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 vascular 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
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 = \[\frac{100000*0.45(0.55)/[(0.05)^2/1.96^2*(100000-1)+0.45*(0.55)]}{1/2}\] = 379
For association between prevalence and predisposing factors, with an odds ratio of 2.0 the samples size² required is
The standard normal deviate for \(\alpha = Z_\alpha = 1.960\)
The standard normal deviate for \(\beta = Z_\beta = 0.842\)
Pooled proportion = \(P = (q_1*P_1) + (q_0*P_0) = 0.373\)
\(A = Z_\alpha\sqrt{P(1-P)/(1/q_1 + 1/q_0)} = 1.905\)
\(B = Z_\beta\sqrt{P(1-P)(1/q_1) + P_0(1-P_0)(1/q_0)} = 0.813\)
\(C = (P_1-P_0)^2 = 0.026\)
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).
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 1 Smoking and PVD

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

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)

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 |     |         |

A hypertensive smoker had 5.2 times risk for having PVD compared to a non-hypertensive 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.
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 (Table 5).

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) (Table 6).

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-HT adults and the difference was statistically significant (p<0.0001) (Table 7).

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%   |            |

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%   |

Table 7. 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%   |

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%   |

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%   |

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.

There was a statistically significant difference in the BMI status of an adult and his/her PVD status (p<0.0001) (Table 9). 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.
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.

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).

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).

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).

| 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|                     |         |

| Table 12 CRP and PVD |
|----------------------|
| C reactive Protein    | PVD   | OR[95% CI] |
| Absent               | Present | p value |
| Elevated             | 21.9%  | 78.1%    | <0.0001 | 12.0[6.5,22.1] |
| Normal               | 77.1%  | 22.9%    |         |               |

| 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 |     |         |
Table 13. 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 |
|-----------------------|------------|-------------------|---------|
| **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 Disease**  |            |                   |         |
| No                    | 1.0        |                   |         |
| Yes                   | 117.1      | 13.6 - 1011       | <0.0001 |
| **Blood Urea**        | 1.8        | 1.4 - 2.4         | <0.0001 |

Given above (Table 13) 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, bedside, 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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