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RESEARCH ARTICLE

TO STUDY OCCURRENCE OF PERIPHERAL ARTERIAL DISEASE IN YOUNG PATIENTS WITH CORONARY ARTERY DISEASE USING ANKLE BRACHIAL INDEX -A SMS HOSPITAL BASED OBSERVATIONAL STUDY

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Abstract

Background: Coronary artery disease (CAD) and peripheral arterial disease (PAD) both are manifestations of systemic atherosclerosis. Many patients with CAD have associated PAD; however, many patients are asymptomatic and thus remain underdiagnosed. Currently, little is known about the actual incidence and clinical implications of asymptomatic PAD in young patients less than 50-year-old undergoing coronary angiography in Indian population, so we will conduct this study to assess the prevalence of previously unrecognized PAD among patients with suspected ischemic heart disease undergoing coronary angiography, and to determine the relationship among PAD, severity of coronary angiographic stenosis, and major cardiovascular risk factors, in western Indian population.

Method: This is an observational study conducted at a tertiary referral hospital. A total of 395 patients referred for coronary angiography without a prior diagnosis of PAD, between January 2023 to June 23 who fulfilling eligibility criteria of study, were included. Patients were evaluated through detailed medical history taking, a questionnaire survey to assess symptoms and functional status, ankle-brachial index (ABI) measurement, and coronary angiography. PAD was considered present if the ABI was< 0.90 in either leg.

Result: In all patients, the prevalence of previously unrecognized PAD was 5.8%. There was significant difference between men and women (7.2% vs 1.1%, P=0.027). Abnormal angiographic results were seen in 63% (249 of 395). The prevalence of PAD was 7.2% in patients with abnormal coronary angiographic result, higher than that in patients with normal results but not statistically significant (3.2%, P=0.119). Patients with PAD were significantly older, and had higher rates of hypertension, dyslipidaemia, diabetes mellitus, current smoking, history of CAD than patients without PAD demonstrating high occurrence of PAD strongly associated with conventional risk factor for CAD. The occurrence of asymptomatic PAD was more among stable ischemic heart disease group(p=0.04). In our analysis, patients with PAD had a more severe form of CAD manifested by a higher frequency of multivessel coronary disease(p=0.002).

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Conclusion: The high occurrence of asymptomatic PAD in young patients with CAD confirms the importance of active screening for PAD by using ABI even in young patients. Routine determination of ABI in the clinical evaluation of all patients with CAD may helpful inidentifyhigh-risk patients.

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Introduction:-

Atherosclerosis is a progressive and diffuse pathological process that can simultaneously affect the coronary and peripheral arteries.1 The prevalence of peripheral arterial disease (PAD) increases with age, ranging from 1% to 3% in the fourth decade to >20% in the eighth decade.2,3

PAD is associated with an increased incidence of multivessel and obstructive coronary artery disease (CAD), and is a risk factor for cardiovascular events.4–7

In most cases, PAD is asymptomatic, and because the ankle-brachial index (ABI) is not routinely measured, PAD is largely underdiagnosed and therefore undertreated.8 Early detection of PAD in patients with CAD is essential for preventing the local progression of the disease and for an effective secondary prevention of future coronary events.9,10ABI measurement is a noninvasive and sensitive method for evaluating atherosclerosis in the lower limbs, with values ≤0.9 indicating the presence of PAD.11

The ABI has been shown to have good sensitivity and specificity for PAD (sensitivity of 69%-73% & specificity of 83%-99% in detecting >50% stenosis), as documented by direct comparisons with angiographic results, and is considered an independent predictor of coronary morbidity and mortality.12–17

Currently, little is known about the actual incidence and clinical implications of asymptomatic PAD in young patients less than 50-year-old undergoing coronary angiography in Indian population. We will conduct this study to assess the prevalence of previously unrecognized PAD among patients with suspected ischemic heart disease undergoing coronary angiography, and to determine the relationship among PAD, severity of coronary angiographic stenosis, and major cardiovascular risk factors in western Indian population.

Objective:-

To study the prevalence of previously unrecognized PAD of the lower limbs in young patients <50 yearsold undergoing coronary angiography with use of ankle brachial index, and to determine the correlation with CAD

To study association of CAD and PAD with various cardiovascular risk factors (HTN, T2DM, SMOKING, HYPERLIPIDEMIA, FAMILY HISTORY OF CVD).

