Original Contribution

Proportion of Peripheral Arterial Disease in Patients with Chronic Kidney Disease

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Among the different complications of chronic kidney diseases, peripheral arterial disease is not uncommon. Though it is an indicator of widespread atherosclerosis, sometimes it is neglected in CKD patients. Our study was done to evaluate the frequency and pattern of PAD in chronic kidney disease patients admitted in a tertiary care hospital of Bangladesh. One hundred (100) admitted patients of CKD were taken by nonrandom purposive sampling considering inclusion and exclusion criteria. After clinical evaluation and Ankle brachial index (ABI) measurement 5 cc venous blood was collected and sent to Clinical Pathology and Biochemistry department of CMCH. Data was collected in a structured proforma and analyzed. Among the 100 patients, 2.0% patient belonged to stage 3, 28.0% were in stage 4 and remaining 70.0% were in stage 5. We found the proportion of PAD in CKD were 18.0%. Among 18 PAD patients, 66.67% were in stage 5, 22.22% in stage 4 and 11.11% in stage 3. Regarding right lower limb 12 patients had some PAD, 3 patients had moderate PAD, 2 patients had borderline and 1 patient had calcified PAD. For left lower limb, 10 patients had some PAD, 4 patients had moderate PAD, 4 patients had borderline PAD. The mean AB) of the PAD patients for right limb was 0.87 and for left limb 0.84. 50.0-55.0% patients were asymptomatic. Among the PAD patients 38.9% had DM, 72.2% had HTN, 33.3% had both DM and HTN, 44.4% had other vascular events, 55.6% were smokers, 33.3% had dyslipidemia and 22.2% had family history of PAD. Renal diseases seem to have a strong association with vascular disease and PAD is not uncommon.

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Key words: Chronic kidney disease, Peripheral arterial disease

Introduction

Cardiovascular diseases including coronary artery disease (CAD), congestive heart failure and peripheral arterial disease (PAD) are common in chronic kidney disease (CKD) patient and have devastating effects in terms of both human suffering and health economics. In comparison to CAD and HF, PAD is neglected in our society, but it is also an important public health problem and associated with quality of life and functional status, even for individuals who are asymptomatic. PAD is a disease process resulting from obstruction of large peripheral arteries, exclusive of the coronary and intracranial cerebrovascular system and most commonly due to atherosclerosis. Most typically it is referred to in relation to the lower limbs. Ankle-brachial index (ABI) is the most accurate and reliable non-invasive marker for diagnosing PAD[1]. ABI is measured by a hand-held Doppler probe, and is the ratio between systolic blood pressure (BP) in the ankle and systolic BP in the arm. The sensitivity and specificity of ABI for the diagnosis of PAD are 95.0% and 100.0% respectively[2]. Normal ABI is 0.9 to 1.4 and value lower than 0.9 is considered as PAD[3].

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This is an indicator of widespread atherosclerosis in other vascular territories, such as the cerebral and coronary circulations[4]. There is also remarkable overlap between PAD, cerebrovascular disease (CBVD) and coronary artery disease (CAD)[5]. PAD is not uncommon in CKD patients. O'Hare AM et al. found about 24.0% CKD patients developed PAD[6]. Now CKD is considered as a risk factor for PAD[4] and the chance of development of PAD in renal patient is greater than two-fold. Leskinen Y et al. 2002[7] PAD is also important because it's progressive nature and risk for amputation and nephrologist feels the impact of amputation on effective dialysis. In ESRD patients, chance of amputation for PAD is more in compare to the general population[8]. It leads to significant morbidity and mortality among end-stage renal disease (ESRD) patients and often coexists with CAD and diabetes which are also responsible for adverse outcomes[9]. But aggressive screening, diagnosis, medical treatment of PAD and revascularization both surgical and nonsurgical prior to amputation may reduce morbidity and mortality. Some risk factors of PAD are un-modifiable e.g, age, male sex, black ethnicity. Traditional modifiable cardio-vascular risk factors are also associated with PAD e.g. tobacco use, hypertension, diabetes, hyperlipidemia. Among the modifiable risk factors tobacco is the most important[10]. PAD is also high in diabetic patient[11]. Abnormal lipid profile is important in the development of atherosclerosis and also related to PAD. There is hardly any study regarding evaluation of peripheral arterial disease in CKD patient in our context on the basis of ABI values. So, this present study was aimed to evaluate the prevalence and pattern of peripheral arterial disease with a particular emphasis on patients with CKD in our community. The findings of this study will help nephrologists and other physicians working in our clinical settings to determine the burden of PAD in our CKD patients and providing best possible management.

