Original Article

Predictors of Autonomic Dysfunction among Predialysis Chronic Kidney Disease Patients in Nigeria

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Abstract

Background: Chronic kidney disease (CKD) is a global public health problem with increasing incidence and mortality in Africa. Autonomic dysfunction (AD) has been implicated as a major contributor to the disease morbidity and mortality, but little is known about the predictors of this dysfunction in African populations. Understanding the predictors of this condition is necessary for early detection and management of CKDs. **Objectives:** This study was designed to determine the predictors of AD in CKD patients in Nigeria. **Materials and Methods:** It was a cross-sectional study of CKD patients at University of Nigeria Teaching Hospital, Enugu, Nigeria. The CKD patients with AD were compared with those without AD and a normal control group. Autonomic function was assessed through noninvasive cardiovascular tests: measurement of resting tachycardia, orthostatic hypotension, heart rate response (HRR) to standing, HRR to Valsalva maneuvre, and HRR to respiration. Data on symptoms of CKD and AD were obtained using a validated questionnaire. **Results:** The mean age of the CKD patients was 41.3 ± 1.5 (range: 21–69) years. Early hospital presentation is associated with significantly less risk of the development of AD ($P < 0.001$). Dizziness, nocturnal diarrhea, and impotence are the major markers/predictors of AD in CKD patients ($P < 0.05$). **Conclusion:** AD is common among predialysis CKD patients in Nigeria, and best predicted by the presence of postural dizziness, nocturnal diarrhea, and impotence in men. Physicians should, therefore, be on the lookout for these features for prompt and adequate management of cases.

Keywords: *Autonomic dysfunction, chronic kidney disease, predialysis patients*

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Introduction

It is increasingly recognized that the burden of chronic kidney disease (CKD) is not limited to its implication on demand for renal replacement therapy, but has a major impact on overall population health. Patients with reduced kidney function represent a population not only at risk for progression of kidney disease and development of end-stage renal disease but also at even greater risk for cardiovascular disease.[1] Indeed cardiovascular morbidity is common in chronic renal failure patients and may be explained in part by abnormalities in cardiovascular autonomic regulation.[2] In spite of this, autonomic neuropathy (AN) in CKD patients has not been extensively studied.[3] In Nigeria, the prevalence of CKD has been documented to be on the increase, yet not many studies have been carried out on autonomic impairment in CKD patients. In predialysis, CKD patients where earlier researchers have reported AN in the order of 40%–63%,[4] little has been done to determine the features or set of features that will best predict the occurrence of autonomic dysfunction (AD) in CKD patients. Most previous authors seem to have concentrated on how AD predicts decline in kidney function.[5,6] Early prediction and diagnosis of AD will mean early intervention and consequent prevention of

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some cardiovascular events. We, therefore, set out in this study to determine the predictors of AD in predialysis CKD patients, in the Southeastern part of Nigeria.

Materials and Methods

We evaluated 80 consenting predialysis CKD patients (Stages 3–5), drawn consecutively from the medical outpatient department and medical wards of University of Nigeria Teaching Hospital (UNTH), Ituku/Ozalla, Enugu, Nigeria, from March 2015 to November 2015. The UNTH, Enugu is the pioneer teaching hospital in southeastern Nigeria. It is owned by the federal government of Nigeria and is currently located at Ituku-Ozalla, at the outskirts of Enugu. Further details of UNTH and Enugu state have been described elsewhere.[7]

Patients with severe cardiac disease, cancer, diabetes, collagen and demyelinating diseases, left ventricular systolic dysfunction, or a history of stroke were excluded from the study. The control consisted of 40 adults matched for age and sex with the cases. These were drawn from among apparently healthy medical students, doctors, nurses, and hospital staff, without symptoms and signs suggestive of renal failure, diabetes mellitus, or heart disease. The study was approved by the institutional review board of UNTH, Enugu, and all participants signed an informed consent before being included in the study.

