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Antihypertensive prescription pattern and determinants of blood pressure control among chronic kidney disease patients

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Abstract

Hypertension is associated with an increased rate of progression of chronic kidney disease (CKD) to end-stage renal disease. It predicts mortality and adverse cardiovascular outcomes in both pre-dialysis CKD patients and those on renal replacement therapy. Thus, judicious use of antihypertensives and good blood pressure (BP) control may reduce morbidity and mortality among these patients. This study aims to assess the determinants of BP control and antihypertensive drug use patterns in CKD patients. A cross-sectional analytical study was conducted among CKD patients presenting to Lagos State University Teaching Hospital between April 2023 and January 2024. Recruited patients were classified into CKD stages 3–5, based on the estimated glomerular filtration rate. Clinical data were collected using a structured, interviewer-administered questionnaire. A total of 163 CKD patients were recruited into this study with a mean age of 54.04 ± 14.47 years. A history of hypertension and diabetes was found in 85.9% and 26.4% of the recruited patients, respectively. Poor BP control was observed in 50% of the subjects. Calcium channel blockers were the most frequently prescribed antihypertensive medications across CKD stages (p=0.046), while anemia and elevated serum creatinine levels were associated with poor BP control. These findings emphasize the importance of addressing anemia and elevated serum creatinine levels in the management of CKD patients.

Keywords: Chronic kidney disease; Hypertension; Blood pressure control; Antihypertensives

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1. Introduction

Chronic kidney disease (CKD) has been increasingly recognized as a global health burden, and it is associated with major morbidity and mortality that demands special attention as one of the growing public health problems.[1,2] CKD is increasing in incidence and prevalence worldwide and is estimated to affect between 10% and 13% of the global population.[1,3-5] CKD has now emerged as a significant public health challenge in sub-Saharan Africa, with a reported prevalence of 13.9% in meta-analyses.[5-7] In 2017, CKD was the 12th leading cause of mortality worldwide, and it resulted in 1.2 million deaths.[2] Moreover, 7.6% of all cardiovascular disease (CVD) deaths (1.4 million) were attributed to impaired kidney function.[3,5] Deaths due to CKD or CKD-attributable CVD are responsible for 4.6% of global all-cause mortality.[3,5]

Hypertension is a major contributing risk factor of CKD globally.[8] CKD, which is considered either a consequence or cause of hypertension, is frequently observed in patients with hypertension and significantly accelerates the hypertension-related risk of cardiovascular events.[8-10] In addition, hypertension is the second most common cause of end-stage renal disease, and it speedily worsens the age-related decrease in renal function if blood pressure (BP) is not optimally controlled.[11,12] Current guidelines recommend a strict BP control (130/80 mmHg) in patients with CKD, although the BP target remains a matter of debate.[1,9,13] Despite the need for aggressive BP control in patients with CKD, previous studies show that only about 27% of CKD patients achieve 140/90 mmHg, and even fewer (11%) reach 130/85 mmHg.[9,14,15] CKD is associated with an elevated office BP and a high ambulatory BP as well as a lack of diurnal BP variation.[13,16] Several studies reported that high ambulatory BP and/or an abnormal circadian BP variation (that is, non-dipper or reverse-dipper) are predictors of combined CVD and poor renal outcomes, better than office BP values in patients with CKD.[15,17]

CVD is the leading cause of hospitalization and mortality in patients with CKD.[1,4] The prevalence of CVD and its risk factors is on the rise in low- and middle-income countries, thereby worsening the burden of CKD.[3,6,18,19] This epidemiological transition may be attributed to the adoption of Western lifestyle changes in nutrition, rapid urbanization, and an aging population, resulting from relatively improved healthcare systems.[20] This has culminated in burgeoning epidemics of cardiovascular risk factors and diseases, such as hypertension, type II diabetes mellitus, obesity, and dyslipidemia, which tend to worsen the cardiovascular burden of CKD patients.[7,18,20,21]

Hypertension-related morbidity in CKD patients includes decompensated left ventricular hypertrophy, heart failure, and ischemic heart disease, which contribute to an increased rate of progression of CKD to end-stage renal disease by further worsening the renal perfusion.[9,22,23] Several studies have shown a significant reduction in hypertension-related morbidity and mortality in both CKD and non-CKD populations when BP is optimally controlled.[10,11,13,14,16]

Despite the benefits of optimal control of BP, the majority of patients with hypertension, including those with CKD, are not optimally controlled, and the magnitude of poor BP control is higher in low- and middle-income countries compared to high-income countries.[6,18,19] Studies on BP profile and its determinants are sparse in this environment. Therefore, this study aims to assess the determinants of BP control and the pattern of antihypertensive use among CKD patients in a Nigerian tertiary hospital.

