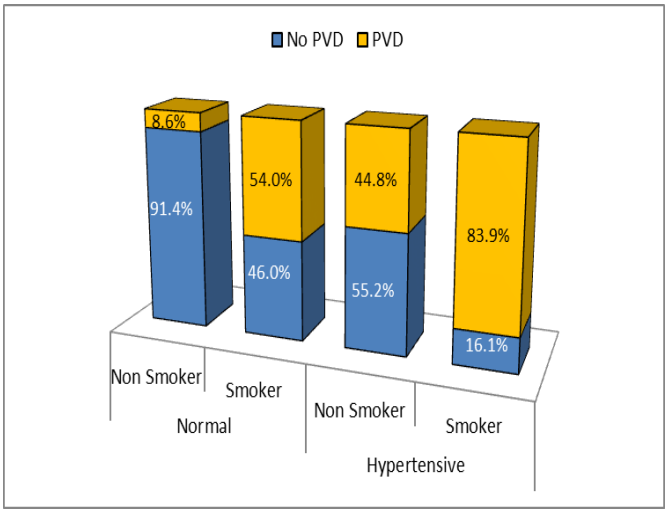
An adult reporting of smoking increased (11.2 times) his/her likelihood of being positive for PVD. The proportion of PVD cases among smokers was 68.8% compared to 16.5% among non-smokers and the difference was statistically significant (p<0.0001) (Table1).

Table 2 Mean Smoking Pack Years and PVD

PVD	N	Smoking Pack years			p value
		Mean	SD	Absolute difference	
Absent	262	1.1	2.7	8.2	<0.0001
Present	130	9.37	7.5		

The intensity of smoking habit as recorded by mean pack years (1.1±2.7) was higher by 8 pack years among PVD cases compared to those who were negative for PVD (9.4±7.5) by ABI (Table2)

Figure 5. Hypertension and Smoking with PVD Prevalence



Hypertension and smoking was combined as a variable and was associated with PVD status (Figure 5). Smokers with history of hypertension had the highest prevalence of PVD 83.9%, compared to a mere 8.6% among non-smokers with no history of hypertension. Compared to a Non Hypertensive Non Smoker, a Non Hypertensive Smoker had 12.4 times and a Hypertensive Smoker had 55.2 times risk of having PVD. There was a statistically significant difference (p-<0.0001) in the PVD proportion between the categories.

Table 3 Laboratory Investigations

Parameter	Mean	SD	Minimum	Maximum
HDL	34.3	5.7	24.0	64.0
TGL	158.7	37.2	84.0	302.0
Urea	23.8	5.0	17.0	54.0
Creatinine	0.7	0.2	0.4	2.1

Laboratory investigations revealed an average HDL of 34.3±5.7 with a maximum of 64.0mg/dL (Table3). The triglyceride levels ranged from 84.0 to 32.0 mg/dL with an average of 158.7 mg/dL. Blood urea was 23.8±5.0 with a maximum of 54.0 mg/dL. Creatinine was 0.7±0.2 mg/dL with a maximum of 2.1. C reactive protein was elevated in less than one-fifth (18.6%, n-73) of the adults included. Coronary artery disease was present in 96 (24.5%) adults.

Table 4 Age and PVD

PVD	n	Age			p value
		Mean	Std. Deviation	Absolute difference	
Absent	262	53.6	7.3	7.9	<0.0001
Present	130	61.5	9.3		

The mean age of those positive (53.6±7.3 years) for PVD was higher than those who were negative (Table 4). The absolute difference between the two mean values was about 8 years and the difference was statistically significant (p<0.0001), suggestive of higher age being a risk factor associated with PVD.

Table 5 Gender and PVD

Sex	PVD		p value	OR[95% CI]
	Absent	Present		
Female	80.2%	19.8%	<0.0001	3.6 [2.3,5.7]
Male	52.6%	47.4%		

There was a marked difference in the proportion of PVD among female adults (19.8%) compared to their male counterparts (47.4%). This statistically significant (p<0.0001) difference in proportion is indicative of men being 3.6 times highly likely to have PVD compared to their women (Table5)

Table 6. History of DM and PVD

Self Reported DM	PVD		p value	OR[95% CI]
	Absent	Present		
No	82.4%	17.6%	<0.0001	8.4 [5.2,13.5]
Yes	35.9%	64.1%		

An adult reporting of having history of DM increased (8.4 times) his/her likelihood of being positive for PVD. The proportion of PVD cases among DM cases was 64.4% compared to 17.6% among non-DM adults and the difference was statistically significant (p<0.0001) (Table6).