Study design

The study was cross-sectional in design. The autonomic nervous function was evaluated in CKD patients under conservative treatment in the hospital during the study. The CKD patients who fulfilled the criteria for AD (AD positive) were consecutively recruited (Group A). The control consisted of two groups namely: CKD patients who did not fulfill the criteria for AD (AD negative) (Group B) and normal individuals drawn from among doctors, nurses, other hospital staff, and patient's relations without symptoms and signs suggestive of renal failure, diabetes mellitus, or heart disease (Group C). The control groups were matched with the case group (Group A) for age, height, weight, body mass index, and sex. A screening questionnaire to identify the symptoms of CKD and AD was pretested on 10 CKD patients assessing care at the Enugu State University Teaching Hospital, Parklane, Enugu, in order to assess its performance. The questionnaire was thereafter reviewed and revised, and then applied to the participants. Anthropometric data including height and weight were collected, and thereafter, the participants had a physical examination and a detailed neurological examination in a quiet room. AD was assessed using a modified Ewing and Clarke's method as used by Köken *et al*.[8] This consisted of five tests: resting tachycardia, heart rate response (HRR) to Valsalva maneuver, HRR to deep breathing, HRR to standing, and blood pressure response to standing. The parasympathetic function was assessed using resting tachycardia, HRR to Valsalva maneuver, HRR to deep breathing, and HRR to standing. The sympathetic function was assessed with blood pressure response to standing (orthostatic hypotension). The supine blood pressure was taken after 10 min of rest, with the cuff of the mercury sphygmomanometer (accoson model, with standard cuff size 15 cm × 55 cm) applied to the right upper arm of the subject. The approximate systolic blood pressure was obtained by palpation. The cuff was then deflated and re-inflated to about 10 mmHg above the approximate systolic value. Phases I and V Korotkoff's sounds were used for systolic and diastolic blood pressure reading, respectively. Electrocardiography (ECG) was done to assess resting heart rate, using a triple lead rhythm strip (Cardiette Autoruler, with facilities for 12 lead ECG). ECG monitoring was done while the participant was lying supine and forcibly exhaling for 10 s against a fixed resistance with an open glottis. The participant blew into an improvised sterile mouthpiece (empty 20 ml syringe) attached to a mercury sphygmomanometer maintaining a pressure of 40 mmHg for 10 s.[8] The longest and shortest R-R intervals were measured with a ruler. The Valsalva Ratio (VR) was calculated; VR = longest RR (after the Valsalva maneuver)/shortest RR (During the Valsalva maneuver). The participant was then asked to breathe deeply and regularly at a rate of 6 breaths/min while sitting up. The electrocardiogram was recorded over three breathing cycles. The average heart rate during deep expiration was subtracted from that during deep inspiration. The average difference found for 6 consecutive inspiration-expiration cycle was taken as the final result.[8] The subject was then asked to stand up from the lying position while the electrocardiogram was recorded. The point of standing was marked on the recording paper. ECG monitoring at a paper speed of 25 mm/s was performed after a rest period in the supine position of 10 min, starting from 1 min before until 30 s after the subject started to stand. The ratio of the R-R interval of the 30th beat after standing (in millimeters) to that of the 15th beat was recorded.[8] Blood pressure of the participant, obtained as already described above, was recorded after 10 min of supine rest and after 2 min in the standing position. If standing was followed by a reduction in systolic blood pressure of at least 20 mmHg or in diastolic blood pressure of at least 10 mmHg within 3 min, orthostatic hypotension was accepted to be present.[8]

Other values obtained during the procedure were interpreted as follows:[8]

HRR to Valsalva maneuver: normal ≥1.21, borderline = 1.11–1.20, abnormal ≤1.10. HRR to deep breathing: normal ≥15 bpm, borderline = 11–14 bpm, abnormal ≤10 bpm. HRR to standing: normal ≥1.04, borderline = 1.01–1.03, and abnormal ≤1.01. Resting tachycardia:- Heart rate ≥100/min at rest.

