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THE PREVALENCE OF PERIPHERAL ARTERIAL DISEASE IN NORMAL POPULATION VERSUS HIGH RISK INDIVIDUALS

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Atherosclerosis is a systemic multifocal disorder of arterial system affecting coronary, cerebral and peripheral vessels. Compared to the highly acknowledged and publicised outcomes such as heart attacks and strokes, peripheral arterial disease [PAD] and its complications are less well recognized. Estimation of ankle brachial index [ABI] as an initial screening test in outpatient department [OPD] yields useful information about the frequency of this disease in the local population. Early detection of disease in normal and high risk asymptomatic population can result in more aggressive guidelines for preventive measures. The sample size of 200 participants aged 40-75 was identified. Among these, 100 belonged to control group with not more than one standard modifiable risk factor, not including diabetes mellitus [DM]. The other 100 participants were included if they had 2 or more standard modifiable risk factors or the presence of DM. ABI measurement was done in both groups by hand held Doppler Ultrasound. PAD was considered present if ABI was 0.9 or less. In the present study among control group, prevalence of PAD was 10% and in high risk asymptomatic group 13%. PAD is a prevalent atherosclerotic syndrome and is associated with a very high risk of myocardial infarction, stroke and death. In the absence of a national program of PAD education and detection many patients will not receive a diagnosis of PAD prior to the occurrence of a morbid or mortal ischaemic event. ABI measurement is the most efficient and objective approach for detecting the presence and severity of disease in primary care settings.

Atherosclerosis is a diffuse and progressive process with variable distribution and clinical presentation depending on the regional circulation involved.[1] Peripheral arterial disease (PAD) is a manifestation of systemic atherosclerosis that is common and is associated with increased risk of death and ischaemic events.[2] Although PAD involves the extra cranial carotid, upper extremity, visceral and renal circulation, the term is usually applied to disease involving the circulation of lower extremity alone. Intermittent claudication, heralded by pain in leg muscles during ambulation is the earliest and the most classical symptom in patients with PAD.[3] Many patients with PAD do not have classical claudication symptoms.[4]

Prevalence of peripheral arterial disease in primary care practice is high, yet physicians awareness of the diagnosis is very low. A simple ankle brachial index [ABI] measurement identified a large number of patients with unrecognized peripheral arterial disease. Atherosclerotic factors were prevalent in PAD patients but the patients received less intensive treatments for lipid disorders and hypertension and were prescribed antiplatelet therapy less frequently than were the patients with cardiovascular disease. These results demonstrate that under diagnosing peripheral arterial disease in primary care practice may be a barrier to effective secondary prevention of high ischaemic cardiovascular risk associated with PAD.[2] In the lower extremity of a supine patient at rest, the ankle systolic blood pressure divided by arm systolic blood pressure is the best indicator of the presence or absence of haemodynamically significant arterial occlusive disease.[2, 5,7,10]

A low ABI reflects the combined effect of many risk factors over time and is a manifestation of overt atherosclerosis. Thus, it would be expected to be a better predictor than any one factor alone.[6]

Ankle-brachial index is reported to be a useful simple test with a sensitivity of 96% and specificity of 94-100% and can be performed in an out patient department [OPD] with a hand held Doppler for the diagnosis of peripheral arterial disease. Peripheral arterial disease is relatively common. The age adjusted prevalence of PAD is 12% among adults. Among those over the age of 75, as many as 20-30% may be affected.[7]

Prevalence of PAD increases with rising age. In youngest age group, prevalence among women was higher; in the oldest category the prevalence among men was higher. These gender differences were not significant. However, the figures on symptomatic patients, cases with concomitant isch-

aemic heart diseases [IHD] or cerebral arterial disease and known cases indicated that proportion of cases with manifestation of atherosclerosis was evidently higher among men.[9] It is imperative that the primary care physicians identify and aggressively treat the modifiable atherosclerotic risk factors such as smoking, dyslipidaemias, hypertension and diabetes mellitus.[7] In the Heart Outcomes Prevention Evaluation (HOPE) study subset, a low ABI was a strong predictor of cardiovascular morbidity and mortality in patients without clinical peripheral arterial disease.[10] The present study was undertaken with the following objectives; demonstrates that PAD is highly prevalent in primary care settings and the estimation of ABI by a hand held doppler as an initial screening test may detect preclinical PAD, reducing the economical burden on health care systems in the developing country like Pakistan.

