Original Research Article

A study of the prevalence and risk factors associated with peripheral vascular disease in type 2 diabetes mellitus patients in Government Dharmapuri Medical College Hospital, Dharmapuri

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Abstract

Introduction: Peripheral vascular disease (PVD) is one of the significant Macro vascular complications of type 2 diabetes mellitus. Peripheral vascular disease assumes importance, for prevention of morbidity and mortality related to diabetic foot. PVD is the single most important factor which raises the incidence of leg amputation risk in type 2 DM patients. While peripheral neuropathy alone leads to, trophic ulcer which has a chronic indolent course provided super added infection is prevented and controlled, the presence of PVD leads to the ischemic foot which leads to rapid spread of infection.

The aim of the study: To investigate the prevalence of PVD among type 2 diabetes patients, to assess the risk factors associated with the development of pvd.to correlate the prevalence of cardiovascular risk factors and vascular complications of type 2 diabetes patients.

Materials and Methods: Cross sectional observational analytical study was conducted. Patients were interviewed with a special note on elicitation of history regarding symptoms of PVD, in the form of intermittent claudication, Ischemic rest pain, history of foot ulcers in the past and present. Smoking was recorded in pack-years of cigarettes smoked. Duration of diabetes since diagnosis was recorded and they were grouped accordingly. The anthropometric measurements were recorded and the body-

mass index was calculated. Waist-hip ratio was also recorded. The blood pressure was recorded in both the upper limbs and both the lower legs using the standard B.P cuff. An comprehensive physical examination was done and findings recorded. Special importance was given to foot examination. Peripheral neuropathy assessment was done using Simmel-Weiss monofilament testing and timed vibration sense perception recordings. Symptoms of peripheral neuropathy were also noted.

Results: The duration of diabetes ranged from newly detected to 28 years, with a mean duration of 8.2 years $\pm$ 6.24 S.D. For patients affected with PVD, the duration of diabetes was found to be longer than others. The mean FPG for the PVD sub group is 173.6mg % $\pm$ 34.9 SD, while for the other subjects the mean FPG is 151.8 mg % $\pm$ 36.3 SD and the difference was statistically significant. (P = 0.006). Among the hypertensive diabetic subjects (n=57), 26.3% had peripheral vascular disease and the prevalence of PVD among normotensive diabetes subjects (n = 55) was 9.1% (P = 0.0329). Smokers among Hypertensive Diabetic males had 58.3% prevalence of PVD (ABI < 1) compared to 14.3% among non – smoking Hypertensive Diabetic males. Difference in the lipid parameters above was all statistically significant. This shows that individuals with a triad of increased LDL – cholesterol, lower HDL – cholesterol (Higher LDL / HDL ratio) and increased triglycerides were more at higher risk for peripheral vascular disease.

Conclusion: As the duration of diabetes increased, the risk of PVD increased. There was relatively poor glycemic control in the PVD sub-set. Hypertension, when associated with Type2 Diabetes raised the risk of PVD nearly threefold. The duration of Hypertension also significantly correlated with the risk of PVD.

Key words

Poor Glycemic Control, Hypertension, Peripheral Vascular Disease, Dyslipidemia.

Introduction

Several population studies have shown that diabetes is a strong risk factor for PVD [4]. In both Diabetic and non-diabetic subjects the prevalence of PVD increases markedly with advancing age. In several studies PVD was found in approximately 20% of the diabetic patients [1]. In the United Kingdom prospective diabetes study (UKPDS) PVD was found in 11% of patients after a follow up period of 6 years from the time of diagnosis of type 2 diabetes. It can be safely concluded based on these population studies that PVD is a highly prevalent disorder, in the elderly diabetic patient [2]. Unfortunately, the awareness of the physicians that these patients have PVD is low, resulting in inadequate preventive measures for reducing lower extremity amputation. Several epidemiological studies and in the UKPDS study symptoms of claudication were reported in only about 25% of the patients with an ABI of <0.8, indicating that for each patient with claudication there are three patients with silent PVD [3]. The reason for asymptomatic PVD could be due to concomitant neuropathy and many elderly patients do not walk far enough to experience symptoms of intermittent claudication. In diabetic patients, the atherosclerotic changes in PVD seem to be more extensive and more aggressive, resulting in faster progression of disease. In diabetic patients with critical limb ischemia, the risk of limb loss is markedly increased, gangrene being reported to develop in 40% of such patients. Diabetes is the leading cause of non-traumatic lower limb amputation and the major reasons for a lower extremity amputation are PVD and / or a deep infection. The anterior tibial, posterior tibial followed next by the peroneal arteries are the common arteries occluded in type 2 diabetic subjects [4].