2. Methods

2.1. Study design and setting

This was a cross-sectional analytical study involving 163 CKD patients. The recruitment period was from April 2023 to January 2024 at the Lagos State University Teaching Hospital (LASUTH), Ikeja, Lagos State. The study population comprised patients with CKD attending the nephrology clinic, which operates 2 days per week and attends to at least 20 CKD patients per clinic day.

Inclusion criteria for this study were adult CKD patients in stages 3–5 with hypertension who had been on antihypertensive medications for at least 6 months and had attended the nephrology clinic for at least 3 consecutive months before the commencement of the study. Patients with underlying cardiac disease, arteriovenous fistula, and clinical evidence of volume overload (pulmonary edema, peripheral congestion, and congestive cardiac failure) were all excluded from this study.

2.2. Sample size determination

The minimum sample size of this study was calculated using Fisher's formula (Equation [1]).[24] A standard normal deviation of 1.96 was used with a confidence level of 95%, a precision of 5% and a proportion of 10.75% obtained from a previous study on the prevalence of CKD.[24]

$$N = \frac{Z^2 pq}{d^2} \quad (1)$$

where N is the sample size, Z is the standard normal deviation, p is the estimated prevalence, q is $1-p$, and d is the desired level of precision. Using Equation (1), a minimum sample size of 148 was derived. Accounting for a 10% (15) expected attrition rate, the minimum sample size was increased to 163 participants. Consequently, a total of 163 CKD patients were recruited for the study.

2.3. Study procedure

Recruited subjects were classified into CKD stages 3–5 based on their estimated glomerular filtration rate (eGFR).

Their clinical history was obtained using a structured questionnaire administered by trained interviewers. Data collected included age, sex, level of education, occupation, and self-reported medication adherence. Adherence to antihypertensive medications was measured using the Morisky Medication Adherence Scale (MMAS)-8, and good adherence was defined as an MMAS score greater than 6 points (out of a total score of 8 points).[25]

CKD was defined as abnormalities of kidney structure or function present for more than 3 months with health implications. Recruited patients were classified into the different stages (3 to 5) of CKD based on the eGFR as follows: stage 3 with eGFR of 30–59 mL/min/1.73m^2, stage 4 with eGFR of 15–29 mL/min/1.73m^2, and stage 5 with eGFR of < 15 mL/min/1.73m^2.[4]

BP was measured by trained staff using a standardized digital sphygmomanometer according to standard protocol, and hypertension was defined as an average of the last two of three measured office systolic BP (SBP) values ≥140 mmHg and/or diastolic BP (DBP) ≥90 mmHg.[26]

A total of 10 mL of venous blood was collected under aseptic procedure from the antecubital fossa of each subject. The blood sample for fasting lipid profile (4 mL) was collected into a plain bottle after the patient fasted overnight for at least 8 h, 1 mL of blood for random blood glucose was collected in fluoride oxalate bottles, 2 mL of blood for packed cell volume (PCV) was collected into ethylenediaminetetraacetic acid bottle, and 3 mL of blood sample for creatinine was collected into lithium heparin bottle.

2.4. Ethical consideration

Approval of the Ethics and Research Committee of LASUTH, Ikeja, Lagos, was obtained before the study commenced. All subjects provided informed consent after a detailed explanation of the study procedure was provided to them by the investigators. All participants understood that patient identifiers would be removed and that data would be stored on a personal computer. The participants also understood that they can willingly withdraw from the study without any negative consequences.

2.5. Data analysis

Data were entered into a personal computer and analyzed using the Statistical Package for the Social Science software (SPSS; version 20, IBM, United States). Missing data were excluded from the analysis. Continuous variables (age, weight, height, body mass index, SBP, DBP, and laboratory values) were recorded and presented as frequencies, percentages, and means ± standard deviation. They were compared using an unpaired Student's *t*-test, where normal distribution was assumed, and skewed data were described with median and percentiles and compared using the Mann–Whitney *U*-test. Categorical variables (gender, religion, education level, history of hypertension and diabetes mellitus, marital status, stage of CKD, prior history of adherence counseling, level of drug adherence, and types of antihypertensives) were presented as tables and pie charts and expressed in percentages. Chi-square test was used to test the differences between categorical variables, while the independent Student's *t*-test was used to determine the differences between two continuous variables. The differences between three continuous variables were tested using a one-way analysis of variance. Logistic regression was performed to determine the predictors of BP control. The level of statistical significance was set at $p<0.05$ with a 95% confidence interval.

