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ORIGINAL ARTICLE

Prevalence of peripheral arterial disease and association with cardiovascular risk factors in patients with end-stage kidney disease in a hospital in Nigeria

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ABSTRACT

Introduction: Peripheral arterial disease (PAD) is not uncommon among patients with end-stage kidney disease (ESKD), but it is usually under-reported. Moreover, PAD is a strong independent risk factor for cardiovascular disease in persons with chronic kidney disease (CKD). The aim of this study was to evaluate the prevalence of PAD and its association with cardiovascular risk factors in Nigerian patients with ESKD.

Methods: This was a retrospective investigation of 122 subjects with ESKD on haemodialysis (HD), who were worked up for renal transplantation at Zenith Medical and Kidney Centre in Gudu, Abuja, Nigeria from February 2020 to March 2021. Data were obtained from the electronic medical records of the hospital and included sex, age, body mass index, history of diabetes, hypertension (HTN), duration of CKD, length of dialysis, lipid profile and lower limb Doppler ultrasound. Cardiovascular risk, measured as atherogenic index (AI), was calculated using the formula log (TG/ HDL-C), where TG = triglyceride and HDL-C = high-density lipoprotein cholesterol. Data analysis was performed using SPSS version 20. Continuous variables were expressed using measures of central tendency whereas categorical variables were expressed as frequency (percentages). Bivariate analysis was used to establish association between each variable, PAD and AI. A chi-square test was used to examine the relationship between categorical variables; a P value <0.05 was considered statistically significant.

Results: Male subjects accounted for 81.1% of the study population. The median duration of CKD was 8 months (range 1–96 months) and the mean duration of dialysis was 10 ± 1.1 months. HTN was the commonest comorbidity factor in these subjects with 98 (80%) hypertensive with a median duration of the condition of 5 years (range 1–32 years); diabetes mellitus (DM) accounted for 44 (36%) patients with a median duration of 15 years (range 1–36 years). The prevalence of PAD among patients with ESKD was 48.4%. AI was associated with dialysis duration. The association between duration of CKD and PAD was positive and significant (rho = –0.245, P = 0.007).

Conclusion: PAD was highly prevalent among patients with ESKD and remains one of the most potent risk markers for cardiovascular morbidity in patients with CKD. Patients with CKD should routinely be examined for PAD and the longer ESKD patients stay on dialysis, the greater the risk of developing cardiovascular disease. Screening for PAD and prompt treatment would be beneficial for pretransplant patients before the procedure.

Keywords: CKD, peripheral arterial disease, cardiovascular risk, Nigeria.

INTRODUCTION

Peripheral vascular disease (PVD) affects over 200 million people worldwide [1]. The prevalence of peripheral arterial disease (PAD) has increased over the last decade by more than 25% from about 160 million to over 200 million, particularly in low-income countries [1]. It is also relatively common among patients with end-stage kidney disease (ESKD), ranging from 35.8% in Italy to 47.2% in Japan, and it can negatively impact outcomes [2,3]. It

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represents the progressive occlusion of peripheral arteries by atherosclerosis and is associated with a high rate of morbidity and mortality, especially in patients with chronic kidney disease (CKD) [4].

CKD has been recognised as a significant independent risk factor of PAD among multiple risk factors. Foley et al. studied 1,091,201 subjects from the Medicare database and observed a 9.6% prevalence of PAD in patients without CKD, and a threefold higher prevalence of 32.6% in CKD patients [5].

There is a great difference in the current recommendations for screening for PAD. The guidelines of the Inter-Society Consensus for the Management of PAD (TASC II), the American College of Cardiology (ACC) and the American Heart Association (AHA) propose a strong recommendation for detecting asymptomatic PAD. This is aimed at a risk-reduction strategy in the form of facilitated secondary prevention, which is particularly important among high-risk populations such as those with ESKD.