Methods

This cross-sectional descriptive study was done in Medicine and nephrology department of CMCH. On the basis of inclusion and exclusion criteria patients of chronic kidney disease were selected. Patient with previous history of amputation of legs due to any cause, vasculitis, thromboembolism or AV fistula in hand were excluded. Aims, objectives and detailed procedure of the study was explained to the patients. After getting informed written consent, detailed history and physical examination was recorded. Brachial pressure of both arms and anterior tibial and post tibial pressure of both ankle was taken using handheld Doppler-8MHz vascular live doc Doppler with Lcd display (L250 series model) (Wallach surgical devices 95 corporate drive, trumbull. CT06611USA). Then ABI for each limb was calculated by using the highest pressure for each lower limb and the highest pressure in both arms and findings of ABI was included in the data sheet. From that ABI presence of PAD and their severity was levelled according toAnkle Brachial Index, Stanford Medicine 25[12]. Then 5 cc venous bloods was collected and sent to the Biochemistry Department of CMCH for measuring se creatinine and eGFR and CKD staging was done according to KDIGO guidelines 2012[13].

Results

Table I: Distribution of socio-demographic factors among the different stages of chronic kidney disease (CKD) patients (N=100)

Socio-demographic factors	CKD Stages			Total (n=100)	Significance (p value)
	Stage 3 (n=02)	Stage 4 (n=28)	Stage 5 (n=70)		
	n (%)	n (%)	n (%)	n (%)	
Sex					
Male	2 (100.0)	22 (78.6)	50 (71.4)	74 (74.0)	$P^1 = 0.536$
Female	00 (00.0)	06 (21.4)	20 (28.6)	26 (26.0)	
Age (years) Mean±SD	52.50±3.54	45.54±15.60	50.57±13.03	49.20±13.79	$P^2 = 0.251$
Age groups (years)					

≤ 20	00 (00.0)	03 (10.7)	01 (01.4)	04 (04.0)	$P^1 = 0.325$
21-40	00 (00.0)	08 (28.6)	17 (24.3)	25 (25.0)	
41-60	2 (100.0)	12 (42.8)	40 (57.2)	54 (54.0)	
61-80	00 (00.0)	05 (17.9)	12 (17.1)	17 (17.0)	
Body weight (Kg) Mean±SD	66.50±3.54	61.11±8.16	61.81±6.22	61.71±6.77	$P^2 = 0.542$

P^1 = Chi-Square test significance; P^2 = ANOVA significance

During this study we found, among 100 patients 74 was male and 26 was female. Most of the patients (70) patients were in stage 5. The mean age of stage 3 was 52.50±3.54. For stage 4 it was 45.54±15.60 and for stage 5 it was 50.57±13.03.Maximam patients of CKD belongs to 41-60 years range and mean body weight was 61.71±6.77.

Table II: Distribution of peripheral arterial disease (PAD) among different CKD stages (N=100)

PAD status	CKD Stages			Total (n=100)	Significance (p value)
	Stage 3 (n=02)	Stage 4 (n=28)	Stage 5 (n= 0)		
	n (%)	n (%)	n (%)	n (%)	
PAD					
Present	02 (11.11)	04 (22.22)	12 (66.67)	18 (100.0)	p<0.005
Absent	00 (00.00)	24 (29.27)	58 (70.73)	82 (100.0)	

Total 18.0% of CKD patient developed PAD. Among them 66.67% were in stage 5, 22.22% in stage 4 and 11.11% in stage 3 which was statistically significant (p<0.005).