The purpose of this study was to find out an early detection of atherosclerosis with ankle brachial index [ABI] in local population, and to compare the frequency of disease in asymptomatic individuals with international data.

SUBJECTS AND METHODS

*Background***:** this study consist of two inter related elements, a prevalence study and a diagnostic study.

General Design: Individuals were selected at random from the general hospitals serving a range of socio-economic and geographical areas of the city. The sample size of 200 participants was identified, they were between 40-75 years of age. Informed consent was sought. One hundred participants belonged to control group with not more than one standard modifiable risk factor [not including DM], the other 100 participants were included if they had 2 or more standard modifiable risk factors or the presence of DM. ABI measurement was done in both groups by hand held doppler ultrasound.

Inclusion Criteria

Control Group

Subjects with 0-1 standard modifiable risk factor not including diabetes mellitus.

High Risk Group

Subjects with two or more standard modifiable risk factors or the presence of diabetes mellitus.

Exclusion Criteria

1. Any patient with evidence of ischaemic heart disease, cerebrovascular disease, history of vascular surgery, amputation or intermittent claudication.
2. Patients with any severe systemic disease.
3. Renal insufficiency patients with serum creatinine >1.5 mmol/L.
4. Patients who had undergone major surgery within the past 3 months.
5. Wheelchair bound patients.
6. Patients with ABI of 1.50 or higher consistent with poorly compressible arteries and inability to gauge arterial perfusion accurately.

Data Collection

Detailed history of presenting complaints, past medical / surgical history, family history and personal history was obtained. Relevant data was obtained from the patient record e.g. hypertension, diabetes mellitus, tobacco smoking, hyperlipidemia, age at menopause and any medication. Subsequently, a standard physical examination was carried out including weight and standing height. A standard bilateral palpation of the femoral, popliteal, posterior tibial and dorsalis pedis arte-ries was performed.

ABI measurement

Arm blood pressure was recorded by routine standard protocol. The arm with higher pressures was taken as index arm. Two more readings were taken on the same arm and the average taken as the index systolic blood pressure in the arm.

In all patients, pedal pulses in posterior tibial and dorsalis pedis arteries were located with the help of a Doppler ultrasound with 8MHz probe. Ankle systolic blood pressure [SBP] in both legs was measured by inflation of the cuff around calf just above the medial malleolus and the ankle pressure read during deflation at the reappearance of the respective foot pulse. The leg with the lower systolic pressure was taken as index leg. Within the index leg, dorsalis pedis artery pressure was taken as index ankle pressure if it was higher than the posterior tibial and vice versa. Two more readings were taken on the same artery and the average recorded.

ABI was calculated by dividing the average systolic blood pressure of the index ankle artery by the average blood pressure of the index arm.

Laboratory Investigations

A sample of fasting blood was taken to measure serum lipid concentrations including total cholesterol, high density lipoproteins, low density lipoproteins, and triglycerides with standard kits. Fasting blood glucose concentration were also measured

Statistical Analysis

Numerical data was statistically analyzed using SPSS (Statistical Package for Social Sciences) Ver-

sion 10 for Windows. Mean ± Standard Deviation was recorded and comparisons made using Student's T-Test. Nominal data was reported as frequencies and percentages and comparisons made by Chi Square (X) Test. Probability <0.05 was considered significant for analysis.

RESULTS

Among 100 control cases 59 were males and 41 females. Out of 100 high risk asymptomatic cases 48 were males and 52 females. Mean age in both groups was 47 and 53 for males and 45 and 52 for females. The details of age distribution and mean ages in various groups and sexes are shown in tables 1, 1a and 2.

Table 1: *Age distribution for males in two groups.*

Age Group (years)	Control group	High risk asymptomatic group
40 – 49	41 (69.49%)	17 (35.41%)
50 – 59	8 (13.56%)	19 (39.58%)
60 – 69	9 (15.25%)	9 (18.75%)
≥ 70	1 (1.69%)	3 (6.25%)
Total	59 (59.0%)	48 (48.0%)

Table 1a: *Age distribution for females in two groups.*

Age Group a(years)	Control group	High risk asymptomatic group
40 – 49	32 (78.05%)	18 (34.61%)
50 – 59	8 (19.51%)	25 (48.08%)
60 – 69	1 (2.44%)	9 (17.31%)
≥ 70	-	-
Total	41 (41.0%)	52 (52.0%)

Table 3 shows height, weight and BMI distribution in the two groups. Among control cases mean weight for males was 71 kg and for females 67.54 Kg. Mean height in males was 165.69 cm and in females it was 158.05 cm. Mean BMI was 25.93 for males and 27.83 for females.