Given the increased incidence of PAD in CKD, the K/DOQI guidelines recommend that CKD patients are screened at the start of dialysis. Screening for PAD and its early diagnosis in this population may be important because of its association with increased mortality in dialysis patients [6,7].

CKD and PAD share common predisposing factors, and there is increasing evidence that CKD represents a strong, independent risk factor for PAD. Ankle brachial index (ABI) is considered to be the gold standard to diagnose PAD in "at risk" individuals, however, the ABI is limited in sensitivity to detect PAD in the presence of arterial calcification, which is more frequent among patients with advanced kidney disease [8]. Thus, ABI values may be falsely normal or even abnormally high (>.4) despite the presence of significant PAD. It is therefore imperative that a high degree of suspicion is maintained by attending physicians when evaluating for PAD in patients with ESKD with normal ABI, and further vascular testing is recommended. Duplex ultrasound evaluation of arterial blood flow velocity represents an accurate diagnostic test in individuals with CKD and can be used with no risk and at low cost.

The objective of this study was to evaluate the prevalence of PAD and its association with cardiovascular risk factors in Nigerian patients with ESKD. We also assessed their pattern of cardiovascular risk.

METHODS

This was a retrospective study of patients with ESKD on haemodialysis, who were worked up for kidney transplantation at the Zenith Medical and Kidney Centre, Abuja Nigeria from February 2020 to March 2021.

Patients' data such as age, gender and past medical history were obtained from the hospital's electronic medical records. Hypertension (HTN) was defined as blood pressure ≥130 mmHg for SBP and/or ≥90 mmHg for DBP or the use of antihypertensive medication. Diabetes was defined as fasting blood sugar ≥7 mmol/L, HBA1C ≥6.5%, or the use of antidiabetic medication.

Subjects were weighed using a standard weighing scale and values recorded to the nearest 0.1 kg, while height was measured with a stadiometer to the nearest 0.1 m. Body mass index (BMI) was calculated as weight (kg) divided by the square of height (m). The first lipid profile test carried out on the first hospital visit was used for this study. Records of subjects who were already started on statins was obtained from the records and as such they were excluded from the study.

The Doppler scans were performed by a consultant radiologist using a linear transducer with a variable ultrasound frequency of 9–15 MHz. These scans were carried out with a GE ultrasound machine (Chicago, Illinois, manufactured in 2019). The examination was performed with the patient in a supine position. Our hospital radiology department follows the guidelines described by Hwang [9] and the arteries scanned were the femoral, popliteal, tibial, peroneal and the dorsalis pedis arteries.

PAD among participants was defined as the presence of intima medial thickening, the presence of plaques, and/or the presence of stenosis.

The atherogenic indices (AI) were calculated using the formula log (TG/HDL-C), where TG = triglyceride and HDL = high-density lipoprotein cholesterol. Cardiovascular risk was classified as low risk (–0.3 to 0.1), medium risk (0.1 to 0.24) or high risk (>0.24) using the AI [10].

Data were analysed using SPSS Statistics for Windows, version 20.0 (IBM Corp., Armonk, New York). Continuous variables were expressed using measures of central tendency whereas categorical variables were expressed as frequency (percentages). A chi-square test was used to examine relationship between categorical variables. Bivariate analysis was used to establish any association between each variable, PAD and AI. Spearman correlation was used to test for any relationship between the duration of CKD and PAD. A P value <0.05 was considered statistically significant.

Ethical approval was granted by the Research and Ethics Committee of the FCT Department of Health, Abuja, Nigeria.

RESULTS

A total of 122 subjects with ESKD were consecutively recruited into this study by a convenience sampling method. The sex and age distribution are shown in Figure 1 with male subjects accounting for 81.1%.