The values for the autonomic function tests, adapted from Köken et al,[8] are as shown in Table 1. Each normal test was scored 0, a borderline test was scored ½, and an abnormal test was scored 1. The 5 test results were summed up with a maximum total score of 5. A total score of 3 and above was considered evidence of AN.[9]

Laboratory evaluation

Venous blood was collected from the participants without using a tourniquet. The results of the following tests were obtained from the participants: serum electrolytes – sodium, potassium, chloride, bicarbonate, calcium, phosphate, serum urea and creatinine, fasting blood glucose and 2 h postprandial glucose estimations, and packed cell volume (PCV). For serum calcium and phosphate estimation; serum calcium – phosphate product above 55 mg/dl was taken as abnormal and reflective of CKD.[10]

An autoanalyzer was used to analyze the blood for serum electrolytes, urea, and creatinine. The glomerular filtration rate (GFR) was estimated using the Cockroft/Gault formula:[11]

For women, this is multiplied by a factor 0.85 to get the GFR.

Abdominal ultrasound for kidney sizes and echotexture was also done.

The diagnosis of CKD was based on the Kidney Disease Outcomes Quality Initiative of the National Kidney Foundation (KDOQI/NKF): 12 epidermal GFR <60 ml/min/1.73 m^2 and/or at least one marker of renal parenchymal damage (e.g., proteinuria), present for ≥3 months.

Data analysis

The statistical package for social sciences (SPSS) version 21 (IBM Inc: Chicago, IL) statistical software was used for data analysis. For continuous variables, mean value and standard deviation were calculated, and the mean compared using independent *t*-test. Categorical variables were compared using the nonparametric tests – Chi-square. Multivariate logistic regression analysis was used to assess for factors associated with AD in CKD patients. All tests were two-tailed, and a $P < 0.05$ considered to be statistically significant.

Results

In all, there were 41 CKD AD +ve patients, 39 CKD AD –ve patients, and 40 normal controls. The mean age of all the participants was 41.3 ± 1.5 (range: 21–69) years. The baseline characteristics of the three groups were similar including age, sex distribution, height, weight, and body mass index ($P > 0.05$). Details are as shown in Table 2.

Some clinical symptoms of autonomic dysfunction in chronic kidney disease patients with and without autonomic dysfunction and normal control group

There were significant differences in the three groups in terms of occurrence of postural dizziness, impotence, dysphagia, and decreased sweat pattern ($P < 0.05$) while altered bowel habit, difficulty in micturition, persistent dry mouth, heat intolerance, and persistent cloudy urine showed no significant difference ($P > 0.05$). Details are as shown in Table 3.

Table 1: Values of autonomic function test

Test	Normal (0)	Borderline (1/2)	Abnormal (1)
HRR to standing (30/15 ratio)	≥1.04	1.01-1.03	≤1.0
HRR to deep breathing (maximum-minimum beats/min)	≥15	11-14	≤10
HRR to Valsalva manoeuvre (Valsalva ratio)	≥1.21	1.11-1.20	≤1.10
Resting tachycardia	<100		≥100
Orthostatic hypotension	<20 systolic and <10 diastolic		≥20 systolic or ≥10 diastolic or both

HRR=Heart rate response

Table 2: Baseline characteristics of the study participants*

Variable	AD +ve (*n*=41)	AD −ve (*n*=39)	Control (*n*=40)	*P*
Age	41.8±1.4	41.1±1.5	41.5±1.7	0.13
Sex distribution, *n* (%)				
Male	20 (48.8)	19 (48.7)	21 (52.5)	0.93
Female	21 (51.2)	20 (51.3)	19 (47.5)	0.93
Weight (kg)	65.4±11.1	65.5±12.6	63.9±11.7	0.80
Height (m)	1.7±0.1	1.7±0.2	1.6±0.4	0.15
Body mass index (kg/m^2)	23.3±3.0	22.7±2.9	22.9±2.8	0.64

*ANOVA for continuous variables, Chi-square test for categorical variables. AD +ve=Autonomic dysfunction present; AD −ve=Autonomic dysfunction absent

