Some Evidence of Risk Factors Associated with Autosomal Dominant Polycystic Kidney Disease in Newly Diagnosed Adult Hypertensive Patients in NAUTH Nnewi, Nigeria

Abstract

Objective: Due to other chronic diseases that are associated with hypertension and kidney disease, little or no attention has been paid to the existence of polycystic kidney disease in Nigeria. The present study aimed at assessing the prevalence of some risk factors of ADPKD among hypertensive adult patients in NAUTH, Nnewi, Anambra State, Nigeria

Study design: A cross-sectional and prospective study

Place and Duration of Study: The study was carried out at Medical out-patient, cardiology and nephrology units of NAUTH Nnewi between February and June, 2019.

Methodology: A total of 160(80 newly diagnosed hypertensive and 80 normotensive subjects) aged between 25-75 years were randomly selected. Estimation of serum electrolytes, urea, creatinine, total calcium, eGFR and total protein, BMI and waist-hip ratio of the subjects were taken were done using standard laboratory methods.

Results: 12.5% of the hypertensive subjects have undergone dialysis, 7.5% had kidney transplant, 13.8% had hematuria, 20% had proteinuria, 27.5% had recurrent kidney infection, 15% had kidney stone, 43.8% experienced abdominal/side pain, 20% have had abdominal hernias and 46.3% had elevated urea/creatinine. Mean values of age, BMI and WHR were significantly higher in hypertensive than control subjects (p =.05). Similarly, serum creatinine, urea, sodium and chloride were significantly higher with lower eGFR in hypertensive when compared with control group (p =.05). eGFR in female was significantly lower compared with male hypertensive (p = .05). The mean SBP and DBP were significantly higher in hypertensive compared with control group (p = .05).

Conclusion, 30% of the hypertensive subjects had multiple signs and symptoms of ADPKD, suggesting evidence of high prevalence of ADPKD in the hypertensive patients. Routine screening of family members with hypertension and symptomatic cases of hypertension using ultrasound imaging is strongly recommended for confirmation of presence PKD.

Keywords: Polycystic kidney disease, hypertension, Risk factors, Nigeria

Introduction

Polycystic kidney disease (ADPKD) is the most common inherited deadly multiple system and progressive disorder characterized by cystic expansion, kidney enlargement and renal insufficiency which can lead to chronic kidney disease with subsequent progression to ESRD.[1] In addition to various extra renal manifestations and genetic mutations, early onset of hypertension is the commonest and fastest modifiable risk factors that progresses to ADPKD with eventual ESRD and death). ESRD due to PKD is less common among black people than among white people because of the higher incidence of ESRD from other causes in black people. [1] However, prevalent rate of ADPKD ranging from 2.4%, - 56.1% have been previously reported in Nigeria.[2]

The disease can be inherited in autosomal dominant (ADPKD) and recessive forms. Autosomal dominant polycystic kidney disease (ADPKD) is the most occurrence and characterized by slow but progressive enlargement of the kidneys with renal failure and hypertension occurring by the fifth to sixth decade of life.[3] The disease occurs in approximately 1:800 to 1:1,000 people and accounts for 2.5% of all cases of end-stage renal disease.[4] Clinically, ADPKD presents over the course of decades with hypertension, flank pain, hematuria, and renal cyst infections in adults. Cyst development is gradual but with massive growth of the kidneys and conserved glomerular filtration rate (GFR) until ages 30–40, followed by a rapid, linear decline after this time, until 70 years, 50% of patients with ADPKD will require dialysis or kidney transplantation while, Autosomal recessive polycystic kidney disease (ARPKD), by contrast, typically presents in a younger patient population.[4] The disease is characterized by cystic dilation of the collecting

ducts of the kidneys, along with dysgenesis of the biliary ductal plate, resulting in congenital hepatic fibrosis and often death in the perinatal period due to respiratory failure. [1]

Diagnosis may be suspected from one or more of the following factors: new onset flank pain or red urine; a positive family history; palpation of enlarged kidneys on physical exam; an incidental finding on abdominal sonogram; or an incidental finding of abnormal kidney function on routine laboratory work (BUN, serum creatinine, or eGFR). Definitive diagnosis is made by ultrasound imaging or abdominal CT exam.[1]The present study therefore, was designed to assess the prevalence of some of the risk factors of ADPKD among the newly diagnosed hypertensive patients attending nephrology unit of NAUTH, Nnewi, Nigeria using these routine laboratory methods.