Table7. History of Hypertension and PVD

Self-reported HT	PVD		p value	OR[95% CI]
	Absent	Present		
No	80.9%	19.1%	<0.0001	7.9 [4.9,12.7]
Yes	35.0%	65.0%		

An adult reporting of having history of HT increases (7.9 times) his/her likelihood of being positive for PVD. The proportion of PVD cases among HT cases was 65.0% compared to 19.1% among non-DM adults and the difference was statistically significant (p<0.0001) (Table7).

Table 8. Clinical Symptoms and PVD

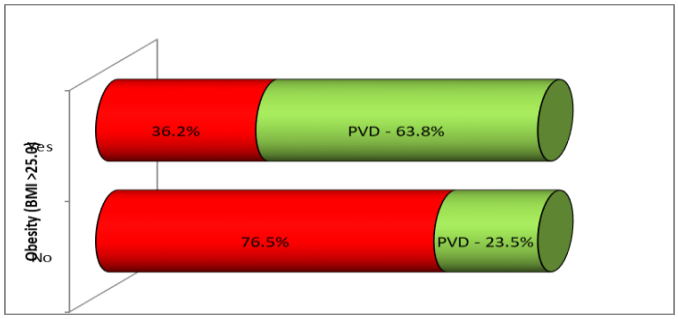
Symptoms	PVD		p value	OR[95% CI]
	Absent	Present		
Present		100.0%	<0.0001	70.8 [4.2,1187.6]
Absent	69.5%	30.5%		

Having clinical symptoms such as claudication pain, ulcer or tissue loss, increased the likelihood of having PVD by 70.8 times compared to those who did not show any. There is a statistically significant (p<0.0001) association between presence of symptoms and PVD.

Table 9 BMI and PVD

BMI	PVD		p value
	Absent	Present	
<18.5	100.0%		<0.0001
18.5-25.0	76.4%	23.6%	
>25	36.2%	63.8%	

Figure 6. BMI and PVD



There was a statistically significant difference in the BMI status of an adult and his/her PVD status (p<0.0001) (Table9). All adults who had BMI less than 18.5 were negative for PVD, while close to one-fourth (23.6%) who were in the 18.5 – 25.0 category were positive for PVD. Two-thirds (63.8%) adults who were obese by having a BMI >25.0 were positive for PVD. Those who were obese (BMI>25.0) were 5.7 times more likely to be positive for PVD compared to those whose BMI was <=25.

Table 10 HDL/Triglyceride

Parameter	n	Mean	SD	Absolute difference	p value
HDL					
PVD – Absent	262	35.7	6.1	4.2	<0.0001
PVD – Present	130	31.4	3.6		
Triglyceride					
PVD - Absent	262	143.8	16.9	44.9	<0.0001
PVD - Present	130	188.7	47.5		

Mean HDL was lower (31.4±3.6) among positive cases compared to those who were negative (35.7±6.1). There was a difference of 4.2 mg/dL between the mean values of HDL when compared to those positive for PVD and those that were not (Table 10). The difference in mean HDL being statistically significant (p<0.0001) suggest low HDL being a risk factor for PVD. Mean TGL was lower (143.8±16.9) among negative cases compared to those who were positive (188.7±47.5) for PVD. The difference of 44.9 mg/dL between the mean TGL values was statistically significant (p<0.0001) suggest high TGL being a risk factor for PVD.

Table11. Renal parameters and PVD

Blood Urea					
PVD - Absent	262	21.5	2.2	6.9	<0.0001
PVD - Present	130	28.5	5.7		
Creatinine					
PVD - Absent	262	0.7	0.1	0.1	<0.0001
PVD - Present	130	0.8	0.2		

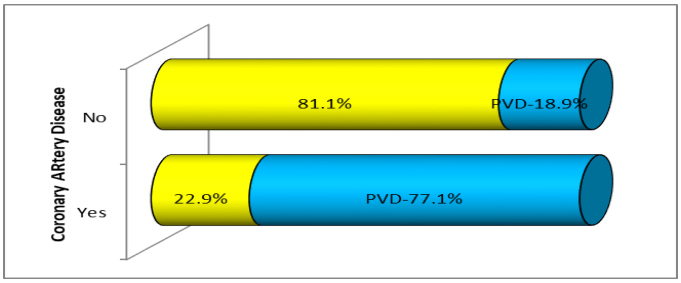
Mean blood urea was lower (21.5±2.2) among negative cases compared to those who were positive (28.5±5.7) for PVD. There was a difference of 6.9 mg/dL between the mean values of blood urea when compared to those positive for PVD and those that were not (Table11). The difference in mean blood urea being statistically significant (p<0.0001). Mean creatinine value was slightly higher (0.8±0.2) among positive cases compared to those who were negative (0.7±0.1). The difference in mean creatinine values was statistically significant (p<0.0001).