Table III: Distribution of age among the PAD patients (N=100)

PAD	Age in years			
	n	Mean±SD	Median	Range
Present	18	49.83±16.50	50.00	16-80
Absent	82	49.06±13.24	50.00	13-80
Total	100	49.20±13.79	50.00	13-80

Among the PAD patients the mean age was 49.83 years and for non PAD patients it was 49.06 years.

Table IV: Distribution of sex among the PAD patients (N=100)

Sex	PAD		Total	p value (χ^2 test)
	Present	Absent		
	n (%)	n (%)		
Male	14 (77.8)	60 (73.2)	74 (74.0)	0.687
Female	04 (22.2)	22 (26.8)	26 (26.0)	
Total	18	82	100	

Among 18 PAD patients 77.8% were male and 22.2% were female. In total, about 18.91% male and 18.18% female has PAD.

Table V: Peripheral arterial disease (PAD) status on the basis Ankle Brachial Index, Stanford Medicine 25[12], among the different stages of chronic kidney disease (CKD) patients (n=100)

PAD status	CKD stages			Total (n=100)
	Stage 3 (n=02)	Stage 4 (n=28)	Stage 5 (n=70)	
	n (%)	n (%)	n (%)	n (%)
PAD (Right Limb)				
Normal	00 (00.0)	24 (85.7)	58 (82.9)	82 (82.0)
Calcification	00 (00.0)	00 (00.0)	01 (01.4)	01 (01.0)
Borderline	00 (00.0)	01 (03.6)	01 (01.4)	02 (02.0)
Some	01 (50.0)	03 (10.7)	08 (11.4)	12 (12.0)
Moderate	01 (50.0)	00 (00.0)	02 (02.9)	03 (03.0)
PAD (Left Limb)				
Normal	00 (00.0)	24 (85.7)	58 (82.9)	82 (82.0)
Calcification	00 (00.0)	00 (00.0)	00 (00.0)	00 (00.0)
Borderline	00 (00.0)	01 (03.6)	03 (04.3)	04 (04.0)
Some	01 (50.0)	03 (10.7)	06 (08.5)	10 (10.0)
Moderate	01 (50.0)	00 (00.0)	03 (04.3)	04 (04.0)

Regarding PAD severity for right limb, 12 patients had some disease, 3 patients had moderate, 2 patients had borderline and 1 patient had calcified disease. For left limb 10 patients had some PAD, 4 patients had moderate PAD, 4 patients had borderline PAD.

VI: Distribution of ankle brachial indices (ABI) among the PAD patients according to CKD stages (n=18)

CKD Stages	Ankle Brachial Index (Right Limb)					
	n	Mean±SD	Median	Range	p value	(ANOVA test)
Stage 3	02	0.76±0.08	0.76	0.71-0.82	0.372	
Stage 4	04	0.88±0.05	0.88	0.82-0.94		
Stage 5	12	0.88±0.12	0.86	0.75-1.13		
Total	18	0.87±0.10	0.86	0.71-1.13		

CKD Stages	Ankle Brachial Index (Left Limb)					
	n	Mean±SD	Median	Range	p value	(ANOVA test)
Stage 3	02	0.83±0.06	0.83	0.79-0.88	0.570	
Stage 4	04	0.88±0.04	0.88	0.83-0.94		
Stage 5	12	0.83±0.09	0.86	0.60-0.93		
Total	18	0.84±0.08	0.87	0.60-0.93		

In case of Right limb, mean ABI of PAD patients for stage 3 was 0.76. In stage 4, it was 0.88 and in stage 5, it was 0.88.

Distribution of ankle brachial index (ABI) in left limb among the PAD patients showing, in stage 3 mean ABI was 0.83. In stage 4, it was 0.88 and in stage 5, it was 0.83.