Material and methods

Study site

The subjects for the study were recruited from Medical out-patient, cardiology and nephrology units of Nnamdi Azikiwe University Teaching Hospital Nnewi, Nigeria.

Study design

This was a cross sectional and prospective study designed to assess the prevalence and some risk factors associated with polycystic kidney disease in newly diagnosed adult hypertensive subjects attending medical out patients, cardiology and nephrology units of Nnamdi Azikiwe University Teaching Hospital (NAUTH), Nnewi, Anambra State, Nigeria between February and June, 2019. A total of 80 hypertensive subjects and 80 normotensive subjects (control group) were randomly selected. Well structured questionnaire was used to ascertain the demographic and risk factors that may be associated the PKD.

Collection of samples, preparation and storage

Five (5) ml of venous blood was collected aseptically from each of the subjects and dispensed into a plain container. The samples were allowed to clot, centrifuged at 5,000 rpm for 5 minutes

and serum separated then stored at 4-6°C. A 24 hours urine sample was also collected from the entire participants.

Inclusion criteria

Newly diagnosed hypertensive subjects, within the age range of 25-75 years who attended medical outpatient clinic, cardiology and nephrology units, NAUTH at the study period and willing to participate were included in the study.

Exclusion criteria

Hypertensive subjects who were already on antihypertensive medications and either HIV or tuberculosis patients were excluded, children or patients less than the age of 25 years, patients above 75 years of age and patients who are unwilling to participate.

Method of sample analysis

Determination of serum Creatinine

Serum creatinine was estimated using Colorimetric method.[5]

Principle for estimation of serum creatinine

Creatinine in alkaline solution reacts with picric acid to form a coloured complex. The amount of complex formed is directly proportional to the creatinine concentration.

Determination of Glomerular filtration rate (eGFR)

The estimated glomerular filtration rate was calculated using the Modification of Diet in Renal Disease (MDRD) formula as described by.[6]

Determination of serum Urea

Serum urea was estimated using Urease-Berthelot method. [7]

Principle for estimation of serum urea

Urea in serum is hydrolyzed to ammonia in the presence of urease. The ammonia is then measured photometrically by Bertholet's reaction.

The Waist-hip ratio

Waist-to-hip ratio (WHR) is the dimensionless ratio of the circumference of the waist to that of the hips. This is calculated as waist measurement divided by hip measurement ($W \div H$).[8]

The waist circumference should be measured at the midpoint between the lower margin of the last palpable rib and the top of the iliac crest, using a stretch-resistant tape that provides a constant 100 g tension. Hip circumference was measured around the widest portion of the buttocks, with the tape parallel to the floor.

Determination of urine protein and albumin

Urine protein was estimated using Turbidimetric method. [9]

Principle for estimation of urine protein and albumin

Proteins are precipitated by dilute trichloroacetic acid in sodium sulphate solution. The turbidity of the resultant uniform suspension is measured in a colorimeter against a known standard while albumin was done using dipstick.

Measurement of blood pressure

The blood pressure was measured using auscultatory method Munter et al. [10] which consists the use of auscultatoric measurement devices such as sphygmomanometer and stethoscope. Hypertension was defined by a systolic blood pressure of >140 mmHg, diastolic blood pressure of >90 mmHg.