Methods:-

Study design-

This will be hospital based cross sectional study

Study location-

Dept of cardiology, SMS medical college and hospital, Jaipur.

Study duration-

One year or till the sample size is reached

Sample size-

395 patients of <50 years age who undergo coronary angiography were studied at 80% study power and alpha error of 0.05

Inclusion criteria-

All patients <50 years old who were undergoing coronary angiography in dept of cardiology, SMS hospital, Jaipur.

Exclusion criteria-
Patients with preexisting confirmed diagnosis of PAD, deformity in the upper and lower limbs, significant lower limb edema, unwillingness, or inability to provide informed consent, and ABI >1.4 (noncompressible arteries).

We obtained the characteristics of the participants, including demographics; atherosclerotic risk factors such as diabetes mellitus, hypertension, hyperlipidemia, and smoking; familial history; past medical history; and functional status.

Atherosclerotic risk factors were defined according to standard definitions.18–20

Patients were considered to have hypertension if they had an elevated systolic blood pressure >140mm Hg and/or a diastolic blood pressure >90mm Hg on several occasions during the hospital stay, were diagnosed as having hypertension, or were prescribed with antihypertensive medications by a treating physician.

Diabetes mellitus was defined according to the standard criteria set by the American Diabetes Association, as follows: fasting serum glucose >126mg/dL, 2-hour glucose level >200mg/dL or glycosylated hemoglobin value >6.4%.

Diabetes mellitus was also diagnosed in patients who had unequivocal hyperglycemia, classical symptoms of diabetes mellitus (polyuria, polydipsia, and unexplained weight loss), and casual plasma glucose level >200mg/dL, and those with a prior diagnosis of diabetes mellitus or who were prescribed with antidiabetic medications by a treating physician.

Patients who were cigarette smokers at enrollment will be considered current smokers. Patients who never smoked and were past smokers who had quit at least 30 days before enrollment will be considered nonsmokers.

Patients were considered to have hypercholesterolemia if they had a past diagnosis by a treating physician, were prescribed with lipid lowering agents, or were found to have a serum total cholesterol level of >240mg/dL during the index admission.

Body mass index was calculated according to the standard formula (body weight [kg]/height [m2]). Obesity was defined as a body mass index of ≥30 kg/m2 .

A family history of premature cerebrovascular disease was defined as myocardial infarction, coronary revascularization, or sudden death before age 55 years in the father or any other male first-degree relative, or before age 65 years in the mother or any other female first-degree relative.

Measurement of ABPI
After resting in the supine and head in midline position for 15 minutes, ABI was measured using the conventional bp measuring instrument and use of HI.dop pocket size doppler device (bistos co. ltd.) with 8 Hz vascular doppler probe.

Blood pressure cuff was tied to all 4 limbs one by one and systolic pressure of all the limbs were measured and the ABI was calculated for each side using the higher systolic pressure of the 2 arms.

For BP measurement of upper arm, cuff was tied at arm and systolic brachial pulse accessed by doppler, and for lower limb, bp cuff was tied just above ankle and dorsal pedis and posterior tibial artery systolic pressure recorded by doppler method.

Patients were identified as having PAD if their ABI was ≤ 0.9 in either leg. Based on the ABPI findings, we were divided the participants into a normal group with no PAD (PAD) and an abnormal group with PAD (PAD+).

Coronary Angiography
All studied patients underwent coronary artery angiography via the femoral/radial approach with a 6-Fr catheter.

All coronary segments were interpreted visually by an experienced cardiologist blinded to participant details. We defined significant stenosis on coronary angiography as >50% stenosis of an epicardial coronary artery.

To assess the extent and severity of the CAD cases, we investigated whether multivessel and left main coronary lesions were involved or not.

Based on the angiographic findings, we divided the participants into a normal group with no significant coronary stenosis (CAD) and an abnormal group with significant coronary stenosis (CAD+).

We compared the results of various observations of our study and abnormal coronary angiographic findings between the PAD+ and PAD- groups. After considering the clinical manifestations, we classified CAD cases into the following: stable ischemic heart disease (SIHD) and acute coronary syndrome (ACS).

Statistical Analysis
We used SPSS software (version 20; Chicago, IL) for data description and analysis.

Continuous variables were reported as mean with standard deviation, unless otherwise indicated. Continuous variables were compared using unpaired t test.

