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Prevalence, clinical profile, and risk factors of peripheral artery disease in an Indian cohort of chronic kidney disease

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ABSTRACT-

Introduction- Patients with chronic kidney disease (CKD) have some additional risk factors including endothelial dysfunction, chronic inflammation, oxidative stress, albuminuria, uremic toxins, pro-thrombotic and pro-calcific states, and microvascular disease leading to development of peripheral arterial disease (PAD) . However, risk factors for the excess risk of PAD among patients with CKD are not well studied.

Aim- To Study clinical profile of Peripheral Arterial Disease in patients of Chronic Kidney Disease.

Material and Methods-: Cross sectional, Observational Study conducted in the department of Medicine, JNU Medical College, Jaipur, Rajasthan, India on 50 patients admitted in Medicine wards with Chronic kidney disease.

Results- Older age of patient, longer duration of CKD, CAD, comorbidity of Diabetes Mellitus, Anemia, higher PTH level, high hsCRP, low eGFR, high Total Cholesterol, high LDL and high Cholesterol, and Albuminuria were found to be significantly associated with development of PAD in patients of CKD

Conclusion - Peripheral artery disease is highly prevalent in patients with CKD in India. Older age, Diabetes, coronary artery disease, advanced CKD stage, albuminuria, and elevated hsCRP levels were identified as risk factors. Early detection of patients with occult PAD may enhance efforts toward proper prevention and treatment.

Keywords- chronic kidney disease (CKD), peripheral arterial disease (PAD).

Introduction

Chronic kidney disease (CKD) is global public health problem. It is estimated that more than 100,000 new cases of end stage renal disease (ESRD) develop annually in India which has significant morbidity and mortality. [1]

A high burden of the global increase in prevalence of CKD is seen in the economically backward countries as a result of the increase in the prevalence of the CKD risk factors, namely, diabetes, hypertension, obesity, and increasing life-expectancy. At present precise estimation

of the burden of CKD and ESRD in India is difficult due to the lack of a comprehensive CKD registry. [2]

More than half of all CKD patient fatalities, according to an analysis of the global survey, were attributable to cardiovascular disease (CVD). [3] The prevalence of peripheral arterial disease (PAD), a progressive form of atherosclerotic occlusive disease that primarily affects the lower limbs, is rising, especially in low- and middle-income nations. [4]

The risk of peripheral arterial disease (PAD) is higher in patients with chronic kidney disease (CKD) compared with those without. In the Atherosclerosis Risk in Communities (ARIC) Study, the age-, gender- and race-adjusted risk for PAD was 82% higher for those with CKD compared with those with normal kidney function. [5] In addition, several studies have shown a relationship between PAD and an elevated risk for cardiovascular disease (CVD) and premature death in patients with CKD and in the general population. [6]

CKD has become one of the most important independent risk factors for development of PAD. Studies have demonstrated that the prevalence of PAD in patients with CKD can range from 12% to 38%. [5,6]

Traditional risk factors such as older age, cigarette smoking, physical inactivity, hypertension, diabetes and dyslipidemia play an important etiopathogenetic role in the development of PAD among patients with CKD but these traditional risk factors alone are not solely responsible for the excess risk of PAD in CKD patients. [7]

There are some additional unique risk factors that may be involved in development of PAD in patients with CKD, including endothelial dysfunction, chronic inflammation, oxidative stress, albuminuria, uremic toxins, pro-thrombotic and pro-calcific states, and microvascular disease .[8] There is dearth of literature on risk factors for the excess risk of PAD among patients with CKD. Identifying novel risk factors for the development of PAD would be key to furthering our understanding of the etiology of PAD in CKD and helping to establish new strategies for the prevention of PAD among patients with CKD.

PAD in late stage can cause lower limb issues, such as ulceration and amputation, and has impact on mortality and mortality. PAD is also associated with an increased risk of concomitant cardiovascular disease and poor quality of life in patients with chronic kidney disease (CKD). [9] Furthermore, poor allograft outcomes and overall mortality are linked to peripheral arterial disease (PAD) in renal transplant recipients. [10]

Ankle-brachial index (ABI) which is the ratio of ankle to brachial systolic blood pressure is a quick, easy, risk-free, noninvasive procedure to objectively assess peripheral blood flow in the lower extremities and is reliable method for screening for the presence and progression of PAD. [11]

Early identification and treatment of PAD may prevent or at least postpone certain negative consequences in patients of CKD. [8] Studies investigating PAD in individuals with chronic kidney disease (CKD) in India are scarce. The purpose of this study was to investigate the clinical profile, prevalence, and associated risk factors of PAD in Indian patients with CKD.

Aim and Objectives-•

To Study clinical profile of Peripheral Arterial Disease in patients of Chronic Kidney Disease.

Material and Methods-: Cross sectional, Observational Study conducted in the department of Medicine, JNU Medical College, Jaipur, Rajasthan, India on 50 patients admitted in Medicine wards with Chronic kidney disease.

Methodology

Demographic characteristics were collected for each participant, including age, sex, height, weight, duration, and stages of CKD. The body mass index was calculated. Relevant risk factors and comorbidities associated with PAD were analyzed, including smoking, hypertension, diabetes mellitus, dyslipidemia, coronary artery disease, cerebrovascular disease, and anemia. The laboratory tests were analyzed and recorded, including serum creatinine, albumin, total and LDL cholesterol, uric acid, phosphate, PTH, high-sensitivity C-reactive protein (hsCRP), hemoglobin level, eGFR and urine checked for albumin; albuminuria was defined when a spot urine dipstick test was positive for albumin and further confirmed by urine albumin/creatinine ratio. All participants underwent detailed history and physical examination; they were asked about PAD symptoms, including intermittent claudication (reproducible pain, cramping, or fatigue in the calf, thigh, or buttock during exercise), coldness, numbness, and resting pain, and they were categorized using the Fontaine classification. [12] The ABI was calculated for all patients using a portable handled Doppler device. The ABI value was calculated by dividing the higher pressure of the arteries at the ankle (dorsalis pedis and posterior tibial) by the higher brachial artery systolic pressure in both arms.