Table 2: *Mean age ±SEM of two groups.*

Sex	Control group	High risk asymptomatic group
Male	47.44 ± 1.11	53.37 ± 1.09
Female	45.39 ± 0.75	51.50 ± 0.93
Total	46.60 ± 0.72	52.40 ±0.71

Among high risk asymptomatic cases mean weight for males was 73.10 Kg and for females 65.1 Kg. Mean height of males was 166 cm in males and 153 cm in females. Mean BMI was 26.88 in males and 28.13 in females.

Table 3: *General characteristics of two groups (Mean ± SEM).*

Parameter	Control asymptomatic group	High risk group
Weight (kg)		
Male	71.0 ± 1.46	73.10 ± 1.75
Female	67.54 ± 1.55	65.71 ± 1.29
Total	69.58 ± 1.08	69.26 ± 1.13
Height (cm)		
Male	165.69 ± 0.85	166.0 ± 0.89
Female	158.05 ± 0.84	153.38 ± 0.80
Total	162.56 ± 0.72	159.44 ± 0.87
BMI		
Male	25.93 ± 0.54	26.88 ± 0.63
Female	27.83 ± 0.66	28.13 ± 0.51
Total	26.71 ± 0.42	27.53 ± 0.41

Body mass index = BMI

Table 3a indicates fasting blood sugar and lipid profile in the two groups. Among control cases, in males mean BSF was 90.66 mg/dl and 97.88 mg/dl in females. Mean total cholesterol was 198.75 mg/dl in males and 203.98 mg/dl in females. Similarly mean serum triglyceride was 196.73 mg/dl in males and 178.17 mg/dl in females. In males mean high density lipoproteins were 44.14 mg/dl and in females 46.39 mg/dl. Similarly mean low density lipoproteins were 113.42 mg/dl in male's and 122.12 mg/dl in females.

Among high risk asymptomatic cases, in males mean BSF was 149.25 mg/dl and in females 161.0 mg/dl. Mean total cholesterol in males was 201.10 mg/dl and in females 207.54 mg/dl. Similarly mean serum triglyceride in males was 271.81 mg/dl and in females 21.67 mg/dl. Mean high density lipoprotein in males was 43.98 mg/dl and in females 48.06 mg/dl. Mean low density lipoprotein in males was 114.06 mg/dl and in females 116.45 mg/dl.

Table 3b shows index blood pressures and ABI in the two groups. Among control cases, in males, mean systolic blood pressure (SBP) in index arm was 121.53 mmHg and in females 120.83 mmHg. Mean SBP in index leg was 122.66 mmHg in males and 118.68 mmHg in females. Mean ankle brachial index (ABI) was 0.99+0.01 in males and 0.99+

0.02 in females. Among high risk asymptomatic cases, in males mean SBP in index arm was 135.19 mmHg and in females 132.71 mmHg. Mean SBP in index leg was 134.90 mmHg in males and 128.23 mmHg in females. Mean ABI was 0.99+0.01 in males and 0.95+0.09 in females.

Table 3a: *Shows fasting blood sugar and lipids.*

Parameter	Control asymptomatic group	High risk group
Blood Sugar Fasting (BSF mg/dl)		
Male	90.66 ± 1.46	149.25 ± 12.22
Female	97.88 ± 4.82	161.0 ± 9.64
Total	93.62 ± 2.17	155.36 ± 7.7
Total-cholesterol (mg/dl)		
Male	198.75 ± 5.23	201.10 ± 6.34
Female	203.98 ± 7.35	207.54 ± 6.91
Total	200.89 ± 4.30	204.45 ± 4.70
Serum triglyceride (mg/dl)		
Male	196.73 ± 14.96	271.81 ± 52.68
Female	178.17 ± 15.90	217.67 ± 23.19
Total	189.12 ± 10.96	243.66 ± 28.0
High Density Lipo protein (mg/dl)		
Male	44.14 ± 1.03	43.98 ± 1.03
Female	46.39 ± 1.15	48.06 ± 1.43
Total	45.06 ± 0.77	46.10 ± 0.91
Low Density Lipo protein (mg/dl)		
Male	113.42 ± 4.47	114.06 ± 4.94
Female	122.12 ± 6.25	116.45 ± 5.8
Total	117.77 ± 3.35	115.34 ± 2.21

