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Prevalence of Peripheral arterial disease in patients of acute coronary syndrome, and its correlation with various established risk factors for atherosclerosis

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Abstract

Background: *Peripheral arterial disease (PAD) is considered as peripheral equivalent of coronary artery disease (CAD). Few studies from India have shown a low and variable prevalence of PAD in high risk population e.g. diabetes but data on patients with clinically manifest CAD is few. This study was done to assess Prevalence of PAD in patients of acute coronary syndrome (ACS), and its co-relation with various established risk factors for atherosclerosis.*

Methods: *Study was done on 120 patients admitted to our hospital with acute coronary syndrome. A detailed medical history and examination was done. High ankle-brachial index (ABI) was calculated with a hand held doppler. PAD was considered present if ABI was less than 0.9.*

Results: *Prevalence of PAD in patients of ACS was 8.33% (n=10) and was highest among patients over 50 years of age (mean age 57.98± 9.99). PAD were more in male (80%) as compared to female (20%) (NS=non significant). 50% had diabetics whereas 30.9% of the patients without PAD had diabetes mellitus (NS), 60% were smokers compared to 23.63% of the patients without PAD had smoker (S=significant), 30% were hypertension compared to 26.3 % of the patients without PAD had hypertension (NS). There were no significant differences in the lipid profile of the two groups.*

Conclusion: *The prevalence of PAD is low even in patients of CAD. Hence PAD screening may not be beneficial to predict cardiovascular events in high risk patients.*

Keywords: *Peripheral arterial disease, acute coronary syndrome, atherosclerosis, ankle-brachial index, diabetes mellitus, hypertension, smoker.*

Introduction

Atherosclerosis is one of the most important and common cause of the death and disability throughout the world. Throughout the last half of the past century, coronary artery atherosclerosis has been a major focus for basic and clinical investigations. Peripheral Arterial Disease (PAD) refers to atherosclerotic and thromboembolic processes that affect the aorta, its visceral arterial branches and arteries of the lower extremities[1]. PAD is a systemic atherosclerotic process associated with high morbidity and mortality and significant impairment of quality of life, yet it remains under diagnosed and under treated. The evidence that both symptomatic and asymptomatic PAD represent an independent risk for cardiovascular morbidity and mortality[2] has triggered resurgence in epidemiological and clinical interest in PAD. The prevalence of coronary artery disease (CAD) is on the rise in the developing world including India. Approximately 30% of patients with CAD may have PAD as the only clinical manifestation of cardiovascular disease (CVD)[3,4]. Traditional risk factors for PAD are similar to those that lead to atherosclerosis in the carotid, coronary and other vascular beds.

Traditional risk factors for peripheral atherosclerosis have been well defined[5,6]. These risk factors include: increasing age, smoking, diabetes and glycemic control, hypertension, fibrinogen levels, hyperlipidemia, low HDL, that are same as for CAD. Negative risk factors include regular physical activity and moderate alcohol consumption[5,7,8-10].

For epidemiological purposes, the most useful noninvasive test to screen for PAD is the ankle-brachial index (ABI) measured by a hand-held Doppler probe. ABI is the ratio between systolic BP in the ankle and systolic BP in the arm[13]. The lower the ABI, the higher the prevalence of 3 or 4 vessel CAD and the lower the prevalence of 1 vessel CAD[14]. In clinical terms, PAD is evident as intermittent claudication (IC) which is defined as ischaemic pain in the calves or gluteal muscles which comes on walking and gets relieved with rest, and more advanced stages are considered as critical (lower) limb ischaemia. The normal value of the ABI ranges from 0.9 to 1.3. PAD is defined as an ABI of less than 0.9. Among PAD patients, lower ABI predicts greater mortality and cardiovascular morbidity[15]. Measurement of ABI is easy to perform, is inexpensive and has a high sensitivity and specificity for PAD. PAD carries a risk that is at least as high as stable angina pectoris. However, PAD is often under diagnosed and the risk underestimated by physicians. Measuring the ABI is a useful tool in this respect, helping physicians both in larger scale population studies as well as during consultation.