Results-

Demographic and baseline characteristics of the study population, stratified by PAD status.

Parameter	No PAD	PAD	Total	P Value
	Mean (SD)	Mean (SD)	Mean (SD)	
No. of Patients	35(70%)	15(30%)	50(100%)	
Mean Age (years)	53.71±8.73	60.20±5.16	55.66±8.34	.012
Male Gender (%)	29(82.86%)	13(86.67%)	42(84%)	0.736
BMI	27.49±1.74	27.27±1.87	27.42±1.76	.705
Duration of CKD	6.03±3.54	9.00±2.73	6.92±3.56	.002
Smoking(%)	5(14.29%)	8(61.54%)	13(26%)	0.004
Dyslipidaemia(%)	7(20%)	6(40%)	13(26%)	0.140
Hypertension	29(82.86%)	15(100%)	44(88%)	0.087
CAD	8(22.86%)	11(73.33%)	19(38%)	0.001
DM	6(17.14%)	11(73.33%)	17(34%)	0.001

Table- 2: Biochemical characteristics of the study population, stratified by PAD status.

Parameter	No PAD	PAD	Total	P Value
	Mean (SD)	Mean (SD)	Mean (SD)	
No. of Patients	35(70%)	15(30%)	50(100%)	
HB	10.37±.64	7.79±1.50	9.59±1.53	<.001
PTH	169.83±91.01	256.53±130.70	195.84±110.63	.010
Phosphorus	3.87±.35	3.69±.20	3.82±.32	.207
Uric Acid	6.26±.66	6.29±.88	6.27±.72	.899
Creatinine	3.07±.80	3.68±.49	3.25±.77	.018
Hs CRP	2.64±.44	5.37±1.66	3.46±1.59	<.001
eGFR	35.01±9.95	28.72±7.87	33.12±9.74	.045

Total Cholesterol (mg/dl)	200.07±22.48	237.83±41.28	218.95±38.06	<.001
LDL Cholesterol (mg/dl)	101.23±13.15	120.67±24.48	110.95±21.81	.002
Albuminuria	8(22.86%)	9(60%)	17(34%)	0.011

Discussion

Peripheral artery disease is highly prevalent in patients with CKD and is an important risk factor for cardiovascular events, lower limb complications, and adverse outcome.[10,13,14]In present study, PAD was diagnosed in 30% of the patients with CKD. An ABI < 0.9, combined with the clinical findings, such as state of pulses and PAD symptoms provide robust background for diagnosis.

The results of the present study showed a significant association between PAD and older age, duration of CKD, diabetes mellitus, and CAD and PAD was significantly associated with some non-traditional risk factors such as albuminuria, reduced GFR, and increased hsCRP.

The results of present study are consistent with the rates reported in several studies, such as the analysis of the United States Renal System database which reported that the prevalence of PAD in any CKD patient was 24.9%,[15] . Similarly, Arroyo et al[16] and Yamasaki et al[17] in a Japanese study reported the prevalence of PAD in 28% and 17.2% of CKD patients, respectively.

Patients with CKD have higher prevalence of PAD, not only due to aggregation of traditional CVD risk factors, but also due to the presence of unique renal risk factors, such as reduced GFR, albuminuria, chronic inflammation, oxidative stress, endothelial dysfunction, and pro-thrombotic state.[10,13,14] Chen et al[5] in their study found that PAD in CKD patients was significantly associated with traditional CVD risk factors, and with many novel risk factors, such as hsCRP, white blood cell count, fibrinogen, albuminuria, HbA1c, insulin resistance, phosphate, alkaline phosphatase, and total PTH, and they concluded that inflammation, prothrombotic state, and oxidative stress are associated with higher risk of PAD among CKD patients.

Bourrier et al[10] in their study found that PAD was common in those with reduced renal function, older males who had a higher burden of comorbidity, including diabetes and CVD, and was associated with low eGFR, raised HbA1C and albuminuria. Matsushita et al[18] found

that albuminuria and eGFR were significantly and independently associated with the development of PAD; these parameters confer a higher risk of incident PAD than traditional risk factors.

Albuminuria is considered a biomarker of endothelial dysfunction and causes structural and functional alterations.[19] The levels of inflammatory mediators, such as CRP, are elevated in CKD patients, and the inflammatory status in CKD worsens both vascular calcification and endothelial dysfunction.[20,21] However Harlacher et al[22], in their study found that phosphate and uric acid contribute to the genesis and progression of CVD in CKD, as they are associated with inflammation and endothelial dysfunction and they reported that PAD prevalence was higher among smokers and patients with dyslipidemia; however, these differences were not statistically significant which is inconsistent with results of present study . Atherosclerosis and intimal arterial calcification play pivotal roles in the development and progression of PAD.[13]

Various cohort studies have reported inconsistent findings regarding PAD prevalence rates, clinical profiles, and related risk factors in CKD patients which may be attributed to diversity in population characteristics, degree of kidney dysfunction, and PAD diagnostic modality used.[5,8,23]

Limitations- This was a single-center study with a relatively small sample size, and as this was an observational cross sectional study, there was an inevitable selection bias in our patients.

Conclusion - Peripheral artery disease was prevalent in patients with CKD in India. Older age, diabetes, coronary artery disease, advanced CKD stage, albuminuria, and elevated hsCRP levels were identified as risk factors. Early detection of patients with occult PAD may enhance efforts toward proper prevention and treatment.

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