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RESEARCH ARTICLE

PERIPHERAL ARTERIAL DISEASE IN CHRONIC KIDNEY DISEASE: A PROSPECTIVE CLINICAL STUDY

Preet Mohinder Sohal, [1] Arti Bhagat, [2] Akriti Gupta, [3] Dinesh Gupta, [4] Jasvinder Singh Sandhu*[5]

[1] Assistant Professor, Department of Nephrology
[2] Resident, Department of Medicine
[3] Resident, Department of Medicine
[4] Professor &Head, Department of Medicine
[5] Professor &Head, Department of Nephrology*

Dayanand Medical College & Hospital, Ludhiana-141001

Corresponding author: Dr Jasvinder Singh Sandhu, MD, DM,Professor and Head,Department of Nephrology, Dayanand Medical College, Ludhiana-141001, Punjab, India

ABSTRACT:

Background: Published data are on peripheral arterial disease (PAD) in non dialysed patients of chronic kidney disease (CKD) is scant. Aim was to noninvasively evaluate the subclinical PAD using ankle-brachial Index and to correlate with the severity of chronic kidney disease. **Material and Methods:** Fifty patients of stage 3 and 4 chronic kidney disease were included. The staging of CKD was based on e-GFR using Cockcroft Gault equation. Peripheral arterial disease was evaluated on the basis of ankle brachial index. **Results:** Fifty patients, 14 in stage 3 and 36 in stage 4 chronic kidney disease were studied. The mean age was 62.4±10.9 years and male to female ratio was 1.6:1. The prevalence of peripheral arterial disease was 20%. Fifty percent of patients with peripheral artery disease were obese compared to 15% without PAD (p=0.017). Clinical profile of CKD with PAD showed that all had type 2 diabetes mellitus, 50% had hypertension. Patients of CKD with peripheral arterial disease had insignificantly higher mean values of serum creatinine, systolic blood pressure and dyslipidemia. Comparing the various variables between CKD with and without PAD, diastolic blood pressure, body mass index and presence of obesity were correlated to peripheral arterial disease. **Conclusion:** There is significant (20%) prevalence of subclinical peripheral arterial disease in non dialysed chronic kidney disease. Routine ankle brachial index measurements in patients of chronic kidney disease would help in diagnosing subclinical peripheral arterial disease and taking measures to halt its progression.

Key Words: Ankle brachial index, chronic kidney disease, peripheral arterial disease

INTRODUCTION:

Chronic kidney disease (CKD) is an independent risk factor for the development of generalized atherosclerosis. Moreover, frequently these patients not only have traditional risk factors such as hypertension, diabetes, or dyslipidemia, but also other non-traditional factors such as inflammation, malnutrition, and oxidative stress, which enhance and accelerate atherosclerosis. Lower extremity peripheral artery disease (PAD) is a significant clinical issue among patients

with CKD. Traditionally, epidemiologic studies of PAD have generally not included CKD as a potential risk factor. However, a growing number of studies have now described an association between PAD and CKD. [1-4] Ankle-brachial index (ABI) is a non-invasive diagnostic test that is easy to perform, reproducible, and efficient in detecting subclinical peripheral arterial disease. It has also been shown to be a strong predictor of cardiovascular disease. An ABI <0.9 is 95% sensitive and 100% specific for angiographically documented PAD for arterial stenosis ≥50% in the lower extremities. [5, 6]

MATERIAL AND METHODS

This cross-sectional observational prospective study was done in a tertiary care medical college hospital. The study was cleared by the Institutional Ethical Committee on human research and approved by State Medical University. Fifty patients of stage 3 and 4 chronic kidney disease (CKD) were included. Chronic kidney disease was defined as per KDIGO guidelines. [7] Staging of CKD was based on the estimated glomerular filtration (eGFR) using Cockcroft Gault equation. [8] Patients of CKD on dialysis, renal transplant recipients, those with revascularisation procedure or limb amputation in the past, those with arteriovenous fistula and the current and reformed smokers were excluded.

After taking a written informed consent, a detailed history and examination was done in each case. Weight, height, body mass index and body surface area were recorded in each patient. Routine investigations were carried out namely hemogram, routine urine, blood urea, serum creatinine, serum electrolytes, blood sugar, HBA1c, lipid profile, X ray chest, ECG and if required colour Doppler of limbs.

Ankle-brachial index was measured after keeping the patient in supine position for five minutes. Systolic blood pressure was recorded in right arm, right ankle, left arm and left ankle. The lower of the two pressures (both arm and both ankle pressures) were taken to calculate ABI.

ABI= systolic pressure ankle divided by systolic pressure brachial artery.

Patients with ABI <0.9 were considered to have peripheral arterial disease. Data were expressed as mean ± SD. Student t test was used to compare the results. P<0.05 was considered as significant.