Table 3: Some clinical symptoms of autonomic dysfunction in chronic kidney disease patients with and without autonomic dysfunction and normal control group*

Symptom	AD +ve, *n* (%)	AD −ve, *n* (%)	Control, *n* (%)	*P*
Postural dizziness	18 (43.9)	4 (10.3)	1 (2.5)	<0.001
Impotence	11 (26.8)	2 (5.1)	1 (2.5)	<0.001
Dysphagia	7 (17.1)	0	1 (2.5)	0.02
Altered bowel habit	12 (27.3)	11 (30.6)	9 (22.5)	0.76
Difficulty in micturition	4 (9.8)	3 (7.7)	1 (2.5)	0.40
Decreased sweat pattern	20 (48.8)	19 (48.7)	7 (17.5)	<0.01
Persistent dry mouth	1 (0)	1 (2.8)	3 (7.5)	0.43
Heat intolerance	11 (26.8)	7 (17.9)	8 (20)	0.60
Cloudy postcoital urine	5 (12.2)	2 (5.6)	1 (2.5)	0.19

*Fisher's exact test for categorical variables. AD +ve=Autonomic dysfunction present; AD −ve=Autonomic dysfunction absent

Table 4: Some clinical symptoms of renal failure in chronic kidney disease patients with and without autonomic dysfunction and normal control group

Symptom	AD +ve, *n* (%)	AD −ve, *n* (%)	Control, *n* (%)	*P*
Nocturia	35 (85.4)	25 (64.1)	13 (32.5)	<0.001
Pruritus	7 (17.1)	11 (28.2)	5 (12.5)	0.19
Hiccups	11 (26.8)	15 (38.5)	3 (17.5)	<0.01
Altered sleep pattern	21 (51.2)	20 (51.3)	11 (27.5)	0.01

*Fisher's exact test for categorical variables. AD +ve=Autonomic dysfunction present; AD −ve=Autonomic dysfunction absent

Two-by-two comparisons between the three groups showed that postural dizziness was commoner in CKD AD +ve than CKD AD –ve ($P < 0.01$), and normal control ($P < 0.001$). There was, however, no difference between CKD AD –ve and normal control ($P = 0.17$). Impotence was more common in CKD AD +ve than CKD AD –ve ($P = 0.02$), and normal control ($P < 0.01$). There was no difference between CKD AD –ve and normal control ($P = 0.54$). Similarly, dysphagia was more common in CKD AD +ve than CKD AD –ve ($P < 0.001$), and normal control ($P = 0.03$). There was no difference between CKD AD –ve and normal control ($P = 0.99$). Decreased sweet pattern was more common in CKD AD +ve than CKD AD –ve ($P < 0.01$), and normal control ($P < 0.01$). It was also more common in CKD AD –ve than normal control ($P < 0.01$).

Some clinical symptoms of renal failure in chronic kidney disease patients with and without autonomic dysfunction and normal control group

There were significant differences in the three groups regarding the occurrence of some symptoms of renal failure including nocturia, hiccups, and altered sleep pattern ($P < 0.05$). Details are as shown in Table 4.

Two-by-two comparisons between the three groups showed that nocturia was more common in CKD AD +ve than normal control ($P < 0.001$), and in CKD AD –ve than normal control ($P < 0.001$). There was, however, no difference between CKD AD +ve and CKD AD –ve ($P = 0.30$). Hiccups was more common in CKD AD +ve than normal control ($P < 0.001$), and in CKD AD –ve than normal control ($P < 0.001$). There was however no difference between CKD AD +ve and CKD AD –ve ($P = 0.11$). Altered sleep pattern was more common in AD +ve than

Table 5: General physical examination findings in chronic kidney disease patients with and without autonomic dysfunction and normal control group

Sign	AD +ve, *n* (%)	AD −ve, *n* (%)	Control, *n* (%)	*P*
Pallor	38 (86.4)	35 (97.2)	7 (17.5)	<0.001
Dehydration	13 (29.7)	7 (19.4)	1 (2.5)	<0.01
Jaundice	1 (2.3)	0	0	-
Pedal edema	18 (40.9)	23 (63.9)	3 (7.5)	<0.001
Ascites	4 (9.1)	9 (25)	1 (2.5)	0.02

