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Prevalence of Carotid Atheromatous Plaques in Pre-Dialysis Chronic Kidney Disease Patients in South East, Nigeria

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Abstract

Background: Chronic kidney disease (CKD) patients have considerably high atherosclerotic changes which predict cardiovascular events; hence, this study evaluated the prevalence of carotid atherosclerotic plaques in pre-dialysis CKD patients at a tertiary institution in south-east, Nigeria. **Materials and Method:** 107 pre-dialysis CKD patients were consecutively recruited for the study. 81 subjects who were screened and had no kidney disease served as control. The control group was sex and age matched with the CKD patients. A pre-tested questionnaire was administered to all participants and physical examination was done. Presence of atheromatous plaques was assessed using doppler ultrasound at 3 sites—distal common carotid artery (CCA), the internal carotid artery (ICA) and the carotid bulb by a single skilled radiologist specialized in doppler ultrasound. **Results:** Atheromatous plaques were significantly increased in CKD patients. 14.2% of CKD patients had atheromatous plaques versus 2.5% in the control group (p value < 0.05). Commonest site of occurrence was at the common carotid artery (CCA-7.5% versus ICA-4.7% versus bulb 1.8%). **Conclusions:** Atheromatous plaques are prevalent in CKD patients. It is recommended that carotid doppler ultrasound should be done in CKD patients to identify patients for possible intervention.

Keywords

Carotid Plaques, CKD, Predialysis, Nigeria

1. Introduction

Chronic kidney disease (CKD) is a global public health problem. It is defined by

the Kidney Disease Outcome Quality Initiative of National Kidney Foundation (K/DOQI-NKF) [1] as either kidney damage (defined as pathologic abnormalities or markers of damage, including abnormalities of blood, or urine test, or imaging studies) with or without decrease in glomerular filtration rate (GFR); or a decrease in GFR < 60 ml/min/1.73m^2; for 3 or more months. CKD is a common disease in Nigeria and other parts of Africa where it is a significant cause of death among patients in the hospital medical ward [2] [3].

CKD is associated with numerous complications which include anaemia, cardiovascular disease (CVD), CKD-mineral and bone disorder, skin disease, gastrointestinal complications, metabolic abnormalities, endocrine abnormalities, muscle dysfunction and uremic neuropathies. CVD remains the leading cause of death in CKD patients long before they get to ESRD. Atherosclerotic changes which predict cardiovascular events are reasonably high in CKD patients. Patients with CKD have higher cardiovascular complications and markedly increased risk of ischemic stroke. They have higher prevalence of premature arterial plaque formation and 20-fold increased cardiovascular mortality compared with individuals with normal kidney function [4] [5]. Factors that are implicated include lipid disorders, increased oxidative stress, chronic inflammation, anaemia, hypertension, hyperhomocysteinemia, disorders of calcium and phosphorus metabolism and metabolic deficiencies of glucose [6] [7]. Presence of atherosclerotic plaques in great arteries e.g. carotid artery is a good indicator of a more generalized atherosclerosis [8].

B-mode ultrasound is an imaging method that has been widely used for detection and measurement of carotid plaques [9] [10]. High-resolution B-mode carotid ultrasound is proven to be an important tool for epidemiological research in different high-risk groups [11].

There are limited studies especially in blacks on the prevalence of carotid plaques in CKD patients; hence, this study evaluated the prevalence of carotid plaques in pre-dialysis CKD patients at different segments of the carotid artery at the University of Nigeria Teaching Hospital, Enugu.

2. Materials and Methods

This study was cross sectional, case control and hospital based between January 2013 and June 2013. The place of study was at the University of Nigeria Teaching Hospital, U.N.T.H, Enugu, a tertiary health institution in south east Nigeria. Informed consent was obtained from all participants and ethical approval was obtained from the Research and Ethics Committee of the University of Nigeria Teaching Hospital, Enugu.

107 consenting pre-dialysis CKD patients were consecutively recruited for the study. 81 subjects who were screened and had no kidney disease served as control in a ratio of 3:2 (patient to control). Controls were drawn from amongst hospital staff, normal subjects attending the hospital for medical examination from the general outpatients department and patients' relatives. The control group was sex and age matched with the CKD patients.

2.1. Sample Size Determination

Prevalence of atherosclerosis in CKD is about 30% [12]. Using average prevalence of CKD in Nigeria of 25% [13], expected prevalence rate of atherosclerosis in CKD was calculated to be 7.5% and allowing for 10% non-response rate, the sample size was thus calculated using the Fisher's formula for sample size determination in health studies [14]

$$n = Z^2 P \times (1 - P) / d^2$$

where n = the minimum sample size

   P = expected prevalence rate %. 30% of 25% = 7.5% was used.