Involvement of deep formal artery and arteries below the knee is the common site of PVD in diabetic subjects with relative sparing of arteries of foot, rendering these distal segments suitable for by-pass surgery [5]. Why atherosclerosis in

diabetic subjects preferably affects lower leg below knee arteries, is at present not well under stood. It is important to realize that foot vessels Dorsalis pedis, plantar and tarsal arteries are spared usually in diabetes subjects with PVD. Strandness and coworkers performed a blinded histological review of amputation specimens prepared with periodic acid Schiff staining and demonstrated no difference between diabetic and non-diabetic specimens. Both groups had similar patterns of atherosclerosis with a paucity of occlusive disease at the arteriolar level. Barner and associates measured the femoro-popliteal bye-pass grafts blood flow rates as a measure of vessel reactivity after infusion of papaverine in to the patient's vascular out flow bed and they recorded no difference between diabetes and non-diabetics [6]. These studies have reinforced the newer theory that a unique small vessel disease does not exist in diabetic foot patients. In the past based on the false presumption that small vessel disease at the level of small foot arteries and arteriolar level, diabetics were not treated as aggressively with revascularization as is now standard. Hyperglycemia seems to be a stronger risk factor for PVD. Inkpad's, each 1% increment in HbA1c was associated with a 28% increase in the risk for PVD [7]. Smoking is also a stronger risk factor for PVD. Both hyperglycemia and smoking can result in the formation of advanced glycation end products, and in enhanced oxidative stress within the vessel wall, resulting in development and progression of PVD. The Framingham offspring study examined 1554 males and 1759 females for PVD. In this population based study the odds ratio for PVD was 2.3 among diabetic vs non-diabetic patients. The Framingham heart study found a strong relationship between the number of cigarettes smoked and the incidence of intermittent claudication and a multivariate analysis identified smoking as a strong single risk factor for development of symptomatic obstructive arterial disease. The occurrence of intermittent claudication is twice as frequent in smokers as non-smokers. In the EDINBURG artery study PVD prevalence strongly and positively related to life time cigarette smoking. Diabetic PVD is associated with an atherogenic dyslipidemia, which is characterized by elevated triglycerides, low level of HDL cholesterol and increased number of small dense LDL particles and elevated LP(a). The association of hypercholesterolemia with atherosclerosis of the lower extremities has been known for 60 years [8]. The Edinburgh artery study reported a higher prevalence of PVD in association with higher serum cholesterol and lower HDL cholesterol in multiple logistic regression analysis. The cardiovascular health study reached similar conclusions among its sample of 5084 subjects aged 65 years or older with PVD defined as an, ABI less than 0.9 [9].

Materials and methods

112 randomly chosen type 2 diabetic subjects attending our Government Dhampuri Medical College Hospital, OP from May 2016 2008 to July 2017 had formed the study sample. Patients who had other potential causes for PVD other than diabetes related factors were excluded from the study.

The exclusion criteria used were:

- Clinical evidence of thromboangitisobliterans.
- Suspected arteritis subjects.
- Patients suffering from hypercoagulable states including hematologic diseases.
- Hypothyroidism
- Collagen vascular disorders
- Valvular heart disease

Duration of diabetes since diagnosis was recorded and they were grouped accordingly. The anthropometric measurements were recorded and the body-mass index was calculated. Waist-hip ratio was also recorded. The blood pressure was recorded in both the upper limbs and both the lower legs using the standard B.P cuff. Hypertension was detected if the upper limb BP was 140/90 or above as per JNC VII norms and if they are already documented to be hypertensive or on anti-hypertensive medications. If patient is a known hypertensive, the duration of hyper tension since diagnosis was

also noted. ABI is calculated by dividing this ankle pressure by the Doppler pressure measured similarly in the right brachial artery. The two consecutive readings were taken. The value for the worse leg was taken in to account.

Statistical Tools

Using this software, range, frequencies, percentages, means, standard deviations, chi square and 'p' values were calculated. Kruskal Wallis chi-square test was used to test the significance of difference between quantitative variables and Yate's test for qualitative variables. A 'p' value less than 0.05 was taken to denote significant relationship.

Results

Fasting plasma glucose was Bio- chemically analyzed for all the subjects. And it ranged from 88 – 290 mg% with a mean FPG of 155.7 mg % ± 36.9 S.D. The control of diabetes was relatively poor among the subjects with PVD, when compared with the rest of the study group. The mean FPG for the PVD sub group was 173.6mg % ± 34.9 SD, while for the other subjects the mean FPG was 151.8 mg % ± 36.3 SD and the difference was statistically significant. (P = 0.006) as per **Table – 1**.

Table - 1: Fasting Plasma Glucose and Lipid Profile parameters.

Parameters	Range in mg%	Mean	SD
F.P. Glucose	88-290	155.7	36.9
LDL	85-164	124.2	16.2
HDL	25-64	33.9	6.1
TGL	84-302	164.9	35.8

Among the hypertensive diabetic subjects, the mean duration of hypertension among PVD subjects was 10.83 year ± 7.79 SD, which was significantly higher than the non – PVD sub group mean of 5.87 year ± 4.75 SD (P = 0.0165) There was a positive linear correlation between the duration of smoking (In pack - years) and risk of development of PVD. Multivariate analysis showed a significant higher risk of PVD among smoking Hypertensive Diabetic males, compared to nonsmoking Hypertensive Diabetic males. Smokers among Hypertensive Diabetic males had 58.3% prevalence of PVD (ABI < 1) compared to 14.3% among non – smoking Hypertensive Diabetic males as per **Table – 2**.