The mean age of the study population was 47.8 ±12.6 years. Normal BMI was recorded in 48%. Underweight was present in 3.5%, whereas overweight and obesity accounted for 30% and 19%, respectively. The median duration of CKD was 8 months (range 1–96 months). HTN was the commonest comorbidity factor in these subjects with a prevalence of 80% and a median duration of 5 years (range 1–32 years). Diabetes mellitus (DM) was present in 44 (36%) subjects and the median duration of diabetes was 15 years (range 1–36 years). The mean duration of smoking was 16.3 ± 2.7 years and the mean duration of dialysis was 10 ± 1.1 months.

The prevalence of PAD in this study population was 48.4%. There were no significant associations between PAD, AI and variables such as age, sex, HTN and DM (Tables 1 and 2). However, there was a significant positive correlation between PAD and age, duration of CKD and duration of dialysis (rho = 0.298, P = 0.001; rho = 0.245, P = 0.007; rho = 0.214, P = 0.020, respectively). There was a weak insignificant positive correlation between duration of HTN and PAD (rho = –0.019, P = 0.834), which was similar to the duration of diabetes and PAD (rho = –0.055, P = 0.550) (Table 3).

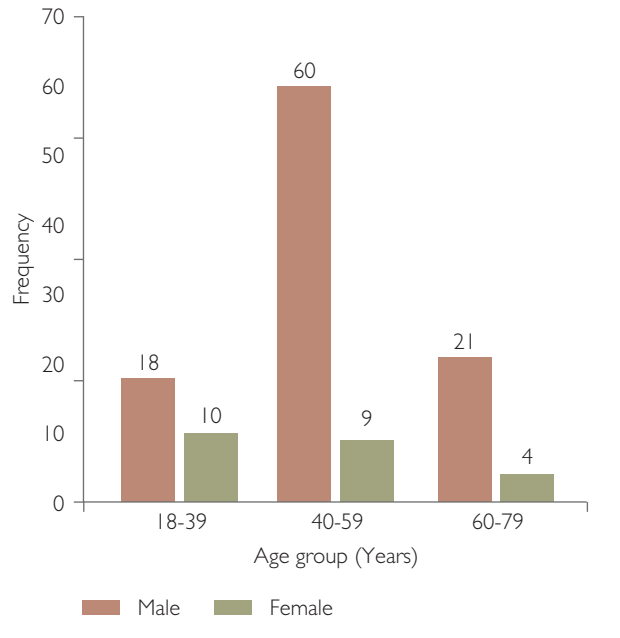

Figure 1. The sex and age distribution of the study population.

Table 1. The association between age, sex, hypertension, diabetes mellitus and PAD.

Variables	PAD Yes n=59 n (%)	PAD No n=63 n (%)	χ^2	P value
Age group (years)			4.250	0.119
18–39	10 (16.9)	18 (28.6)		
40–59	33 (55.9)	36 (57.1)		
60–79	16 (27.2)	9 (14.3)		
Sex			0.756	0.385
Male	46 (78.0)	53 (84.1)		
Female	13 (22.0)	10 (15.9)		
Hypertension			0.076	0.782
Yes	48 (81.4)	50 (79.4)		
Diabetes			0.074	0.786
Yes	37 (62.7)	41 (65.1)		

Table 2. The association between sex, age, hypertension, diabetes mellitus and AI.

Variables	AI Low n=57 n (%)	AI Medium n=13 n (%)	AI High n=52 n (%)	χ^2	P value
Age group (years)				3.559	0.469
18–39	17(29.8)	2 (15.4)	9 (17.3)		
40–59	28(49.1)	9 (69.2)	32 (61.5)		
60–79	12(21.1)	2 (15.4)	11 (21.2)		
Sex				1.623	0.444
Male	49(86.0)	10(76.9)	40 (76.9)		
Female	8 (14.0)	3 (23.1)	12 (23.1)		
Hypertension				3.252	0.197
Yes	47(82.5)	8 (61.5)	43 (82.7)		
Diabetes				1.534	0.464
Yes	39(68.4)	9 (69.2)	30 (57.7)		

The atherogenic index recorded 52 (43%) subjects at high risk, 13 (11%) at medium risk and 57 (47%) at low risk.