Table VII: Distribution of types of limb ischemia among the PAD patients (n=100)

Types of ischemia (Right limb)	PAD		Total
	Present	Absent	
	n (%)	n (%)	n (%)
Asymptomatic	10 (55.6)	00 (00.0)	10 (10.0)
Night pain	01 (05.6)	00 (00.0)	01 (01.0)
Intermittent claudication	07 (38.9)	00 (00.0)	07 (07.0)
Total	18	82	100

Types of ischemia (Left limb)	PAD		Total
	Present	Absent	
	n (%)	n (%)	n (%)
Asymptomatic	9 (50.0)	0 (00.0)	9 (09.0)
Night pain	2 (11.1)	0 (00.0)	2 (02.0)
Intermittent claudication	7 (38.9)	0 (00.0)	7 (07.0)
Total	18	82	100

Regarding presentations of right limb PAD patients 55.6% were asymptomatic, 38.9% had intermittent claudication and 5.6% had night pain and for left limb PAD, 50.0% were asymptomatic, 38.9% had intermittent claudication and 2.0% had night pain.

Table VIII: Distribution of risk factors among the PAD patients (n=100)

Risk factors		PAD		Total	p value (χ^2 test)
		Present	Absent		
		n (%)	n (%)	n (%)	
Diabetes mellitus	Present	7 (38.9)	41 (50.0)	48 (48.0)	0.393
	Absent	11 (61.1)	41 (50.0)	52 (52.0)	
Hypertension	Present	13 (72.2)	64 (78.0)	77 (77.0)	0.595
	Absent	05 (27.8)	18 (22.0)	23 (23.0)	
DM and hypertension	Present	06 (33.3)	35 (42.7)	41 (41.0)	0.465
	Absent	12 (66.7)	47 (57.3)	59 (59.0)	
Other vascular events*	Present	08 (44.4)	07 (8.5)	15 (15.0)	0.001
	Absent	10 (55.6)	75 (91.5)	85 (85.0)	
Smoking	Present	10 (55.6)	46 (56.1)	56 (56.0)	0.967
	Absent	08 (44.4)	36 (43.9)	44 (44.0)	
Dyslipidemia	Present	06 (33.3)	12 (14.6)	18 (18.0)	0.061
	Absent	12 (66.7)	70 (85.4)	82 (82.0)	
Family history of PAD	Present	04 (22.2)	02 (02.4)	06 (06.0)	0.001
	Absent	14 (77.8)	80 (97.6)	94 (94.0)	

* Other vascular events include IHD, stroke

The studied PAD patients had various risk factors like DM (38.9%), HTN (72.2%), both DM and HTN (33.3%), other vascular events (44.4%), smoking (55.6%), dyslipidemia (33.3%) and family history of PAD (22.2%).Among these risk factors other vascular events and positive family history were found statistically significant.