3. Results

A total of 163 CKD patients were recruited into this study. Table 1 shows the socio-demographic characteristics of the patients. The majority of respondents were elderly (42.9%), and the mean age of the patients was 54.04 ± 14.47 years. More than half (51.5%) of study participants were male. About 39.3% of the patients completed tertiary education, with 85.9% and 26.4% having a history of hypertension and diabetes, respectively. Most respondents had no prior adherence counseling for their medications, and the majority reported poor adherence to their antihypertensive medications.

Table 2 shows the pattern of antihypertensive medication use in the participants. Calcium channel blockers (CCBs) were the most frequently prescribed antihypertensive across the stages of CKD (69.3%, $p=0.046$), either as monotherapy or in combination with other antihypertensives, while beta-blockers were the least prescribed (17.8%).

Figure 1 shows the proportion and pattern of antihypertensive use. Monotherapy was prescribed in 17% of the subjects, while a three-drug antihypertensive combination is the most common pattern of prescription. A five-drug combination was used in 13% of the subjects.

When the various clinical and laboratory parameters were compared across the stages of CKD in Table 3, the serum bicarbonate level decreased as the CKD progressed ($p<0.001$). The mean hematocrit level was also significantly lower in CKD stage 5 patients, compared to the other two groups ($p<0.001$).

Tables 4 and 5 show the relationship between the socio-demographic and laboratory parameters of the study participants and BP control. Anemia and higher serum

Table 1. Socio-demographic characteristics of the patients (*n*=163)

Characteristics	Frequency	Percentage
Age		
Young (<40 years)	31	19.0
Middle age (40–60 years)	62	38.0
Elderly (> 60 years)	70	42.9
Gender		
Male	84	51.5
Female	79	48.5
Religion		
Christianity	123	75.5
Islam	40	24.5
Educational level		
None	10	6.1
Primary	33	20.2
Secondary	56	34.4
Tertiary	64	39.3
History of hypertension		
Yes	140	85.9
No	23	14.1
Marital status		
Single	14	8.6
Married	133	81.6
Divorced	2	1.2
Widow	14	8.6
History of diabetes		
Yes	43	26.4
No	120	73.6
Stages of CKD		
Stage 3	71	43.6
Stage 4	49	30.0
Stage 5	43	26.4
Prior adherence counseling		
Yes	11	6.7
No	152	93.3
Level of drug adherence		
Good	34	20.9
Poor	129	79.1

Abbreviation: CKD: Chronic kidney disease.

creatinine levels were found to be associated with poorer BP control.

Table 6 shows the association between BP and the subjects' parameters. There was a negative correlation between BP and the eGFR and PCV, while a positive correlation between serum creatinine and BP was observed.

Table 2. Pattern of antihypertensive drug use among patients

Antihypertensives	CKD stage			Total *n* (%)	*p*-value
	Stage 3 (*n* = 70)	Stage 4 (*n* = 49)	Stage 5 (*n* = 44)		
Diuretic					
Yes	35	26	21	82 (50.3)	0.756
No	35	23	23	81 (49.7)	
ACEi					
Yes	24	23	16	63 (38.7)	0.292
No	46	26	28	100 (61.3)	
CCB					
Yes	42	38	33	113 (69.3)	0.046
No	28	11	11	50 (30.7)	
Beta-blockers					
Yes	9	11	9	29 (17.8)	0.387
No	61	38	35	134 (82.2)	
Centrally acting					
Yes	16	16	18	50 (30.7)	0.203
No	54	33	26	113 (69.3)	
ARB					
Yes	19	10	19	48 (29.5)	0.101
No	51	39	25	115 (70.5)	
Others					
Yes	11	15	21	47 (28.9)	0.193

Abbreviations: ACEi: Angiotensin-converting enzyme inhibitor; ARB: Angiotensin receptor blocker; CCB: Calcium channel blocker; CKD: Chronic kidney disease.