RESULTS

The mean age of patients was 62.4±10.9 years. There was male preponderance (62%). Approximately 1/4th (22%) of patients were obese; none had severe or morbid obesity. Most of patients (72%) had stage 4 chronic kidney disease. Majority (74%) of patients had diabetic CKD and 1/4th (24%) had hypertensive nephropathy. Hypercholesterolemia and hypertriglyceridemia were present in 28% and 22% of patients. Twenty percent of patients had peripheral arterial disease with ankle brachial index <0.09. None of patients had ABI <0.04 or >1.3. (Table 1)

On comparing the various variables amongst patients with and without PAD, the body mass index, presence of obesity and diastolic blood pressure were significantly correlated to peripheral arterial disease. (Table 2)

Table 1: Showing the patient characteristics

Variable	**Number of patients N (%) 50 (100%)**
Sex	
Male	31 (62%)
Female	19 (38%)
Age in years Mean ± SD	62.4±10.9
Obesity	
Non-obese	39 (78%)
Obese	11 (22%)
Ankle Brachial Index	
<0.09	10 (20%)
>0.09	40 (80%)
Renal Function Tests:	
(mg/dL) Mean ±SD	
Blood Urea	66.4±33.0
S.Creatinine	3.5±1.4
eGFR (ml/mt.)	25.0±12.3
Stage of CKD	
Stage 3	14 (28%)
Stage 4	36 (72%)
Co morbidities	
T2DM+HTN	16 (32%)
T2DM	21 (42%)
HTN	12 (24%)
Others	01 (2%)
Lipids: (mg/dL) Mean ±SD	
S. Cholesterol	163.7±56.2
S. Triglyceride	148.5±67.9
S. LDL	99.3±54.2
S. HDL	46.7±27.5

N=Number of patients, T2DM= Type 2 diabetes mellitus, HTN=Hypertension, LDL= Low density lipoproteins, HDL= high density lipoproteins

Table 2: Comparing various variables between patients of chronic kidney disease with and without peripheral arterial disease

Variable	With PAD ABI (<0.9) N (%)10 (20%)	Without PADABI (>0.9) N (%) 40 (80%)	P value
Sex			
Male	4 (40%)	27 (67.5%)	
Female	6 (60%)	13 (32.5%)	0.2156
Age in years			
Mean ± SD	59.5±9.9	63.2±11.1	0.3412
Obesity			
Non-obese	5 (50%)	34 (80%)	
Obese	5 (50%)	06 (15%)	0.0496*
Renal Function Tests:			
(mg/dL) Mean ±SD			
Blood Urea	52.4±24.4	70.2±34.1	0.128
S.Creatinine	3.9±1.4	3.4±1.4	0.293
eGFR (ml/mt.)	24.0±12.5	25.3±12.3	0.775
Stage of CKD			
Stage 3	3 (21.4%)	11 (78.6%)	
Stage 4	7 (19.4%)	29 (80.6%)	0.8749
Co morbidities			
T2DM+HTN	5 (50%)	11 (21.5%)	
T2DM	5 (50%)	16 (40%)	0.1834
HTN	0	12 (30%)	
Others	0	01 (2.5%)	
Lipids			
(mg/dL) Mean ±SD			
S. Cholesterol	185.1±71.1	158.4±51.5	0.181
S. Triglyceride	182.5±62.5	140.0±67.3	0.077
S. LDL	122.6±69.4	93.4±49.1	0.130
S. HDL	48.3±23.0	46.3±28.8	0.845
Morphometry:			
Mean ±SD			
Systolic blood pressure	139.2 ±13	134±16.5	0.432
Diastolic BP	82.6 ±6.5	77±6.6	0.020*
Weight (kg)	79.7±4.8	70.3±12.5	0.025*
Height (cm)	167.9±8.0	168.3±6.2	0.849
BMI (kg/m^2)	29.7±2.5	25.9±4.4	0.013*

*Significant, N=Number of patients, ABI=Ankle brachial index, T2DM= Type 2 diabetes mellitus, HTN=Hypertension, LDL= Low density lipoproteins, HDL= high density lipoproteins

DISCUSSION

We observed a significantly high (20%) prevalence of asymptomatic lower extremity peripheral arterial disease in stage 3 and 4 chronic kidney disease. There are few published data on PAD in CKD population (GFR<60 ml/min) with a reported prevalence of 24% to 37%. [4,9,10] The prevalence of PAD in our study was slightly less than reported by other workers because we excluded smokers and those with symptomatic PAD. In our study patients with PAD were more likely to be older, females and type 2 diabetic CKD as compared to those without PAD.

Few studies have reported the correlation between peripheral arterial disease (PAD) and stages of CKD. The prevalence of asymptomatic PAD increased with more advanced stage of CKD. The mean ABI of stage 4 and 5 CKD patients was lower than that of stage 1 and 2 ($p < 0.05$), [11] However, no such correlation was observed in our study.

A variety of non invasive tests are available to evaluate for the presence and severity of PAD. These include assessment of intermittent claudication, ankle-brachial index (ABI), toe-brachial index (TBI), exercise treadmill test etc. In a recent meta-analysis the pooled sensitivity and specificity of ABI ≤ 0.90 for PAD diagnosis were 75% and 86%. [12] ABI may be less reliable in identifying PAD among patients with CKD with medial arterial calcification, which can result in falsely elevated lower extremity blood pressure readings due to arterial incompressibility. An estimated prevalence of medial arterial calcification was reported as 24% among patients with kidney dysfunction. [13] If the ABI is elevated (≥1.3), the TBI may provide a more accurate assessment, as medial artery calcification is less likely to interfere with toe pressure measurements [14] An ABI <0.90 and a TBI <0.60 are considered abnormal. [14] None of our patients had ABI >1.3 or <0.4 to suggest medial artery calcification or severe PAD.

Despite the reported high incidence of mortality in patients of chronic kidney disease with PAD, [15] there are no data to support screening for PAD in patients with CKD. [16]

In conclusion, there is a high prevalence of asymptomatic peripheral arterial disease in non-dialysed patients of chronic kidney disease (eGFR <60 ml/mt.). The diastolic blood pressure, body mass index and presence of obesity correlate with the occurrence of peripheral arterial disease in these patients. The use of a simple non invasive ankle-brachial index in routine clinical nephrology practice would help a long way in diagnosing peripheral arterial disease and preventing its morbidity in patients of chronic kidney disease.

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