Table - 2: Other Qualitative Parameter among the patients.

Parameter	Cases	
	No	%
Smoking among males (65)		
Smokers	27	41.5
Non-Smokers	38	58.5
Hyper Tension		
Present	57	50.9
Absent	55	49.1
Symptoms of PVD		
Symptomatic	11	9.8
Asymptomatic	101	90.2
PVD		
Present	20	17.9
Absent	92	82.1
CEVD		
Present	7	6.3
Absent	105	93.8
CAD		
Present	23	20.5
Absent	89	79.5
Nephropathy		
Yes	8	7.1
No	104	92.9
Fundus		
Normal	86	76.8
Abnormal	26	23.2
Neuropathy		
Yes	86	76.8
No	26	23.2

One patient presented with intermittent claudication symptoms, but the ABI was more than 1, the patient was referred for further investigations to vascular surgery department, in the form of post – exercise recording of ABI, duplex Doppler scanning of lower limb vessels, X-ray of legs for screening of extensive moncke bergs medial calcification of arteries.

Interesting observation to note is that patients with mild PVD (ABI > 0.8 to < 1), had relatively no symptoms, and as the ABI values decline, there was a trend towards development of symptoms. But, however, there were also asymptomatic patients even in the severe PVD group (**Table – 3**).

Table – 3: Severity of PVD among the subjects.

Severity of PVD	**Cases**	
	No	**%**
Moderate (ABI – 0.6 to <1)	15	13.4
Severe (ABI < 0.6)	5	4.5
Normal (ABI >1)	92	82.1
Total	112	100

Discussion

Prevalence of peripheral vascular disease in this study was 17.9% which was comparable to the prevalence as described in other studies. A meta-analysis has presented age and gender adjusted results of the prevalence of PVD ranging from 5.5% to 26.7% [10]. In the UKPDS PVD was rare at the time of diagnosis but after 6 years of follow up 11% of the patients had PVD [11]. Thus, it is to be noted that PVD is a significant complication of type 2 diabetes. The symptoms of intermittent claudication are seen only in 50% of the patients affected with PVD in this study. It is comparable with other studies, where the prevalence of symptoms among PVD patients was only approximately 50%. The prevalence of PVD was 20% among males and 14.9% among females in the study group. Diabetes seems to repeal the protective effect of female gender on PVD when compared to non-diabetics as seen in other epidemiological studies [12]. The higher prevalence among males could be partially due to smoking. As the duration of diabetes increased, the risk of PVD increased in the study group. The large multi centric UKPDS study also has categorically proved that the duration of hyperglycemia has a definite role in PVD. Fasting plasma glucose was higher among the PVD subset, indicating relatively poor glycemic control when compared to the rest of the study group. In the large multi centric UKPDS, as the HBA1C increased by every 1%, there was an increase of 28% in PVD prevalence [13]. Tight glycemic control in general reduces peripheral arterial disease and risk of amputation. Hypertension associated with diabetes raised the risk of PVD, nearly threefold in the study subjects. Another interesting observation noted in the study group was that the duration of hypertension also significantly correlated with the risk of PVD. In the cardiovascular health study, hypertensive patients had a 50% increased risk of PVD, in a multivariate analysis adjusted for age, smoking, diabetes dyslipidemia. In the study group, smokers had more than fourfold increased risk of having PVD, compared to non-smokers [14]. Thus smoking was found to be the single most important risk factor in comparison to other risk factors. A multivariate analysis by kannel, identified smoking as the strongest risk factor for development of PVD. In this study, smoking in a diabetic hypertensive exponentially increased the risk of PVD. Smoking is the single most modifiable risk factor and hence smokers must be actively counseled for cessation of smoking. In the study group, LDL cholesterol and serum triglycerides was relatively higher for PVD subset and the HDL cholesterol was low [15]. The cardiovascular health study and the Edinburg artery study reported higher prevalence of PVD in association with higher LDL, and lower HDL cholesterol in multiple logistic regression analysis. Type 2 Diabetic patients are more prone to have silent CAD as well as PVD. Co-morbid coronary artery disease had a higher concordance rate (>50%) in the study group subjects affected with PVD [16]. This indicates that an atherosclerotic disease in peripheral arteries should be considered as an indicator of generalized cardio-vascular disease and active secondary preventive measures to be started for prevention of further cardiovascular events. It is imperative to record the ABI – periodically in all Type 2 diabetics, since an ABI of <1 is CAD equivalent [17]. This assumes importance since many of the patients with ABI < 1 are asymptomatic. The prevalence of PVD was 42.5% among patients with diabetic retinopathy in the study group and this underscores the

importance of screening for PVD among patients with diabetic retinopathy [18].

Conclusion

Prevalence of peripheral vascular disease is about 18% in the present study. This must be viewed seriously considering the huge type 2 diabetic population. Thus, a significant proportion of type 2 diabetic subjects are affected by PVD, and hence due importance to be given for screening and prevention of PVD among type 2 diabetes patients. Central obesity, Uncontrolled hyperglycemia, 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 [19, 20].

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