We used the Chi-square test to compare the categorical variables. A multivariate logistic regression model was used to identify the independent risk factors for PAD. The model included prespecified risk factors of old age, hypertension, diabetes mellitus, hyperlipidemia, current smoking, previous coronary artery disease, and a history of stroke.

We analysed the results and express them as odds ratios (ORs) for the comparison of risk with 95% confidence intervals (CIs). We considered $P<0.05$ as indicating statistical significance.

Results:-

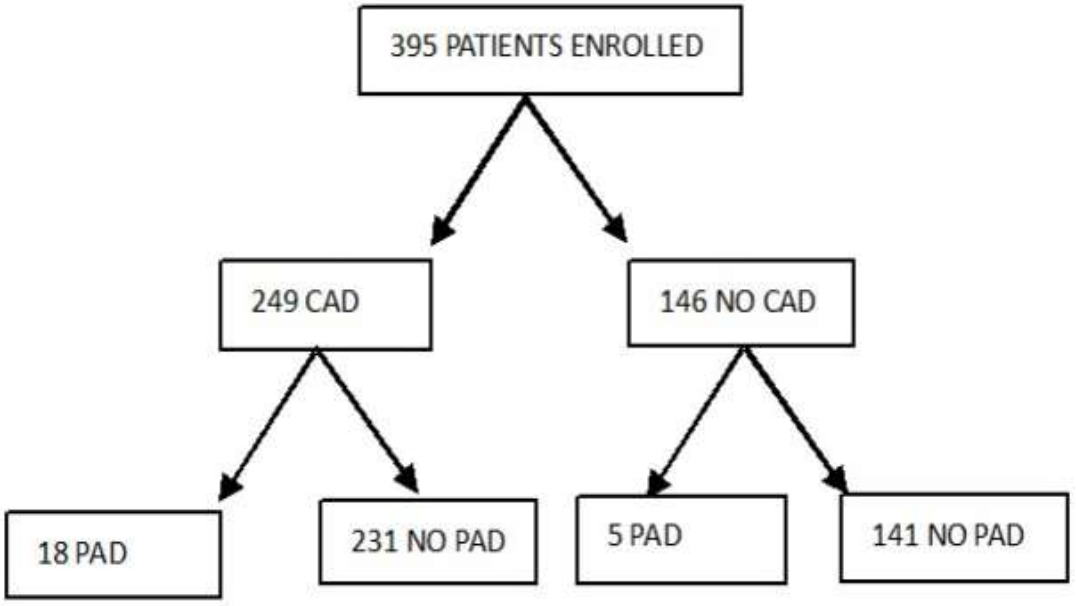

Figure 1:- Participant flow chart. ABI=ankle-brachial index, CAD=coronary artery disease, PAD=peripheral arterial disease.

Table 1:- Sociodemographic,clinical, and angiographic profile of study participants:

VARIABLES	Total participants(n=395)	**VARIABLES (CONT.)**	Total participants(n=395)
AGE (MEAN±SD)	43.1±5.5	TROP POSITIVE	170 (43%)
18-30 YEARS	18(4.6%)	BMI (MEAN±SD)	23.7+-1.5

31-40 YEARS	83(21%)	**NYHA FUNCTIONAL CLASS**	
41-<50YEARS	294(74.4%)	I	368 (93.2%)
GENDER		II	15 (3.8%)
FEMALE	92 (23.3%)	III	4 (1%)
MALE	303 (76.7%)	IV	6 (1.5%)
CLINICAL SUBGROUP		LVEF(%)	48.5+-9.3
ACS	328 (83%)	ABI-RT LL	1.14+-0.1
CSAP	50 (12.7%)	ABI-LT LL	1.16+-0.08
RISK FACTORS		PAD+	23 (5.8%)
SMOKING	227 (57.5%)	PAD-	372 (94.2%)
HYPERTENSION	133 (33.7%)	ANGIOGRAPHIC PARAMETERS	
DIABETES	57 (14.4%)	CAD+	249 (63%)
FAMILY HISTORY	13 (3.3%)	CAD-	146 (37%)
CAD	45 (11.4%)	SINGLE VESSEL DIS.	101
CVA	8 (2%)	MULTIVESSEL DIS.	148
DYSLIPIDEMIA	59 (14.9%)	LM DISEASE	11

ABI Ankle brachial index, ACS- Acute coronary syndrome, BMI Body mass index, CAD Coronary artery disease, CSAP Chronic stable angina pectoris, CVA Cerebrovascular accidents, LVEF Left ventricle ejection fraction, RT LL Right lower limb, LT LL Left lower limb, TROP Troponoin, SD Standard deviation.