Statistical analyses

All the statistical analyses were performed using SPSS version 19.0 (SPSS Inc., Chicago, IL). Continuous variables were expressed as mean ± standard deviation. Student *t* -test was used to

compare the continuous variables between the groups. Correlation of the parameters with PKD was determined using the Pearson's correlation coefficient. $P < 0.05$ was considered statistically significant.

Results

Table 1 shows that none of the hypertensive subjects have been diagnosed of PKD and, a frequency of 10(12.5 %) hypertensive subjects have undergone dialysis, 6(7.5 %) had kidney transplant. Also 80 (100 %) of the participants are known to be hypertensive, 11 (13.8 %) had hematuria, 16 (20 %) had proteinuria, 22 (27.5 %) had recurrent kidney infection, 12 (15 %) had kidney stone, 35 (43.8 %) experienced abdominal or side pain, 16 (20 %) have had abdominal hernias and 37 (46.3 %) had elevated urea or creatinine. Results also showed that 26 (32.5 %) of the hypertensive subjects experienced one sign or symptom of PKD, 30 (37.5 %) experienced double symptoms and 24 (30 %) experienced multiple symptoms (3 or more symptoms) of PKD.

Table 2 showed no significant difference in the mean height and hip measurement of the hypertensive subjects and control groups ($p > .05$). The mean age, body mass index (BMI), weight, waist-hip ratio (WHR) and waist measurement were significantly increased in the hypertensive subjects ($p = .05$).

In table 3 there were no significant difference in the mean potassium (K^+), total protein (TP) between the hypertensive subjects and control group ($p = .05$). The mean systolic blood pressure (SBP), diastolic blood pressure (DBP), levels of creatinine (Cr), estimated glomerular filtration rate (eGFR) and urea were significantly increased in the hypertensive subjects when compared to with control group ($p = .05$), while the mean sodium (Na^+) and chloride (Cl^-) were significantly lower in the hypertensive subjects ($p = .05$).

In table 4 there were no significant difference in mean age, weight, height, BMI, waist and hip between female hypertensive and male hypertensive subjects ($p > .05$). The mean WHR was significantly increased in female hypertensive subjects ($p = .05$).

In table 5 there were no significant difference in mean Na^+, K^+, Cl^-, urea, creatinine, total protein, SBP and DBP between female hypertensive and male hypertensive ($p > .05$). However,

the mean eGFR was significantly lower in female hypertensive compared with the male counterpart (p = .05).

In table 6, there were no significant difference in the mean values of weight, height, BMI and hip between female hypertensive and female control groups (p > .05). The mean age, waist and WHR was significantly increased in female hypertensive compared with the male counterpart (p = .05).

Table 7 shows no significant difference for the mean K^+, urea and total protein between female hypertensive and female control subjects (p > .05). The mean Na^+, Cl and eGFR were significantly lower in female hypertensive (p = .05) while, the mean Creatinine, SBP and DBP were significantly increased in the hypertensive females (p = .05).

In table 8, there were no significant difference for mean K^+, urea, total protein and eGFR between male hypertensive and male control (p > .05). The mean Na^+, and Cl^- were significantly lower in male hypertensive than in control (p = .05). The mean Creatinine, SBP and DBP were significantly increased in hypertensive male compared with male control (p = .05).

Table 1: Frequency and percentage of variables from hypertensive subjects

Variables		**frequency (n=80)**	**percentage (%)**
Sex	Male	36	45
	Female	44	55
Definitive diagnosis	Yes	0	0
	No	80	100
Dialysis	Yes	10	12.5
	No	70	87.5
Kidney transplant	Yes	6	7.5
	No	74	92.5
Check all that apply	Hypertension	80	100
	Hematuria	11	13.8

Proteinuria	16	20	
History of kidney stone	12	15	
Recurrent kidney infection	22	27.5	
Abdominal/side pain	35	43.8	
History of abdominal hernias	8	10	
Elevated BUN or creatinine	37	46.3	
Single symptoms	26	32.5	
Double symptoms	30	37.5	
Multiple symptoms	24	30	