The prevalence of PAD in India has been reported to vary from 6-20%. Two recent large studies from south India namely by Mohan et al[16] and CUPS[17] found prevalence of PAD in diabetics to be 3.9% and 6.3% respectively. Two recent studies in North India, one by Agarwal et al[18] and other by Madhu et al[19] found the prevalence of PAD in diabetics to be 18.1% and 13.73% respectively. Unfortunately, there is no available data from our country evaluating the prevalence of PAD in patients with CAD in India.

Patients and Methods

This study was done over a period of one academic year from September 2012 to August 2013 in the Department of Medicine, BRD Medical College and associated Nehru Chikitsalya, Gorakhpur in patients diagnosed with ACS.

Patients

In this study, patients were selected as per following criteria:

Inclusion Criteria

Criteria for the diagnosis of coronary artery disease:

- Typical history of angina pectoris.
- History of myocardial infarction/ thrombolytic therapy.

- ECG showing evidence of pathology 'q' waves and ST-T and T-wave changes suggestive of ischemic heart disease.
- Biomarkers (Troponine I, CK-MB).

Criteria for traditional cardiovascular risk factors:

Criteria for diabetes mellitus-

- Patients with known case of diabetes with regular or irregular treatment.

Criteria for hypertension

- Patients with known case of hypertension with regular or irregular treatment.

Criteria for diagnosis of dyslipidemia

- Patients who have Total cholesterol >200 mg/dl, triglycerides >150mg/dl, high density lipoprotein (HDL) cholesterol <40mg/dl or low density lipoprotein (LDL) >100mg/dl, Non HDL >130mg/dl.
- Patients, receiving treatment with lipid lowering drugs diagnosed by other physician.

Smoking

Each patient was classified as a non-smoker, active smoker, or ex-smoker by history of smoking (age of starting and stopping if an ex-smoker and family history of premature CAD). The smoker was also evaluated as to their exposure, calculating this as the packet-year index and the number of years as a smoker.

The patients were evaluated for their detailed clinical history including personal details, present history, past history, family history, treatment history followed by clinical examination including general and systemic examinations and ankle-brachial index (ABI) measurement.

Ankle-Brachial Index- measurement was done by Doppler machine, model number MINIDOP D580, manufactured by EMCO, Baroda, India.

The criterion for assessment of PAD in the present study was a decreased ABI, measured using a peripheral Doppler. This method is considered to be reliable for detecting PAD and has been validated in previous several studies. Earlier studies have suggested that an ABI<0.9 has a sensitivity of 95% for detecting angiogram positive disease, whereas a ratio of >0.9 almost always excludes PAD. ABI is therefore, considered a suitable method to assess PAD for epidemiological and clinical studies.

The examination was followed by laboratory investigations including hemoglobin concentration, total and differential leucocyte count, serum creatinine, serum SGPT/SGOT, urine examination-R/M, blood sugar, HB1AC%, serum lipid profile, cardiac profile, ECG, chest X-rays.

Exclusion Criteria

- Patients age <20 years.
- Chronic advanced renal insufficiency with a serum creatinine > 4mg/dl.

Statistical Analysis

Wherever possible the data was analysed for statistical significance. Student's t test was used to compare continuous variables. The chi-square test or Fisher exact test was used for categorical variables. P-values less than 0.05 were considered statistically significant.

Results

Demographic Profile-(**Table no. 1**) Our study included 120 patients, 75 male (62.5%) and 45female (37.5%). Mean age was 57.98 ± 9.99 years. Out of 120 patients, 39(32.5%) had diabetes, 34 (28.33%) hypertension and 32 (26.66%) patients were found to be smokers. 20 (16.66%) patients had history of alcohol intake and 25 patients (20.83%) were found to be obese (BMI>25).74 patients (61.66%) had STEMI and 46 patients (38.33%) had NSTEMI/Unstable angina. 12 patients (10%) had past history of CAD. 39 (32.5%) patients found to had LDL chol. >100mg/dl. Maximum numbers of patients were belonged to the lower class (58.33%), whereas 37.5% were from middle socioeconomic class and only 4.16% patients were from the upper socioeconomic class. Premature CAD was present in 13.3% of the patients (Premature CAD was defined as occurrence of CAD at age ≤ 45 years).