Table 12 CRP and PVD

C reactive Protein	PVD		p value	OR[95% CI]
	Absent	Present		
Elevated	21.9%	78.1%	<0.0001	12.0[6.5,22.1]
Normal	77.1%	22.9%		

A laboratory report suggesting elevated c reactive protein increases (12.0 times) an adult's likelihood of being positive for PVD. The proportion of PVD cases among elevated c reactive protein cases was 78.1% compared to 22.9% among normal adults and the difference was statistically significant (p<0.0001) (Table12).

Figure7. CAD and PVD



A laboratory report suggesting CAD increases (14.4 times) an adult's likelihood of being positive for PVD. The proportion of PVD cases among CAD patients cases was 77.1% compared to 18.9% among normal adults and the difference was statistically significant (p<0.0001) (Figure7).

Table13. Multivariate Logistic Regression Analysis of Perivascular Disease Status with Demographic, Lifestyle choices and Laboratory Parameters

Independent Variables	Odds Ratio	95.0% C.I. for OR		p value
		Lower Limit	Upper Limit	
Age	1.1	1.01	1.3	0.023
Diabetes				
No	1.0			
Yes	12.8	2.4	69.2	0.003
Hypertension*Smoking				
No HT No Smoker	1.0			
No HT Smoker	14.0	1.6	125.8	0.001
HT Smoker	54.5	5.6	533.5	
HT Non Smoker	42.7	3.9	463.9	
Obesity				
No	1.0			
Yes	10.3	1.6	66.7	0.015
HDL	0.8	0.7	0.97	0.024
TGL	1.1	1.0	1.1	<0.0001
Coronary Artery Disease				
No	1.0			
Yes	117.1	13.6	1011	<0.0001
Blood Urea	1.8	1.4	2.4	<0.0001

Given above (Table13) is the multivariate odds ratio with 95% CI of the statistically significantly contributing variables to the PVD status. One year increase in age among adults >40, increased the risk of having PVD by 1.1 times. An adult with diabetic history accessing a general surgery department had 12.8 times more likely to have PVD in reference to a person without history of diabetes. A marked increase in the odds were noticed in the combined variable of hypertension and smoking. Compared to non hypertensive-non smoker, a hypertensive-smoker had 54.5 times and a hypertensive- non-smoker had 42.7 times more likelihood of having PVD. A smoking history is confounded by history of hypertension significantly indicative of PVD.

Conclusions

Prevalence of peripheral vascular disease is about 24.2% in the present study. This has to be viewed seriously considering the huge type 2 diabetic and hypertensive population. Thus a significant proportion of elderly patients with multiple co-morbidities are affected by PVD, and hence due importance to be given for screening and prevention of PVD among these high risk populations. About 69.5% of the PVD patients are totally asymptomatic and hence the need for active screening with estimation of ABI is to be done annually for all elderly high risk populations. This is important for prevention of lower extremity amputation. Central obesity, uncontrolled diabetes, hypertension, high LDL cholesterol, high triglycerides, low-HDL cholesterol and smoking are the modifiable risk factors associated with development of PVD. Advancing age and male gender were found to be the non modifiable risk factors for development of PVD. Concordance rate for co-morbid CAD was very high (>70%) in PVD patients and hence active screening for CAD in all the PVD patients has to be done, even if there is no CAD symptoms. PVD has to be given due importance, and ABI has to be estimated in all elderly patients, particularly those with high risk life style. Low ABI is associated with cardiovascular complications.

Thus, ABI is a good indicator of underlying complications of diabetes mellitus, particularly CAD. ABI estimation is a non invasive cheap, bed-side, and rapid test with a high degree of validity and predictive power and which does not need specially trained persons or costly equipments. Hence, ABI estimation should be done annually for all elderly patients, particularly those with high-risk life style habits for a disease free survival.

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