   Z = standard deviation value at 95% confidence interval (1.96)

   d = Sampling error tolerated (5.0%).

   n = 106

   Allowing for 10% non-response rate, appropriate sample size was

$$n = 100/90 \times 106 = 117$$

Estimated sample size was 117. 117 consenting CKD patients were consecutively recruited however 10 out of them did not complete the study; hence the study population was 107.

2.2. Data Collection

A pre-tested questionnaire designed by the researchers was administered to all participants to collect socio demographic and other relevant information regarding when diagnosis of CKD was made and current medications like use of anti hypertensives and lipid lowering agents. Anthropometic data comprising height and weight were collected and a detailed physical examination was done at the point of recruitment of patients/control subjects into the study.

After a brief explanation of the procedure, each participant was placed in supine position with the neck extended. Presence of atheromatous plaques was assessed using doppler ultrasound at 3 sites—distal common carotid artery (CCA), the internal carotid artery(ICA) and the carotid bulb by a single skilled radiologist specialized in doppler ultrasound using a high resolution B mode ultrasonography (specifications—Sonosite M Turbo P03318 04 2009 Sonosite, Inc, Bothell,WA,98021 USA) with 6 - 13 MHZ Transducer.

A plaque was defined as a focal structure that encroaches into the arterial lumen of at least 0.5 mm or 50% of the surrounding intima media thickness value or demonstrates a thickness of 1.5 mm as measured from the media-adventitia interface to the intima-lumen interface [15].

2.3. Glomerular Filtration Rate Measurement

Creatinine clearance was calculated using the Modification of Diet in Renal Disease (MDRD) formula and the degree of renal impairment was classified using the NKF/KDOQI.

2.4. Statistical Analysis

Statistical analysis was done using the Statistical Package for Social Science (SSPS Inc, Chicago, IL) version 20 statistical software. The frequencies, mean, standard deviation were generated. Numerical variables were analysed with z test and categorical variables with chi square. A p value of less than 0.05 was taken as statistically significant.

3. Results

One hundred and seven pre-dialysis patients with stages 2 to 5 CKD, and 81 control subjects were consecutively recruited for the study. The patients were made up of 63 males (58.9%) and (41.1%) female while the control group was made up of 44 males (54.3%) and 37 (45.7%) females (see Table 1). There were no statistical significant difference in the age and gender of the study of population and controls, as the patients were age and sex matched. Mean ages of CKD patients and the control subjects were 41.81 ± 13.95 years and 40.56 ± 13.05 years respectively. The mean BMI of patients and control subjects were similar (see Table 3).

11 patients (10.6%) had stage 2 CKD, 28 patients (26.2%) had stage 3 CKD, 44 (41.1%) had stage 4 while 24 (22.4%) had stage 5 CKD. The highest number of patients was found to have stage 4 disease (see Table 2).

Atheromatous plaques were significantly increased in CKD patients.15 (14.2%) CKD patients had atheromatous plaques versus 2.5% in the control group (see Table 3). Atheromatous plaques were increased in advanced stages of CKD (see Figure 1). Commonest site of occurrence was at the common carotid artery (CCA-7.5% versus ICA-4.7% versus bulb 1.8%; see Table 4).
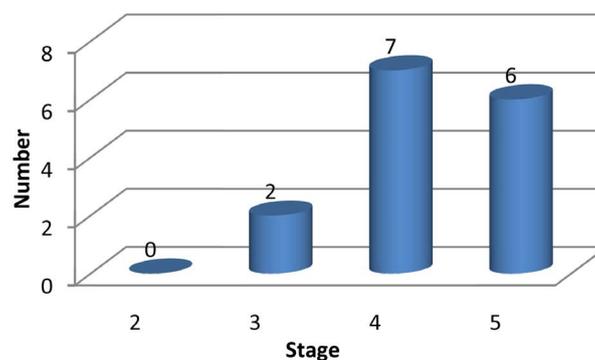

Figure 1. Atheromatous plaques and CKD stages.

Table 1. Sex distribution of the study population.

Sex	CKD	Control	Total	P-Value
Male	63 (58.9%)	44 (54.3%)	107 (56.9%)	
Female	44 (41.1%)	37 (45.7%)	81 (43.1%)	
Total	107 (100%).	81 (100%)	188 (100%)	0.532

Table 2. CKD stages of patients.

CKD Stages	No Of Patients	(%)
Stage 2	11	10.6
Stage 3	28	26.2
Stage 4	44	41.1
Stage 5	24	22.4
TOTAL	107	100

Table 3. Characteristics and general data of CKD patients and control subjects.

Parameter	CKD	Control	P-Value
Age (years)	41.81 ± 13.95	40.56 ± 13.05	0.530
Weight (kg)	64.74 ± 24.38	68.8 ± 14.95	0.054
Height (m)	1.67 ± 0.10	1.68 ± 0.09	0.479
BMI (kg/m^2)	23.92 ± 3.30	24.75 ± 4.22	0.132
Creatinine (umol/l)	324 ± 182.5	87.6 ± 17.2	<0.001
eGFR (mls/min)	27.93 ± 16.17	96 ± 15.3	<0.001
Atheromatous plaques	15	2	<0.05
Lipid lowering agents	56 patients (52%)	0	<0.001
Antihypertensive agents	71 patients (66%)	0	<0.001

Table 4. Atheromatous plaques in CKD patients and control group.