Table 2:- Clinical characteristic of patients with or without PAD.

Variables	**PAD+(n=23)**	**PAD-(n=372)**	**P value**
Age (mean±sd)	45.2±3.3	42.9±5.5	**0.05**
18-30 years	0	18	
31-40 years	2	81	
41-<50years	21	273	
Gender			
Female	1(1.1%)	91	**0.027**
Male	22	281	
Clinical subgroup			
ACS	15(4.6%)	313	**0.004**
CSAP	8(16%)	47	
TROP Positive	10(5.8%	160	0.991
BMI (Mean±SD)	23.1±1.4	23.7±1.5	0.109
Risk factors			
Current smoker	19	208	**0.012**
Hypertension	13	120	**0.017**
Diabetes	11	46	**<0.001**
Family history	0	13	
/o CAD	5	40	0.108
CVA	0	8	
Dyslipidemia	4	55	0.734
NYHA functional class			
I	20	348	0.816
II	3	14	
III	0	4	
IV	0	6	
LVEF(%)	50.7±6.5	48.3±9.4	0.222
ABI-RT LL	0.99±0.09	1.15±0.07	**<0.001**
ABI-LT LL	1.03±0.06	1.17±0.09	**<0.001**

ANGIOGRAPHIC PARAMETERS			
CAD+	18	231	0.119
CAD-	5	141	
Single vessel dis.	1	100	
MULTIVESSEL DIS.	17	131	**0.002**
LM DISEASE	2	9	

ABI Ankle brachial index, ACS- Acute coronary syndrome, BMI Body mass index, CAD Coronary artery disease, CSAP Chronic stable angina pectoris, CVA Cerebrovascular accidents, LVEF Left ventricle ejection fraction, RT LL Right lower limb, LT LL Left lower limb, TROP Troponoin, SD Standard deviation.

Table 3:-The distribution of ankle brachial index (ABI) values in both lower limbs and their relation to severity of peripheral arterial disease.

Severity (ABI value)	Right	Left	Total
Mild (0.89–0.7)	11	8	19(82.6%)
Moderate (0.69–0.4	3	1	4(17.4%)
Severe (<0.4)	0	0	0
Normal (>0.9)	381	386	767
TOTAL	395	395	790

Table 4:- Predictors of peripheral artery disease in patients with CAD Multivariate.

Variables	**Odds ratio**	**95%CI**	**P-Value**
AGE	1.037	(0.8851, 1.2136)	0.657
EF	1.044	(0.9681, 1.1265)	0.262
SEX	1.488	(0.0776, 28.5266)	0.792
HTN	4.205	(1.1147, 15.8643)	**0.034**
DIABETES	20.756	(4.2014, 102.5437)	**<0.001**
CURRENT SMOKER	11.698	(1.4370, 95.2310)	**0.022**
HYPERLIPIDEMIA	0.303	(0.0461, 2.0006)	0.215
H/O CAD	1.954	(0.4390, 8.6988)	0.379
MULTIVESSEL CAD	6.132	(0.7398, 50.8329)	0.093
LM DISEASE	1.636	(0.2095, 12.7686)	0.639

We studied all the 395 consecutive patients managed in SMS hospital, Jaipur who were fulfilling inclusion criteria of our study. Out of 395 patients,231 (58.5%) diagnosed as having CAD alone, 18 (4.6%) with CAD and PAD, and 146 (37%) without CAD, out of which 5 (1.3%) with PAD without CAD (Fig. 1). The prevalence of asymptomatic PAD was 7.2% in young patients of less than 50-year-oldwith CAD, which was higher than that in patients with normal coronaries (4.5%) but statistically not significant. Table 1. shows the baseline demographic and clinical characteristics of the patients. Patients with PAD were significantly older, and had higher rates of hypertension, dyslipidaemia, diabetes mellitus, current smoking, history of CAD than patients without PAD. We find significant differences in the prevalence of PAD between male (5.6%) and female (0.3%) patients. The prevalence of CAD among PAD+ and PAD- patients was 78.3% and 62.1%, respectively (P=.119). Patients with multivessel CAD had a 6-fold higher risk of being diagnosed as having previously unrecognized PAD compared with those with single-vessel CAD (adjusted OR 6.13, 95% CI: 0.74–50.83).