There was a significant weak positive correlation between dialysis duration, PAD and AI (rho = 0.195, P = 0.046, and rho = 0.101, P = 0.028, respectively). Other associations were not significant (Table 4).

DISCUSSION

PAD was highly prevalent among patients with ESKD in our sample of Nigerian patients and it remains one of the most

Table 3. Correlations between variables and PAD.

Variables	Correlation coefficient#	P value
Age	0.298	0.001*
Sex	0.079	0.389
Duration of CKD	0.245	0.007*
HTN	0.025	0.784
DM	0.025	0.788
HTN duration	0.019	0.834
DM duration	0.055	0.550
Smoking duration	0.154	0.091
Dialysis duration	0.214	0.020*

*Statistically significant; #Spearman correlation. PAD, peripheral arterial disease; CKD, chronic kidney disease; HTN, hypertension; DM, diabetes mellitus.

Table 4. Correlations between variables and AI.

Variables	Correlation coefficient#	P value
Age	0.035	0.716
Sex	0.091	0.342
Duration of CKD	-0.058	0.550
Smoking duration	-0.068	0.481
Dialysis duration	0.195	0.046*
PAD	0.101	0.028*
BMI	0.006	0.952

*Statistically significant; #Spearman correlation. AI, Atherogenic index; CKD, chronic kidney disease; PAD, peripheral arterial disease; BMI, body mass index.

potent risk markers for cardiovascular morbidity. Increasing age, duration of CKD, and dialysis duration were significantly associated with PAD. This is not unexpected as most of the conditions that lead to ESKD are also involved in the aetiology of PAD, so that the longer the duration of ESKD the greater the risk of PAD. Cardiovascular risk among our sample of patients was also relatively high and associated with length of dialysis and the presence of PAD.

The majority of the subjects were middle aged with a mean age of 47.8 years. This is similar to the report of a multicentre study to determine the prevalence of CKD and risk factors in North-Central Nigeria, which showed that CKD was most prevalent among the middle-aged urban population with a mean age of 44 years [11].

In our study, more than two-thirds of the subjects (81%) were males. In contrast, a community-based study showed that CKD was more common among females [12]. This could be because their study was community-based whereas ours was hospital-based. Males are generally more economically advantaged than females, which may significantly influence their health-seeking behaviours, especially since ESKD is expensive to manage and health insurance coverage is limited.

A significant number of our subjects were hypertensive (80%). It cannot be established from this study if HTN was the cause of the ESKD or if it was a consequence of kidney disease. HTN has been documented as one of the commonest causes of CKD, especially in people of African descent [13].

Diabetes mellitus (DM) was present in 64% of the study population. This is usually seen to be a problem in developed countries and it is the most common cause of ESKD in North America and Europe [14].

The prevalence of PAD in this study based on Doppler scanning was 48%. This is higher than the prevalence documented in previous studies where it was recorded as 24–37% in a group of patients with CKD [15-17], and was reported in 28% of patients with CKD/ESKD in the USA [15]. The findings from the Dialysis Outcomes and Practice Patterns Study (DOPPS) described an overall PAD prevalence of 25.3% among patients on HD that was accompanied by significant geographic variations. In European countries, PAD prevalence was 17.5–37.8%, whereas in Japan the corresponding value was significantly lower at 11.5% [18]. The variation in PAD prevalence in our study compared with other reports could be due to several reasons: the diagnostic criteria for PAD in ESKD patients were not uniform, or the different populations were genetically varied, or the inclusion criteria in the various studies may have been different. The prevalence of PAD has increased over the last decade, particularly in low-to-middle-income countries [1]. Among patients on haemodialysis, which includes all the subjects in our study, the prevalence of PAD was much higher, ranging from 17% to 48% [17,19].