Discussion

This study regarding the proportion of peripheral arterial disease in chronic kidney disease was done between January 2015 to June 2015, in a tertiary care hospital of Chattagram where 100 cases of chronic kidney disease were included as per inclusion criteria. Gender distribution of this study showed 74.0% were male and 26.0% were female. Another study regarding the same topic showed 63.9% were male[14]. In this study male predominance may be due to lack of health seeking behavior among the female. Among the 100 patients 2.0% patient belonged to stage 3, 28.0% stage 4 and remaining 70.0% stage 5. It represents the fact that most of the CKD patients were diagnosed and become symptomatic in or above stage 3B[13] and hospitalized later on. A study done by Pakistan Institute of Medical Sciences shows Twenty-five patients (34.7%) were in stage 3 CKD, 20 patients (27.8%) were in stage 4 CKD and 27 patients (37.5%) were in stage 5 CKD[14]. Another study had the study population with 2.1%, 16.5%, 34.5%, 22.2% and 24.7% in CKD stage 1, 2, 3, 4 and 5 respectively[15]. The mean age distribution of this study group was 49.20 with a standard deviation of ±13.79. This was similar to that found by Sheikh where the mean age was 52.7 years[16]. In another study the mean age of the patients was 53.22±12.8 years[14]. Maximum patients of our CKD belonged to 41-60 years range. In the 2003-2006 NHANES study, the prevalence of CKD in people ages 60 was 24.5 percent. And in people between the ages of 20 and 39 was below 0.5 percent (Kidney Disease Statistics for the United States 2012)[17] that signified the agerelated renal dysfunction. We have found that among 100 patients 82.0% have no PAD and 18.0% have PAD. Maritim MC et al. found 11.9% patient of CKD developed PAD[15]. In another study of NHANES on 2229 patients, a 24.0% PAD prevalence rate was observed in patients with estimated GFR <60 ml/min/1.73m^2 [6]. 66.67% of our PAD patients were in stage 5, 22.22% were in stage 4 and 11.11% were in stage 3. Maritim MC et al. 2007 also found majority of PAD patients had advanced CKD disease, with 74.0% in stage 4 and 5 and 90.0% in stage 3 and above[15]. Among the PAD patients mean age was 49.83 years and the mean age of non PAD patients was 49.06 years which is more or less similar to another study showing the mean age of the patients with PAD was 51.9±14.6 years and the mean age of the patients without PAD was 53.7±12.2 years[14]. The mean age was 54.49±18.36 years in male and 49.45±17.89 years for female in a study of NICVD on PAD[18]. Sex distribution of PAD patients showed 77.8% are male and 22.2% are female. In a study on PAD in our country shows most of the patients were male (69 out of 89) patients[18]. In 100 patients about 18.91% male and 18.18% female had PAD. Similar result is found in another study, 21.74% male and 38.5% female had PAD[14]. Distribution of peripheral arterial disease (PAD) status in right limb showing among 100 patients, 82.0% were normal, 12.0% had some PAD, 3.0% had moderate PAD, 2.0% had borderline and 1.0% had calcification with average ABI in PAD is 0.87 and in left limb 82.0% were normal, 10.0% had some PAD, 4.0% had moderate PAD, 4.0% had borderline and no patients had calcification with average ABI in PAD is 0.84. A Pakistani study showed 18.1% had mild to moderate PAD with ABI of 0.41-0.90 and 9.7% had severe PVD with ABI of 0.00-0.40[14]. Another Kenyan study shows 1.5% had severe PAD, 5.2% moderate PAD and 5.2% mild PAD[15]. In right limb among 18 PAD patient 66.67% had some, 16.67% had moderate and 11.11% had mild disease and in case of left limb among 18 PAD patient 55.55% had some, 22.22% had moderate and 22.22% had mild disease. In a Kenyan study, out of 23 patients with PAD, 43.5% had mild PAD (ABI 0.71-0.90), 43.5% had moderate PAD (ABI 0.41-0.70) and 13.0% had severe PAD (ABI 0.41)[15]. Most of the PAD patients were found asymptomatic. In right limb among the PAD patients 55.6% were asymptomatic, 38.9% had intermittent claudication and 5.6% had night pain and in left limb 50.0% were asymptomatic, 38.9% had intermittent claudication and 11.1% had night pain. In another study on PAD in primary care medical practices, 30.0% to 60.0% of patients with PAD reported no exertional leg symptoms and 45.0% to 50.0% reported exertional leg symptoms[19]. Another study showed 50.0% patients were asymptomatic and 47.8% of PAD patients presented with intermittent Claudication[15]. In the Spanish study 30.0% of the PAD patients had intermittent claudication[20]. The underlying reason for the increased risk of PAD among patients with CKD was not well understood. In this study, we found that traditional risk factors such as age, cigarette smoking,

diabetes and hypertension were presentin PAD with CKD patients that suggest the relationship of these factors with PAD. In our 18 PAD patients 38.9% had DM, 72.2% had HTN, 33.3% had both DM and HTN, 44.4% had other vascular events, 55.6% were smokers, 33.3% had dyslipidemia and 22.2% had positive family history. The commonest risk factor in another studyon PAD was hypertension 46.1%, followed by diabetes 30.3%, family history of atherosclerotic coronary and peripheral vascular diseases 27.0%, smoking 23.6%, dyslipidaemia 13.5%[18]. PAD was found to be associated with hypertension (74.0%), diabetes mellitus (56.0%), cigarette use (47.0%) and dyslipidemia (43.0%) in a similar study[15].

Conclusion

In conclusion proportion of PAD among CKD patients is not low. Majority of the PAD patients were in advanced CKD stage 4-5 and they had mild to moderate PAD. More than half of the patients with PAD were asymptomatic.

Limitation of the study

Small sample size. The ability to find out the association between PAD and risk factors was limited by a small number of patients with PAD. Absence of long term follow-up. Cross-sectional study may not bring out associations in on-going disease.

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