*Fisher's exact test for categorical variables. AD +ve=Autonomic dysfunction present; AD −ve=Autonomic dysfunction absent

Table 6: Neurological examination findings in the chronic kidney disease patients with and without autonomic dysfunction and normal control group*

Signs	AD +ve, *n* (%)	AD −ve, *n* (%)	Control, *n* (%)	*P*
Asterixis	26 (59.1)	22 (61.1)	1 (2.5)	<0.001
Drowsiness	5 (11.4)	3 (8.3)	1 (2.5)	0.25
Impaired memory				
Immediate	3 (6.8)	1 (2.8)	0	-
Short	3 (6.8)	1 (2.8)	0	-
Long	4 (9.1)	2 (8.3)	0	-
Impaired orientation	2 (4.5)	1 (2.8)	0	-
Impaired judgment	6 (13.6)	2 (5.6)	0	-
Altered muscle tone	5 (11.4)	1 (2.8)	0	-
Altered muscle power	5 (11.4)	1 (2.8)	0	-
Impaired reflexes				
Biceps jerk	4 (9.1)	1 (2.8)	0	-
Triceps	3 (6.8)	6 (16.7)	0	-
Supinator jerk	6 (13.6)	2 (5.6)	0	-
Knee jerk	10 (22.7)	9 (25.0)	1 (2.5)	0.01
Ankle jerk	8 (18.2)	6 (16.7)	1 (2.5)	0.06
Impaired sensation				
Pinprick	2 (4.5)	0	0	-
Temperature	4 (9.1)	1 (2.8)	0	-
Joint position	0	0	0	-
Vibration sense	4 (9.1)	1 (2.8)	0	-
Gait (impaired)	9 (20.5)	1 (19.4)	0	-

*Fisher's exact test for categorical variables. AD +ve=Autonomic dysfunction present; AD −ve=Autonomic dysfunction absent

Table 7: Mean values of biochemical and laboratory indices among chronic kidney disease patients with and without autonomic dysfunction and normal control group*

Variable	Mean±SD			*P*
	AD +ve	AD −ve	Control	
Urea	32.64±4.7	29.25±4.3	4.38±0.9	<0.001
Creatinine	743.84±45.4	684.67±39.8	99.55±7.3	<0.001
Calcium	1.96±0.1	1.99±0.1	2.39±0.2	<0.001
Sodium	134.86±8.1	134.97±8.1	137.73±8.2	0.21
Potassium	5.43±0.8	5.51±0.8	3.83±0.7	<0.001
Chloride	98.80±7.3	100.21±7.6	98.18±7.3	0.45
Bicarbonate	20.97±3.1	20.39±3.1	25.80±3.8	<0.001
Phosphate	2.29±0.3	2.15±0.3	1.10±0.1	<0.001
PCV	22.66±3.8	22.59±3.6	33.93±4.7	<0.001
GFR	10.61±1.9	11.28±1.9	108.25±8.4	<0.001
Ca/PO_4 index	55.28±8.4	51.33±8.5	3.96±0.6	<0.001
Uric acid	0.63±0.08	0.60±0.08	0.21±0.07	<0.001

*ANOVA for continuous variables. AD +ve=Autonomic dysfunction present; AD −ve=Autonomic dysfunction absent; PCV=Packed cell volume; GFR=Glomerular filtration rate; Ca/PO4=Calcium-phosphate; SD=Standard deviation

Table 8: Predictive symptoms of autonomic dysfunction in chronic kidney disease patients*