Table 2 Anthropometric parameters between hypertensive group and control group (Mean ± SD)

Variables	**Hypertensive group (n=80)**	**Control group (n=80)**	**t-value**	**p-value**
Age (yr)	59.50±10.94	51.37±7.01	10.02	0.000*
Weight (kg)	76.08±19.05	67.57±16.25	1.135	0.045*
Height (M)	1.61±1.31	1.61±0.13	0.011	0.795
BMI (kg/m^2)	29.61±7.33	25.81±5.56	2.382	0.017*
Waist (cm)	107±17.59	9 4.38±14.14	0.385	0.003*
Hip (cm)	97.38±12.80	94.20±14.14	0.276	0.304
WHR	1.11±0.16	1.00±0.11	2.151	0.002*

*Statistically significant p-values at = .05.

Table 3: Serum electrolytes levels, Urea, Cr, TP, eGFR, SBP and DBP hypertensive subjects and control group (Mean ± SD)

Variables	Hypertensive group (n=80)	Control group (n=80)	t-value	p-value
Na^+(mmol/l)	140.70±2.87	133.52±9.67	15.403	0.000*
K^+(mmol/l)	4.48±0.88	4.43±0.47	13.202	0.771
Cl^- (mmol/l)	101.70±2.31	96.36±6.53	11.727	0.000*
Urea (mg/dl)	54.72±40.18	38.60±10.69	13.772	0.035*
Cr (mg/dl)	3.04±0.27	2.49±0.25	34.854	0.000*
TP (g/l)	7.19±1.72	6.70±0.99	2.039	0.163
eGFR (ml/min/1.73m^2)	59.04±33.70	82.53±38.16	2.880	0.001
SBP (mmHg)	151.38±32.57	111.35±8.67	41.54	0.000*
DBP (mmHg)	108.60±24.78	88.00±10.05	8.704	0.000*

*statistically significant p-values at = .05

Table 4: Anthropometric parameters between hypertensive female and hypertensive male (Mean ± SD)

Variables	female hypertensive (n=36)	male hypertensive (n=44)	t-value	p-value
Age (yr)	60.73±10.24	56.48±11.67	0.511	0.012*
Weight (kg)	76.57±18.45	75.19±19.88	0.260	0.801

Height (M)	1.59±0.14	1.65±0.12	0.920	0.096
BMI (kg/m^2)	30.78±7.59	27.65±6.62	0.256	1.333
Waist (cm)	110.93±17.62	100.44±17.50	0.443	0.861
Hip (cm)	97.17±13.25	97.81±12.12	0.968	0.801
WHR	1.15±0.17	1.03±0.10	0.816	0.019*

*statistically significant p-values at = .05

Table 5: Serum electrolytes levels, Urea, Cr, TP, and eGFR between female hypertensive and male hypertensive (Mean ± SD)

Variables	**female hypertensive (n=44)**	**male hypertensive (n=36)**	**t-value**	**p-value**
Na^+(mmol/l)	132.43±10.67	135.10±7.74	0.481	0.334
K^+(mmol/l)	4.53±0.90	4.42±0.83	0.066	0.671
Cl^- (mmol/l)	95.50±7.18	97.76±5.20	1.223	0.223
Urea (mg/dl)	55.30±41.89	53.05±37.71	0.057	0.845
Cr (mg/dl)	2.25±1.06	2.01±0.88	0.446	0.406
TP (g/l)	7.22±1.97	7.14±1.26	1.932	0.873
eGFR ($ml/min/1.73m^2$)	58.87±28.54	84.76±34.91	3.810	0.005*
SBP (mmHg)	148.90±35.14	153.80±28.68	2.641	0.598
DBP (mmHg)	110.13±26.17	105.80±22.22	0.469	0.544