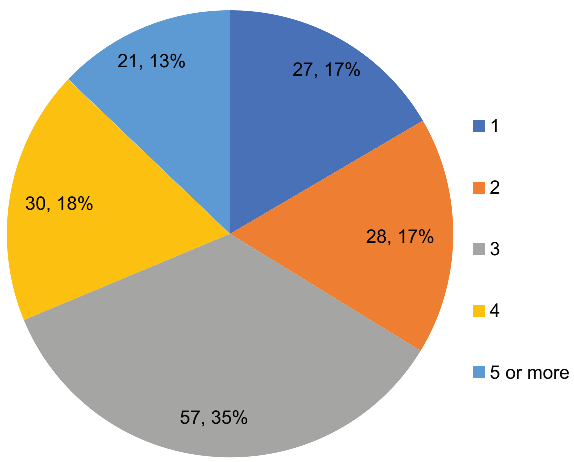

Figure 1. Proportion and the number of antihypertensive medications used

4. Discussion

Hypertension is a common complication of CKD and a significant risk factor for disease progression.[6] Poor

Table 3. Relationship between clinical/laboratory parameters and chronic kidney disease staging

Lab parameters	CKD staging			*p*-value
	Stage 3	Stage 4	Stage 5	
Age	57.4±15.4	53.9±14.6	49.9±13.5	0.032
Weight (kg)	70.5±14.8	74.2±17.6	68.7±16.1	0.734
BMI (kg/m^2)	26.2±5.5	26.7±6.4	24.8±5.6	0.256
SBP (mmHg)	142.9±26.4	148.5±27.7	145.4±29.8	0.567
DBP (mmHg)	82.8±14.3	85.8±15.6	86.7±17.3	0.337
Sodium ion (mmol/L)	141.9±6.9	138.8±6.1	140.2±7.0	0.044
Potassium ion (mmol/L)	4.0±0.6	4.4±0.8	4.5±0.8	0.044
Bicarbonate ion (mmol/L)	23.1±3.4	19.9±4.3	18.2±4.3	<0.001
TCH (mmol/L)	201.2±59.9	193.6±48.2	193.3±45.4	0.692
PCV (%)	36.6±5.8	32.5±7.9	27.2±7.5	<0.001

Abbreviations: BMI: Body mass index; CKD: Chronic kidney disease; DBP: Diastolic blood pressure; SBP: Systolic blood pressure; TCH: Total cholesterol; PCV: Packed cell volume.

BP control is common among CKD patients, and this contributes to adverse events among this subset of patients. Therefore, it is crucial to identify and address the predictors of poor BP control, as this is likely to improve outcomes in CKD patients.[6] This study, therefore, aimed to assess the determinants of BP control and the pattern of antihypertensive use among CKD patients in our locality.

The most frequently prescribed antihypertensive medication in our cohort was CCBs. This finding is similar to the result of Ogundele *et al*, who reported CCBs as the most frequently prescribed antihypertensive among their study population.[27] This is probably because CCBs are the most prescribed medications in essential hypertension in this locality and, thus, translate to prescriptions in CKD patients. This may also be attributed to the fact that CCBs are more readily available and affordable in this environment, where most patients pay out of pocket for medications and health care services.[28] The cost of medications has been shown to affect prescription patterns and patient adherence.[28] Beta-blockers are the least commonly prescribed antihypertensives among our cohorts, probably because some guidelines have removed beta-blockers as the first-line medication for BP control.[26] Surprisingly, despite the proven efficacy of diuretics in managing fluid overload and water retention, the use of diuretics was not as common as that of CCBs. In our study, angiotensin-converting enzyme inhibitors and angiotensin receptor blockers were used in 38.7% and 29.5%, respectively. Combined renin-angiotensin-aldosterone system (RAAS) blockers were used by 68.2% of patients, which is comparable to the use of CCBs in this study. Previous studies have shown that increased

Table 4. Relationship between socio-demographic parameters and blood pressure control