Site	CKD Patients	Control	P-Value
CCA	8 (7.5%)	1 (1.2%)	<0.001
ICA	5 (4.7%)	1 (1.2%)	0.19
Bulb	2 (1.8%0	0	0.52
Total	15 (14.0%)	2 (2.5%)	<0.05

4. Discussion

A rising prevalence of chronic kidney disease has been observed globally in recent times [16] [17]. CKD is a common disease in Nigeria and it has contributed significantly to morbidity, mortality and premature death [17]. This study showed that there were more male CKD patients than female patients. This is similar to ratios found for end stage kidney disease in south western Nigeria [18]. The male gender has been observed to be a non-modifiable risk factor for CKD. The patients were mostly young/middle aged patients as against the geriatric kidney patients in developed countries. Studies in most part of sub-Saharan African countries showed that kidney disease occurs in relatively younger age [18].

Atherosclerosis which is a leading cause of cardiovascular diseases is associated with increased mortality. Atherosclerosis varies with ethnicity and it is

found to be higher among blacks. All participants in this study were blacks. Studies have demonstrated a high prevalence of endothelial dysfunction, a critical early event in atherogenesis in African-Americans [19]. Katoka evaluated coronary atherosclerosis in two groups (African-Americans versus Caucasians). The study demonstrated a greater increase in atheroma volume and faster progression of atheromatous lesions in the African American group when compared to the Caucasian group. The findings suggested more aggressive form of atherosclerosis that requires intensification of secondary prevention strategies in African-Americans [20]. Some other studies however suggest greater coronary atherosclerosis among whites than blacks [21] [22].

Patients with CKD have higher mortality rates hence it is important to ascertain factors contributing to cardiovascular deaths in this group of patients. This study showed a higher prevalence of atheromatous lesions in CKD. This can be explained by the fact that in CKD, there is accelerated atherosclerotic changes and premature arterial plaque formation compared with individuals with normal kidney function [5] [23] [24]. Jaroslav *et al.* [25] demonstrated that unstable atherosclerotic plaques are found more frequently in carotid artery disease patients with CKD than in those with normal renal function. CKD also leads to additional changes in plaque composition, such as reduced cellularity, reduced collagen, and increased inflammation, which may lead to plaque instability and rupture. These morphologic differences in plaque composition are associated with an increased prevalence of cerebrovascular events in patients with CKD [26] [27]. Other studies also demonstrated higher prevalence of carotid plaques in CKD patients. Pascazio *et al.* [28] showed that the number of patients with carotid plaques were significantly higher in the CKD dialytic cases versus normal control.

In this study, it was observed that carotid plaques were more in patients with stages 3, 4 and 5 CKD. This is similar to findings from some previous studies. Satoshi *et al.* studied 368 subjects who underwent trans esophageal echocardiography and carotid ultrasonography, and measured estimated glomerular filtration rate (eGFR). It was observed that carotid plaques were more frequent in patients with CKD stage 3b or higher [29]. Kobayashi *et al.* demonstrated an independent association between stages of reduced eGFR and a higher prevalence of silent brain infarction [26]. Afolabi *et al.* also observed that carotid intima media thickness correlated significantly with reduction in eGFR in CKD patients [30] However, our findings were different from the study by Makiko *et al.* in Japan which included 1003 patients aged ≥ 50 years who underwent carotid ultrasonography. Patients with end-stage renal failure were excluded. Kidney function was not associated with calcified plaque [31].

In patients with CKD, atheromatous cardiovascular disease remains a major cause of morbidity and mortality.

This study collaborates a higher prevalence of carotid plaques in CKD patients which predicts greater cardiovascular events. Presence of carotid plaques is considered as surrogate end point for cardiovascular disease and B-mode ultrasound

is an imaging method that has been widely used to detect and measure carotid plaques. High resolution images of the full thickness of the artery wall are generated with intravascular ultrasound, permitting precise quantitation of atheromatous burden and progression on serial evaluation. It is relatively cheap and available in Nigeria hence it can be of great benefit in this regard. Early identification of patients with carotid plaques and intervention will reduce deaths from cardiovascular events in these patients.

Our study had some limitations. Many of the CKD patients were already on medications which included antihypertensive and lipid lowering agents. This could have influenced the strength of the study. In addition, other factors contributing to atherosclerosis were not fully explored in this study.

5. Conclusions and Recommendations

Atheromatous plaques are more prevalent in CKD patients. It is recommended that carotid doppler ultrasound should be done in CKD patients to identify patients for possible intervention.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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