Table 1: Demographic Profile and Prevalence of Risk Factors Among Study Subjects (n=120)

S. No.	Risk factors	No. of patients	Percentage
1.	Mean age	57.98±9.99	
2.	Gender: Male	75	62.5%
	Female	45	37.5%
3.	Diagnosis: STEMI	74	61.66%
	UA /NSTEMI	46	38.33%
4.	Socioeconomic status: Lower	70	58.33%
	Middle	45	37.5%
	Upper	5	4.16%
5.	Hypertension	34	28.33%
6	Diabetes	39	32.5%
7.	Smoker	32	26.66%
8.	Obesity (BMI >25 kg/m^2	25	20.83%
9.	Past history of CAD	12	10%
10.	LDL-C >100mg/dl	39	32.5%
11.	Alcohol intake	20	16.66%
12.	Premature CAD	16	13.3%

Table 2. Prevalence of PAD in Study Population

Total	**No PAD**	**PAD**		
N=120	110 (91.6%)	10 (8.33%)	Male	Female
			8(80%)	2(20%)

The above table shows prevalence of PAD, PAD was present 8.33% of study population (n=120).

Table 3 Comparison of various risk factor in patients with or without PAD

Risk factors		**Patients with PAD (10), ABI<0.9**	**Patients without PAD(110), ABI>0.9**	**p-value**
AGE (years)	Mean	57.98±9.99	58.9±9.72	
Sex	Male	8	67	>.05
	Female	2	43	
BMI	<25	7	88	>.05
	>25	3	22	
S.cholesterol (mg/dl)	<200	6	76	>.05
	>200	4	34	
S.triglyceride (mg/dl)	<150	8	90	>.05
	>150	2	20	
S.HDL cholesterol (mg/dl)	<40	2	8	>.05
	>40	8	102	
S.LDL cholesterol (mg/dl)	<100	6	73	>.05
	>100	4	37	
Non HDL cholesterol (mg/dl)	<130	5	53	>.05
	>130	5	57	
Diabetes	Yes	5	34	>.05
	No	5	76	
Hypertension	Yes	3	31	>.05
	No	7	79	
Smoking	Yes	6	26	<.05
	No	4	84	

Table-3. shows various risk factor for atherosclerosis- On observing the atherosclerotic risk factors in total population it was found that males and females proportions were unequal (62.5% males and 37.5% females). Out of total 10 patients with PAD, 8 patients (80%) were male and 2 patients (20%) female. Majority of patients in the present study were above the age of 50 years (mean age 58.9 ± 9.72). Out of total 10 patients with PAD, all patients were above the age of 50 years (mean age 57.98 ± 9.99). 25 patients (20.83%) were found to be obese (BMI>25). Out of total 10 patients with PAD, 3 patients (30%) found to had obese. On the basis of serum fasting lipid profile, out of 110 patients who had CAD but no PAD the serum cholesterol of 34 patients (30.9%) were above 200mg/dl, serum triglyceride level of 20 patients (18.18%) above 150 mg/dl, serum HDL cholesterol level of 8 patients (7.27%) below the normal range (40mg/dl), serum LDL cholesterol level of 37 patients (33.63%) above 100 mg/dl, and serum non HDL cholesterol of 57 patients(51.8%) was above 130mg/dl. In the 10 patients with PAD, the serum cholesterol of 4 patients (40%) was above 200mg/dl, serum triglyceride level of 2 patients (20%) above 150 mg/dl, serum HDL cholesterol level of 2 patients (20%) below the normal range (40mg/dl), serum LDL cholesterol level of 4 patients (40%) above 100 mg/dl, and serum non HDL cholesterol of 5 patients (50%) above the 130mg/dl. Out of 110 patients with CAD, 26 (23.6%) patients were found to be smokers, 34 (34.9%) had diabetes and 31 (28.18%) had hypertension. Out of total 10 patients who had PAD, 6 patients (60%) were smoker, 5 patients (50%) were diabetes and 3 patients (30%) were hypertensive.