Socio-demographic parameters	Blood pressure control		*p*-value
	Controlled (*n* = 82)	Uncontrolled (*n* = 81)	
Age			
Young (<40 years)	16	15	0.216
Middle age (40–60 years)	26	36	
Elderly (>60 years)	40	30	
Gender			
Male	42	42	0.530
Female	40	39	
Religion			
Christianity	58	64	0.135
Islam	24	17	
Education			
None	9	2	0.077
Primary	18	15	
Secondary	30	26	
Tertiary	25	38	
Anti-hypertensive use			
Yes	75	72	< 0.001
No	7	9	
History of diabetes			
Yes	23	20	0.379
No	59	61	
Cigarette smoking			
Yes	3	2	0.506
No	79	79	
Alcohol consumption			
Yes	7	5	0.391
No	75	76	
Erythropoietin use			
Yes	15	17	0.555
No	67	64	
CKD stage			
Stage 3	40	31	0.396
Stage 4	22	27	
Stage 5	20	23	
Anemia			
Yes	57	45	0.046
No	25	36	
Obesity			
Underweight	5	3	0.085
Normal	44	29	
Overweight	21	29	
Obesity	12	20	

Abbreviation: CKD: Chronic kidney disease.

Table 5. Relationship between patients' parameters and blood pressure control

Parameters	BP control		*p*-value
	Controlled (mean±SD)	Uncontrolled (mean±SD)	
Age	55.7±15.4	53.0±14.2	0.142
Weight	67.2±13.6	75.2±17.4	0.463
BMI	24.7±5.4	27.2±5.9	0.543
Duration of hypertension	10.2±2.5	9.6±2.3	0.251
eGFR	31.1±17.5	26.3±16.0	0.088
Creatinine	3.5±0.3	4.4±0.5	0.029
PCV	32.4±7.3	33.6±7.6	0.782
TCH	199.6±53.2	194.6±53.4	0.955
Number of medications	3.5±1.1	4.5±2.2	0.061
Level of drug adherence (MMAS-8)	6.3±1.5	3.4±2.5	0.006

Abbreviations: BMI: Body mass index; BP: Blood pressure; eGFR: Estimated glomerular filtration rate; MMAS: Morisky Medication Adherence Scale; PCV: Packed cell volume; SD: Standard deviation; TCH: Total cholesterol.

Table 6. Logistic regression showing the association between patients' parameters and blood pressure

Parameters	Blood pressure		*p*-value
	Odds ratio	95% CI	
Age	0.66	0.4510–0.9453	0.142
Weight	1.99	1.3623–2.9054	0.463
BMI	1.33	1.0287–2.1455	0.543
Duration of hypertension	1.46	1.7457–2.0003	0.251
Level of education	0.49	1.8456–3.7322	0.811
eGFR	0.41	−1.329–−0.1738	0.003
Creatinine	0.65	0.4500–0.9410	0.003
PCV	0.32	−2.1493–−0.1913	0.004
TCH	0.22	−0.2881–−0.3801	0.955
Number of medications	0.67	0.0596–0.3012	0.674
Prior adherence counseling	0.41	0.1561–0.8881	0.765
Level of drug adherence	0.73	0.0438–0.2850	0.555

Abbreviations: BMI: Body mass index; CI: Confidence interval; eGFR: Estimated glomerular filtration rate; PCV: Packed cell volume; TCH: Total cholesterol.

RAAS activation and fluid overload are major drivers of poor BP control in CKD patients; therefore, the use of RAAS blockers is associated with better BP control in these patients.[6] In a meta-analysis of 17 cohort studies, involving a total of 34,602 individuals with CKD, de Pinho *et al.*[29] demonstrated a wide variation in antihypertensive prescription patterns. RAAS blockers were prescribed for 54% to 91% of cohort participants, 11% to 79% for diuretics, 22% to 70% for beta-blockers, and 27% to 75% for calcium-channel blockers. The prescription pattern in our study fits into this wide variation.[6,29]

However, a striking finding in our study was that antihypertensive monotherapy was still observed in some of our patients in the face of uncontrolled BP, despite most guides recommending multiple drug therapy as well as combination therapy.[9,26] Even though the majority of our patients have been prescribed two or more medications, the poor BP control observed in this study may be due to physician inertia in up-titrating the antihypertensive medications. Physician inertia has been reported in previous studies, though this was not assessed in the present study.[30,31]