PAD increases with age and is 4.5–14.5% more prevalent among individuals aged ≥65 years [20]. In our study, increasing age significantly correlated with PAD, which was found to be especially common among middle-aged persons (56%). This can be explained by the fact that ESKD, which is an independent risk factor for PAD, is most common in this age group. Additionally, studies have shown that haemodialysis is a risk factor for developing PAD, and as many as 17–48% of ESKD patients develop PAD while on dialysis [17,19]. One study reported a coronary artery disease co-prevalence of 65% in patients with CKD who have PAD [21].

It is valuable to note that many patients on HD with PAD can avoid or at least delay vascular or cardiovascular events, and even death if PAD is diagnosed in time and adequately managed. It was not unexpected for more males to have ESKD with a higher prevalence of PAD as shown in Table 1. This can be attributed to the male preponderance in this study. PAD was more prevalent in those with HTN (81%), which is considered a risk factor for vascular disorders, including PAD. In one study 5–55% of patients with PAD also demonstrated HTN [22]. Our finding of the majority of subjects with DM having PAD (63%) is not unusual, because DM is known to increase the risk of PAD and to accelerate its course [23]. There was a significant correlation between duration of CKD and PAD in our study. CKD has been reported to be an independent risk factor for PAD. The risk of PAD increases as GFR values decrease and is even worse for those on dialysis, after adjusting for multiple confounding variables [24,25].

The cardiovascular risk derived from the atherogenic index among patients with ESKD in this study put the latter at high risk in 43% of cases. This is not unexpected as studies have shown that individuals with CKD are at increased risk for cardiovascular diseases, which include specific conditions such as coronary artery disease and congestive heart failure [26-28]. The subjects in our study were patients with ESKD, who were being worked up for kidney transplantation and in whom this study revealed a high PAD prevalence. Interestingly, PAD is not considered a contraindication to renal transplantation. The American Society of Transplantation and the American Heart Association recommend a preoperative noninvasive screening for coronary artery disease, given the high rate of concurrence of PAD and coronary artery disease in the presence of PAD. These organizations recommend treatment if the patient becomes symptomatic with PAD [29,30].

Some authors have demonstrated that renal allograft transplantation may retard the progression of PAD in CKD patients by various mechanisms such as by the reduction or removal of the non-dialyzable mediators of PAD and the use of immunosuppressives [31,32]. Additionally, drugs used for immunosuppression such as tacrolimus, and antimetabolites, such as mycophenolate mofetil, have the ability to contribute to slowing the progression of PAD after transplantation through their anti-proliferative effects on neointimal hyperplasia [31,32]. Other studies have shown a reduction in risk of dying from PAD after renal transplantation and a twofold reduction in 5-year mortality for PAD patients compared to those remaining on the waiting list [hazard ratio (HR) 0.440, $P < 0.001$][33,34].

Limitations of the study

This was a single-centre retrospective study that involved a relatively small number of patients. The study population included ESKD patients on HD awaiting renal transplantation; a long-term follow-up after renal transplantation to monitor the progress of PAD and cardiovascular risk would generate more robust data and better understanding. Also, as with other retrospective, cross-sectional studies, there may be some recall and detection bias in the data collection.

CONCLUSION

PAD is an under-diagnosed disease among patients with ESKD, and it remains one of the most potent risk markers for cardiovascular morbidity in patients with CKD. The cardiovascular risk measured by AI was highest in middle-aged patients with ESKD on haemodialysis and in those with HTN and diabetes; an association between age, duration of CKD, length of time on dialysis, PAD and cardiovascular risk was established. Patients with CKD should routinely be examined for PAD and the longer ESKD patients stay on dialysis, the greater the risk of developing cardiovascular disease. Screening for PAD and prompt treatment would be beneficial for pretransplant patients before the procedure.

Conflicts of interest

The authors declare no conflict of interest in this research.

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