Variables	*B*	SE	df	*P*	*R*	OR
Micturition difficulty	3.0044	1.9127	1	0.1162	0.0649	20.1735
Postural dizziness	2.1269	1.0234	1	0.0377	0.1446	8.3888
Altered sweating pattern	3.4736	1.9044	1	0.0681	0.1094	32.2539
Heat intolerance	0.6414	0.8600	1	0.4557	0.0000	1.8992
Impotence	4.1265	1.9141	1	0.0311	0.1546	0.0161
Cloudy postcoital urine	1.8281	1.1806	1	0.1215	0.0599	0.1607
Dysphagia	2.7827	1.5542	1	0.0734	0.1043	0.0619
Altered bowel habit	0.0086	0.7385	1	0.9907	0.0000	0.9914
Presence of diarrhea	2.7851	1.7240	1	0.1062	0.0742	0.0617
Nocturnal diarrhea	8.1690	3.4867	1	0.0191	0.1774	29.0934
Constipation	2.8303	3.3088	1	0.3923	0.0000	0.0590
Persistent dry mouth	1.7508	91.5789	1	0.9847	0.0000	0.1736

*Logistic regression analysis. SE=Standard error; OR=Odd's ratio

normal control (P = 0.01), and in CKD AD –ve than normal control (P = 0.01). There was however no difference between CKD AD +ve and CKD AD –ve (P = 0.45).

Duration of symptoms of renal failure in chronic kidney disease patients with and without autonomic dysfunction

Within the first 16 weeks of onset of symptoms, there were significantly less patients with AD than without AD presenting to the nephrology clinic (71.8%, 28/39 vs. 17.1%, 7/41; odd ratio [OD]: 5.67; 95% confidence interval [CI]: 2.0–15.9; P < 0.001). Thereafter, significantly more patients presented with AD than without AD (82.9%, 34/41 vs. 28.2%, 11/39; OD: 12.4; 95% CI: 4.2–36.1; P < 0.001).

General physical examination findings in chronic kidney disease patients with and without autonomic dysfunction and normal control group

There were significant differences in the three groups regarding the occurrence of some general physical signs of renal failure including pallor, dehydration, pedal edema, and ascites (P < 0.05). Details are as shown in Table 5.

Two-by-two comparisons between the three groups showed that pallor was more common in CKD AD +ve than normal control (P < 0.001), and in CKD AD –ve than normal control (P < 0.001). There was however no difference between CKD AD +ve and CKD AD –ve (P = 0.09). Dehydration was more common in CKD AD +ve than normal control (P < 0.01), and in CKD AD –ve than normal control (P < 0.01). There was however no difference between CKD AD +ve and CKD AD –ve (P = 0.30). Pedal edema was more common in CKD AD +ve than normal control (P < 0.001), and in CKD AD –ve than normal control (P < 0.001). It was also more common in CKD AD +ve than CKD AD –ve (P < 0.04). Ascites was more common in CKD AD +ve than normal control (P = 0.02), and in CKD AD –ve than normal control (P = 0.02). There was however no difference between CKD AD +ve and CKD AD –ve (P = 0.06).

Neurological examination findings in chronic kidney disease patients with and without autonomic dysfunction and normal control group

Following neurological examination of the three groups of participants, there were significant differences regarding the occurrences of asterixis and knee-jerk (P < 0.05). Other neurological features including drowsiness, impaired memory, and impaired sensations did not show any significant difference between the three groups (P > 0.05). Details are as shown in Table 6.

Two-by-two comparisons between the three groups showed that asterixis was more common in CKD AD +ve than normal control (P < 0.001), and in CKD AD –ve than normal control (P < 0.001). There was however no difference between CKD AD +ve and CKD AD –ve (P = 0.85). Similarly, ankle jerk was more common in CKD AD +ve than normal control (P < 0.01), and in CKD AD –ve than normal control (P < 0.01). There was

however no difference between CKD AD +ve and CKD AD –ve ($P = 0.86$).

Mean values of biochemical and laboratory indices among chronic kidney disease patients with and without autonomic dysfunction and normal control group

There were strong significant differences in the three groups regarding mean serum concentrations of laboratory and biochemical indices including urea, creatinine, calcium, potassium, bicarbonate, phosphate, PCV, GFR, Ca. PO4 index, and uric acid ($P < 0.001$). Details are as shown in Table 7.