The prevalence of poor BP control among study participants was over 90% as most participants had SBP above 140 mmHg. This is similar to the high prevalence of uncontrolled BP found in a previous study by Mamven *et al.*[6] Despite 80% of the participants claiming to be on at least one antihypertensive drug, more than 50% still had uncontrolled BP. This was, however, not surprising as the majority of our subjects self-reported poor drug compliance, and they had no form of medication adherence counseling despite multiple clinic visits. Even though studies have shown that self-reporting of medication adherence may overestimate adherence from bias, most of the patients in this study still had poor medication adherence. Poor adherence to medications, aside from clinicians' inertia, has been reported as a common occurrence in patients with CKD.[6,18,30,32,33] This may contribute to our findings. Some of the reasons previously attributed to poor medication adherence include lack of formal medication adherence counseling, as was observed in this study, high pill burdens, nausea and vomiting, depression, lack of social support, and lack of motivation.[7,21] High pill burden has been reported as common in CKD patients.[32,34]

Predictors of poor BP control in the previous study by Mamvem *et al.*[6] were age and the number of anti-hypertensive medications. This was at variance with our findings, likely because about 50% of the subjects in Mamvem *et al.*'s[6] study had end-stage renal disease (ESRD) compared to about 27% in our subjects. ESRD patients have been reported to have a substantially higher pill burden and increased risk of drug-related problems, which have been associated with reduced medication adherence due to polypharmacy and the adverse effects arising from drug–drug interactions.[32,34] Subeesh *et al.*[34] reported an average of 9.16 ± 3.01 drugs per prescription in their ESRD patients, while Al-Ramahi *et al.*[32] reported a prescription of up to 15 different medications (7.87 ± 2.44) with up to 930 potential drug–drug interactions. These drug–drug interactions may be responsible for the poor BP control in some CKD patients.

Although the majority (94%) of our subjects had received some form of formal school education, this was not significantly associated with BP control (p=0.077). This finding further buttresses the fact that compliance with medications and consequent BP control go beyond the level of formal education. Other factors that have been previously documented to aid BP control include patient-healthcare provider communication, patient medication adherence education, and counseling.[35-37] These are important in achieving better BP control by ensuring drug adherence.[17,23]

Our study also demonstrated an association between anemia, serum creatinine, and BP control. This aligns with the studies by Li and Collins[38] and Odeyemi *et al.*[39] The prevalence of anemia increases with the severity/stage of CKD, and serum creatinine also rises as CKD progresses. Therefore, without adequate and optimal drug intervention, BP control is poorer as CKD progresses, which aligns with previous studies.[2,5,13,14] Flack *et al.*[40] established an association between the presence of either micro- or macro-albuminuria and low eGFR to poor BP control. However, the direct association between CKD stage and BP control was not established in this study. Similarly, there was no established relationship between socio-demographic parameters—such as gender, body mass index, cigarette smoking, and alcohol—and BP control in our study. However, our study may be limited by not assessing other known factors that have been shown to affect BP, such as diet, lifestyle, and exercise. Physical activity, dietary habits, sodium intake, and psychosocial support have been shown to be determinants of BP control.

Finally, this study found that anemia and reduced eGFR in CKD patients are associated with poor BP control. However, our findings need to be confirmed in a larger multicenter longitudinal observational study.

5. Limitations

The present study has several limitations. Causality cannot be inferred due to the cross-sectional design of the study, and a single-center study like ours may not be generalizable across regions. We used a self-reporting method to assess medication adherence in this study, which may not be entirely reliable, as patients may overestimate or underestimate their adherence. Furthermore, we relied on office BP monitoring in this study and did not assess 24-h BP control. We, therefore, recommend a larger, prospective, and multicenter study using ambulatory BP monitoring.

6. Conclusion

This study provides valuable insights into the determinants of BP control in CKD patients. The findings emphasized the need to achieve better BP control and the importance of addressing anemia and elevated serum creatinine, as well as optimizing antihypertensive medication use for better BP management.

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Conflict of Interest

The authors declare that they have no competing interests.

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Ethical approval and consent to participate

The approval of the Ethics and Research Committee of Lagos State University Teaching Hospital, Ikeja, Lagos, was obtained before the study commenced (approval ID: LREC/10/06/636). All subjects provided their informed consent after the investigators provided a detailed explanation of the study procedures. All participants understand that all patient identifiers will be removed and that the data will be stored on a personal computer. The participants also understood that they can willingly withdraw from the study without any negative consequences.

Consent for publication

All participants provided informed consent for the publication of the findings derived from this study. Where applicable, participants gave explicit permission for the publication of any data, images, or information that could potentially reveal their identity. The authors affirm that all relevant consent forms have been obtained and are available on reasonable request.

Availability of data

Data can be obtained on reasonable request to the authors.

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