Table 3b: *Shows index blood pressure and ABI.*

Parameter	Control Group asymptomatic	High risk
SBP (mmHg) in index arm		
Male	121.53 ± 1.89	135.19 ± 2.17
Female	120.83 ± 2.04	132.71 ± 2.19
Total	121.24 ± 1.39	133.9 ± 1.54
SBP (mmHg) in index-leg (Doppler)		
Male	122.66 ± 2.32	134.90 ± 2.06
Female	118.68 ± 2.47	128.23 ± 2.58
Total	121.03 ± 1.71	131.43 ± 1.69
ABI (Doppler)		
Male	0.99 ± 0.01	0.99 ± 0.01
Female	0.99 ± 0.02	0.95 ± 0.09
Total	0.99 ± 0.01	0.97 ± 0.008

Students' t test was used to compare weight, height, BMI and FBS among various groups in both sexes. Among male controls versus high risk asymptomatic only FBS was found to be significantly higher among high risk asymptomatics ($p<0.001$). Among female controls versus high risk asymptomatic, height and BSF were found to be significantly higher among high risk asymptomatics ($p < 0.001$). Among male controls versus high risk asymptomatic SBP in index arm and SBP in index leg were found to be significantly higher among high risk asymptomatics ($p < 0.001$) and ($p < 0.001$). Among female controls versus high risk asymptomatics SBP in index arm and SBP in index leg were found to be significantly higher among high risk asymptomatics ($p<0.001$) and ($p<0.05$).

Table 4a, 4b and 4c show the general characteristics of the two groups. In control group 15 cases had I/C. In high risk asymptomatic vs controls 46 vs 13 cases were hypertensive, 73 cases were diabetic and 13 cases were dyslipidaemic.

In controls 8 cases had F/H of CAD, 21 cases had F/H of hypertension and 23 cases and F/H of

Table 4a: *General characteristics of two groups*

		Control group	High risk asymptomatic group
Intermittent claudications			
Male	Positive	6	
	Negative	53	
Female	Positive	9	-
	Negative	32	52
Total Positive		**15 (15.0%)**	**-**
Total Negative		**85(85.0%)**	**100(100.0%)**
History of hypertension			
Male	Yes	9	25
	No	50	23
Female	Yes	4	21
	No	37	31
Total Positive		**13**	**46**
Total Negative		**87**	**54**
History of diabetes mellitus			
Male	Yes	-	30
	No	59	18
Female	Yes	43	
	No	41	9
Total Positive		**0**	**73**
Total Negative		**100**	**27**

		Control group	High risk asymptomatic group
History of lipids			
Male	Yes	-	6
	No	59	42
Female	Yes	-	7
	No	41	45
Total Positive		**0**	**13**
Total Negative		**100**	**87**

DM. In high risk asymptomatics 8 cases had F/H of CAD, 18 cases had F/H of hypertension and 51 cases had F/H of DM. In high risk asymptomatic group 57 cases were taking oral hypoglycaemic drugs and 10 cases were using insulin. In controls 10 cases vs 32 in high risk asymptomatics were using antihypertensives. In controls 11 cases vs 18 cases in high risk asymptomatics were smokers. Most of them were smoked upto 10 cigarettes/day.

Table 4b:

		Control asymptomatic group	High risk group
Family history CAD			
Male	Yes	4	5
	No	55	43
Female	Yes	4	3
No	37	49	11
Total Positive		**8**	**8**
Total Negative		**92**	**92**
Family history of hypertension			
Male	Yes	11	14
	No	48	34
Female	Yes	10	4
	No	31	48
Total Positive		**21**	**18**
Total Negative		**79**	**82**
Family history of diabetes mellitus			
Male	Yes	9	20
	No	50	28
Female	Yes	14	31
	No	27	21
Total Positive		**23**	**51**
Total Negative		**77**	**49**