*statistically significant p-values at = .05

Table 6: Anthropometric parameters between female hypertensive and female control (Mean ± SD)

Variables	female hypertensive (n=44)	female control (n=44)	t-value	p-value
Age (yr)	60.73±10.24	52.00±6.52	5.235	0.007*
Weight (kg)	76.57±18.45	72.08±17.92	0.129	0.464
Height (M)	1.59±0.14	1.63±0.11	0.295	0.305
BMI (kg/m^2)	30.30±7.59	27.03±5.83	1.003	0.120
Waist (cm)	110.93±17.62	95.62±18.98	0.148	0.014*
Hip (cm)	97.17±13.25	93.38±13.44	0.985	0.397
WHR	1.15±0.17	1.02±0.12	1.427	0.019*

*statistically significant p-values at = .05

Table 7: Serum electrolytes levels, Urea, Cr, TP and eGFR between female hypertensive and female control (Mean ± SD)

Variables	female hypertensive (n=44)	female control (n=44)	t-value	p-value
Na^+(mmol/l)	140.92±2.62	132.43±10.67	6.285	0.007*
K^+(mmol/l)	4.53±0.90	4.54±0.37	7.901	0.438
Cl^- (mmol/l)	101.46±2.03	95.50±7.18	6.314	0.006*

Urea (mg/dl)	55.30±41.89	39.08±14.54	3.677	0.183
Cr (mg/dl)	2.25±1.06	1.13±0.40	10.22	0.001*
TP (g/l)	7.22±1.97	6.82±0.87	2.900	0.496
eGFR (ml/min/1.73m^2)	58.87±28.54	82.23±34.22	0.464	0.025*
SBP (mmHg)	149.70±35.46	113.79±8.42	25.87	0.001*
DBP (mmHg)	110.47±26.55	90.14±8.71	6.170	0.008*

*statistically significant p-values at = .05

Table 8: Serum electrolytes levels, Urea, Cr, TP, eGFR between male hypertensive and male control (Mean ± SD)

Variables	**male hypertensive (n=36)**	**male control (n=36)**	**t-value**	**p-value**
Na^+(mmol/l)	140.94±2.70	135.43±7.74	10.19	0.007*
K^+ (mmol/l)	4.42±0.83	4.34±0.54	4.385	0.721
Cl^- (mmol/l)	102.0±2.58	97.76±5.20	3.168	0.005*
Urea (mg/dl)	53.05±37.78	38.31±7.17	10.327	0.133
Cr (mg/dl)	2.01±0.88	1.05±0.24	32.657	0.000*
TP (g/l)	7.14±1.26	6.59±1.13	0.249	0.177
eGFR (ml/min/1.73m^2)	84.76±34.91	82.06±24.23	5.108	0.793

SBP (mmHg)	153.90±28.68	109.81±8.67	13.23	0.000*
DBP (mmHg)	105.8±22.23	86.62±11.21	3.500	0.003*

*statistically significant p-values at = .05

Discussion

Due to other chronic diseases that are associated with hypertension and kidney disease, little or no attention has been paid to the existence of polycystic kidney disease in Nigeria, especially in the study environment. ADPKD is the primary cause of renal failure and hypertension has become the most common and early marker of polycystic kidney disease which can result to sudden renal function loss. [1] As in our in study, the significant evidence of hematuria, recurrent kidney infections, abdominal side pains/hernias and proteinuria in the hypertensive patients strongly indicates symptoms of autosomal dominant polycystic kidney disease.[3] The relationship between hypertension and ADPKD has earlier been reported.[1] PKD is an inheritable disease with more or less no definitive treatment, the treatment aims at reducing the signs and symptoms of the disease.[12] Early or frequent episodes of gross hematuria have contributed severely to renal dysfunction and chronic iron toxicity. It has also been shown that increased levels of proteinuria and urinary albumin excretion correlated with higher risk of severe renal disease and progression to ADPKD.[12] Hematuria in ADPKD has been linked with hemorrhage in the cysts or cyst rapture into collecting ducts while, proteinuria occurs due to impaired reabsorption of proteins by cyst-lined tubular epithelia which may not occur at the initial stage of the disease.[13] The multiple urinary tract infections (UTIs) observed in this study could result to more rapid decline in renal function. The observation was in line with the previous study by. [1, 7, 14] However, it is uncertain whether UTIs play a significant role in the loss of renal function in ADPKD. Furthermore, the kidney stone as observed has been very common in those with ADPKD than in the general population. [14] Other symptoms as observed in this study such as abdominal side pain and hernias or a combination have been documented as early and most common symptoms seen in those with PKD.[1, 12, 13, 14] The authors attributed the pains to cyst formation and organ enlargement including the kidneys and liver.