Two-by-two comparisons between the three groups showed that all the above indices had strong significant difference between CKD AD +ve and normal control ($P < 0.001$), and between CKD AD –ve and normal control ($P < 0.001$). Apart from creatinine which was significantly higher in CKD AD +ve than CKD AD –ve ($P = 0.02$), other indices showed no significant difference between CKD AD +ve and CKD AD –ve ($P > 0.05$).

Predictors of autonomic dysfunction in chronic kidney disease patients

Following a multiple logistic regression analysis, it was observed that postural dizziness, impotence in men, and nocturnal diarrhea were symptoms that best predicted the presence of AD in CKD patients. Details are as shown in Table 8.

Discussion

This study has demonstrated that postural dizziness, impotence in men and nocturnal diarrhea are the major markers/predictors of AD in CKD patients. This finding partly agrees with the report by Campese *et al*. in which postural dizziness was associated with AD in 65% of the patients.[12] However, it contrasts with the work of Sanya in Western Nigeria, where an alteration in bowel habits, decreased sweat pattern, and persistent dry mouth were the observed predictors of AD, while postural dizziness was not.[9] These discrepancies are difficult to explain, however, may be patient dependent as some of the patients might not have fully appreciated the questions asked them even when they were well explained to them.

This study has also demonstrated a significant relationship between the duration of renal failure and the development of AD. With longer duration of symptoms, the likelihood of development of AD increases. In fact, CKD patients who presented after more than 16 weeks from onset of symptoms are approximately 12 times more likely to develop AD than those who presented earlier. This interesting finding suggests that public enlightenment campaigns on the need for early hospital presentation may reduce the incidence and complications of AD in CKD patients. This observation is similar to the work of Campese *et al*. which demonstrated a significant increase in the incidence of AD in CKD patients as the duration of symptoms before presentation increases.[12]

This study also observed a significant difference between the mean values of creatinine in CKD patients with and without AD, and normal control group. It suggests a possible correlation between severity of uremia and AD. This observation is similar to other related studies[4,9,12] in which the severity of uremia and duration of CKD were significantly associated with the development of AD. Although the mean GFR of patients with AD was lower than that of patients without AD, the observed difference was not statistically significant. A possible explanation for this observed lack of difference in GFR despite observed significant difference in creatinine level may be due to other factors (order than creatinine) involved in the determination of GFR such as patient's age and body weight.

Other biochemical and laboratory factors including sodium, potassium, bicarbonate, calcium– phosphate product (Ca/PO4 index), and PCV did not show any significant difference between CKD +ve and CKD –ve patients indicating that the serum levels of these indices do not predict AD in the study population. This is however in contrast with studies from Toronto, Canada, where AD was found to be associated with Ca. PO4 index and PCV.[13,14]

Although some studies have shown that AD can reduce the renal release of erythropoietin probably by renal denervation, leading to the development of anemia,[15,16] this study did not observe any association with PCV between CKD patients with and without AD.

The limitations of this study include the fact that it is a "one hospital-based" study and hence limits generalization of its findings to the entire population. Furthermore, the very small frequencies and wide confidence intervals observed in some of the outcome measures of interest suggest that a larger sample size would have improved the study's precision and external validity; however, it is unlikely that it would have had a significant effect on the magnitude and direction of the estimates. In spite of these limitations, the study is relevant as it has started the process of filling the knowledge gap on the predictors of AD in CKD patients in Nigeria. A major strength of this study is the accurate tests performed to diagnose AD. Furthermore, the study is prospective in design with reduced likelihood of recall bias.

Conclusion

AD is a common problem among predialysis CKD patients in southeastern Nigeria, and best predicted by the presence of postural dizziness, nocturnal diarrhea, and impotence in men. The managing physicians should, therefore, be on the lookout for these features for prompt and adequate management of cases. Public enlightenment campaigns on the need for early hospital presentation may help reduce the incidence and complications of AD in CKD patients.

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Conflicts of interest

There are no conflicts of interest.

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