Table 4c

		Control asymptomatic group	High risk group
Oral hypoglycemic			
Male	Yes	-	23
	No	59	25
Female	Yes	-	34
	No	41	18
Total Positive		**-**	**57**
Total Negative		**100**	**43**
Insulin			
Male	Yes	-	2
	No	59	46
Female	Yes	-	8
	No	41	44
Total Positive		-	10
Total Negative		**100**	**90**
Antihypertensive			
Male	Yes	8	18
	No	51	30
Female	Yes	2	14
	No	39	38
Total Positive		**10**	**32**
Total Negative		**90**	**68**
Smokers			
Male	Yes	10	18
	No	49	30
		Control asymptomatic	**High risk group**
Female	Yes	1	-
	No	40	52
Total Positive		**11**	**18**
Total Negative		**89**	**82**
Number of cigarettes per day			
Male	5 – 10	5	9
	11 – 20	5	5
	20 – 30	-	3
	> 30	-	1
Total	**Male**	**10**	**18**
Female	3	1	-

Table 5 shows the distribution of ABI in males and females of both groups. In control group out

of 59 males 54 cases had ABI in the range of 0.9-1.4 and 5 cases had ABI in the range of 0.7-0.9. In high risk asymptomatic group out of 48 males 45 cases had ABI in the range of 0.9 - 1.4 and 3 cases had ABI in the range of 0.7-0.9. Among 41 female controls 35 had ABI in the range of 0.9-1.4 and 5 had ABI in the range of 0.7-0.9 whereas 1 case had ABI of >1.4. In high risk asymptomatic group among 52 females 42 had ABI in the range of 0.9-1.4 and 10 had ABI in the range of0.7-0.9.

Table 5: *Distribution of ABI In Both Groups.*

Group	<0.7		0.7-0.9		0.9-1.4		>1.4		Total	
	M	F	M	F	M	F	M	F	M	F
Control	-	-	5	5	54	35	-	1	59	41
High risk Asymptomatic	-	-	3	10	45	42	-	-	48	52

DISCUSSION

Peripheral arterial disease [PAD] is a progressive disease, which has a variable prevalence depending on the method of diagnosis, age sex, race and the geographic area. Although the clinical history and physical examinations are key elements in the evaluation of patients with chronic lower extremity ischaemia, physiological testing with modern noninvasive techniques has become an essential component of the pretreatment evaluation and post treatment follow up.[11]

PAD affects more than 27 million people in North America and Europe.[12] According to the results from the National Health and Nutrition Examination Survey 1999-2000, (NHANES), PAD affects about 5 million US adults. As the US population ages, PAD is likely to become an increasing problem. If risk factors remain stable, it is expected that an estimated seven million individuals aged 40 years & over, will have PAD by the year 2020 in USA.[12] The prevalence estimates in the present study are consistent with those observed in US community based studies such as the Framingham Offspring Study, and the Atherosclerosis Risk in Communities Study, and among elderly individuals in the Honolulu Heart Program, and the Cardiovascular Health Study. The prevalence of PAD in these studies which used similar diagnostic criteria, ranged from 3% to 4% among middle aged adults and between 13% and 14% in the elderly. More then 95% of the individuals with PAD had at least one traditional cardiovascular risk factor and the majority had multiple risk factors.[13] Our results from control group indicate that among 40-75 year old subjects the prevalence of PAD was 10% and in asymptomatic group it was 13%. In Belgium and Israel, among 40-60 years old asymptomatic subjects, the prevalence of an ABI < 0.9 was about 4%, whereas among 60 years olds in Denmark the prevalence was nearly 12%.[14] These results were lower than 10% and 13% observed in our study, probably due to the younger populations studied. In an earlier study conducted on a selected population of pharmaceutical workers in Basle, the prevalence of arterial occlusion in asymptomatic men aged 60-64 years was 6%.[14] Although it is difficult to compare studies because of the differences in study populations and tests used, our figure of 10% and 13% of population aged 40-75 years having major asymptomatic PAD among control group and high risk asymptomatic group respectively, is of a similar order of magnitude and is based on the application of the same technique to all the indi-viduals. The conclusion that having PAD puts an individual at a much higher risk which is comparable to the reference population, is therefore a justified one, and a message that needs to be emphasized. Even though the majority of PAD subjects remain asymptomatic; they remain a high risk population probably even higher than those with single cardiovascular risk factor.[15] The increased mortality risk can presumably be reduced by appropriate life style and pharmacological intervention within a primary care setting for which early detection by ABI estimation during routine primary care office visits is highly recommended.

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