Table 2. shows the distribution of ABI values in both lower limbs and their relation to the severity of PAD. Of the ABI recordings, 2.3% were abnormal on the left side and 3.5% were abnormal on the right side. The severity of PAD was more prevalent in the right lower limb (right ABPI, 0.76±0.11; left ABPI, 0.78±0.08).

In the logistic regression analysis, the factors independently associated with a greater risk of having PAD were age hypertension(p=0.034), diabetes(<0.001) and smoking(0,022), were all independently associated with PAD(table 4).

Discussion:-

This study aims to investigate occurrence and predictors of asymptomatic PAD among patients undergoing coronary angiography in SMS hospital, Jaipur. Our study shows an overall prevalence of asymptomatic PAD in patients with and without CAD of 7.2% and 3.4%, respectively. Because of the lack of awareness among physicians and a lack of symptoms in patients led to the failure of diagnosing PAD. This high occurrence of asymptomatic PAD in young patients of less than 50 years of age who were diagnosed coronary artery disease by angiography is comparable to the prevalence reported in other populations, such as the cohorts in Germany, Switzerland, France, Japan, and Turkey.21–24 Likewise, in the Arabian Gulf, Kumar et al. reported a prevalence of asymptomatic PAD of 13.7% in patients with a single previous coronary or cerebrovascular event.23

In the present study, we found that increasing age, hypertension, diabetes mellitus, hyperlipidaemia, current smoking, previous CAD were the main predictors of PAD in patients with CAD. When analysing age in our study population, the prevalence was 4.6% in patients younger than 30 years. The prevalence increased to 21% in the age group 31 to 40 years and was 74.4% in the age group of 41 to less than 50 years. These findings are consistent with the results of similar studies.25–27 Most of our study participants were males (76.7%), whereas females comprised only 23.3%. The occurrence of PAD was 7.2% among males and 1.1% among females, with statistical significance (P=0.027). Some of the studies showsthat prevalence in men being slightly higher than that in women, whereas other studies showed that women were more likely to develop PAD than men.28–31 In our study, PAD occurred on the right side in 3.5% and on the left side in 2.28%. Other studies also showed a unilateral predisposition of the disease to the right or left side, as in our study.32,33 no obvious reasons for this predisposition.

Based on ABI, the study population was divided into mild, moderate, and severe disease and 82.6% of subjects were reported to have had mild disease (ABI 0.7–0.89). Doobay and Anand have shown that a low ABI between 0.8 and 0.9 has a high specificity of 92% to predict CAD and 87% for cardiovascular mortality.34

Lee et al. have shown that ABI Prior reportsshows that smoking, hypertension, and history of cerebrovascular disease were predictors of PAD.35,36 Our results suggested that there were significant differences in the prevalence of PAD according to the patients' clinical presentation of either stable ischemic heart disease or acute coronary syndrome with occurrence of asymptomatic PAD was more among stable ischemic heart disease group(p=0.04). In our analysis, patients with PAD had a more severe form of CAD manifested by a higher frequency of multivessel coronary disease. This finding is consistent with previous reports, suggesting a greater burden of atherosclerotic disease and a later presentation, and this may provide a possible explanation for the poor outcome of patients with concomitant CAD and PAD than those without PAD.37–38. So, making a diagnosis of PAD in a patient with CAD should prompt the clinician to be more aggressive with risk factor intervention and to have a higher clinical index of suspicion for possible PAD symptoms. Also, those patients should be considered an exceptionally high-risk group.

Limitations

This study has several limitations. First, patients with ischemic heart disease which selected for angiography had high-risk demographic and clinical profiles which arealso associated with a high prevalence of PAD. Consequently, this may have biased the study results toward a higher prevalence of PAD. Second, this study of PAD based on ABI measurement only, without lower limb angiogram; therefore, it cannot exactlyshow the true of underlying atherosclerosis. Third, this study does not provide information about the outcome of patients with CAD according to the presence or absence of PAD.

Conclusion:-

Our study demonstrated that the occurrence of asymptomatic PAD in young patients with angiographically confirmed coronary artery disease and was strongly associated with higher incidence of cardiovascular risk factors like hypertension, smoking, and diabetes and with stable ischemic heart disease and multivessel disease. The high occurrence of asymptomatic PAD in young patients with CAD confirms the importance of active screening for PAD by using ABI even in young patients. Routine determination of ABI in the clinical evaluation of all patients with CAD may helpful in identify high-risk patients.

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