Discussion

PAD has been considered as a marker of asymptomatic CAD in high risk patients and also as a poor prognostic indicator in patients of CAD. Data about prevalence of PAD in Indian population is variable. PAD has been studied in diabetic patients where the prevalence reported

varies from 3.6 - 6.9% in South Indian population[16,17] in a community based setting and North India 13.7-18.1%[18,19] in diabetic patients in a hospital based setting. Community based datas from western nation also shows a varying prevalence percentage (4-20%).

PAD prevalence has also been studied in patients with CAD, mostly in patients undergoing intervention with ACS. The varying prevalence has been reported as 2.6%,[21] 18.9%,[23] 26%,[22,24] 40%[20]. Indian data is from the study by Agarwal et al, in diabetic patients, where they found 26.8% of prevalence of PAD in diabetic patients with CAD. We found a total prevalence of PAD in ACS to be 8.3% which is much lower as compared to western data. Although the total no. of diabetics were only 39, 5 had PAD (12.8%). This also is low as compared to data by Agarwal et al. Males had a higher frequency (10.66%) of PAD than females (4.44%), supporting the earlier publications.

The prevalence of PAD increases with age. In the Framingham Heart Study, subjects 65 years of age or older were at increased risk for development of PAD[25]. A strong association between advanced age (≥ 70 years) and PAD prevalence was also noted in the NHANES report: prevalence was 4.3% in subjects aged 40 years or older compared with 14.5% in those aged 70 years or older[26]. In our study PAD was present in 57.98 ± 9.99 years of age.

Lu et al[27] demonstrated that smoking is an important risk factor not only for CAD, but also for PAD. The results found in our study agree with published results as the frequency of smoking was significantly greater in patients with PAD than in those without PAD (<0.05).

Previous studies have shown that in patients of ACS, PAD is more in patient who have previous diabetes[29] or hypertension,[28] that is a result of interaction of various factors. We did not find any difference in the prevalence of either diabetes or hypertension between the patient with or without PAD. Yet again PAD patients were a small number (n=10).More than half of patients with an abnormally decreased ABI do not have symptoms of PAD.[30] In our study none of the patient had symptoms.

Cohort/case control studies have shown an increased incidence of CAD in patients with PAD. All the types of studies have stressed on the coexistence of PAD and CAD. Both have been postulated to have similar risk factors especially the traditional risk factors (diabetes, hypertension, smoking and dyslipidemia). We found a very low prevalence of PAD in our study in contrast to previous published data. We also did not find any difference in the various risk factors of atherosclerosis in patients with or without PAD. Because our sample size of PAD was small, our data may not be statistically valid, though in a previous unpublished work, we had also found a low prevalence of PAD in diabetes & hypertension. In contrast to the western data, the Indian population has been shown to have a different risk and clinical profile .Such also appears to be the case with screening of PAD to detect early CAD. With a low prevalence of PAD even in patient with CAD, screening would not be feasible.

Conclusion

ACS was found in younger patients (mean age 57.98±9.9 years) in our study. No traditional risk factors of atherosclerosis was present in 45% patients with ACS. Non HDL levels more than 130 was present in 52.5% patients and could be considered as major risk factor for atherosclerosis in Indian population. The prevalence of PAD is low even in patients of CAD. Hence PAD screening may not be beneficial to predict cardiovascular events in high risk patients. The role of traditional risk factors of cardiovascular disease also needs to be relooked in Indian scenario.

Conflicts of interest: None
Source of Funding: None
Ethical Issue: None

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