The result showed that 37(46.3%) of the hypertensive subjects had elevated urea or creatinine. At the onset of PKD, serum creatinine is usually within the normal range but gradually rises as the cystic damage to the kidney becomes more severe.[15] Results also showed that 26 (32.5%) of the hypertensive subjects had just one of the sign or symptom of PKD, 30(37.5%) of them had two, while 24 (30%) had multiple signs and symptoms of PKD. However, it is not surprising that most of our study participants presented most of the symptoms of ADPKD because they are newly diagnosed hypertensive who had not been on medications for hypertension. Many people with hypertension do not seek medical service on time rather; they indulge in drinking herbal medicine and other practices thereby delaying the treatment until there conditions became worse. The activation of renin-angiotensin aldosterone system (RAAS) and sympathetic nervous system are the predominant causes of hypertension in ADPKD. Left ventricular hypertrophy (LVH) also causes high BP and increases cardiovascular risk in the affected individuals. [1, 12, 16]Early detection and treatment of hypertension could prevent the formation of cyst and cardiovascular complications with reduction in end organ damage and mortality. [12]

Out of 80 hypertensive subjects; 10 (12.5%) of the hypertensive subjects have undergone dialysis and 6 (7.5%) had kidney transplant. The observation is in line with the treatment and management of ADPKD. [12] Polycystic kidney disease is characterized by slow enlargement of the kidney, gradual Cyst development and growth with renal failure occurring by the fifth- sixth decade (50-60 years) of life. Yet despite the massive growth of the kidneys, the glomerular filtration rate (GFR) in these patients is typically conserved until ages 30–40, followed by a rapid, linear decline after this time and by the age of 70, 50% of patients with PKD will require dialysis or kidney transplantation. [1, 3] Type of PKD1 mutations can also influence the renal outcome in ADPKD.

The mean age of the hypertensive subjects was significantly higher compared with control and significantly lowers in men than in female counterparts. Age has been reported to be among the common risk factor of ADPKD.[16] A median between ages of 30 - 58 years have been documented previously for increased incidences of ESRD due to ADPKD thereby, making age a significant factor for onset of cardiovascular diseases including hypertension and CKD which may lead to PKD with subsequent progression to end-stage renal disease (ESRD). [12, 16] Several other studies have reported more critical illnesses in men than women, with earlier onset of hypertension, more severe hypertension, and earlier onset of ESRD and thus, ADPKD. [17]

BMI and WHR were also significantly increased in the hypertensive subjects compared with control group. Based on gender, the mean WHR was significantly higher in female hypertensive compared with their male counterparts and female control. As in our study, increases in BMI together with WHR are factors that predisposes individual to ADPKD. [18] People with high BMI are heading towards overweight and obesity and this predisposes those individuals to cardiovascular diseases including hypertension which are risk factor for kidney disease and ESRD with eventual decline in eGFR in the general population.[15]Additionally, some previous researchers have strongly implicated overweight and obesity with rate of progression to early stage ADPKD. [18] The later indicated that common pathways may be implicated in both ADPKD and obesity. However, the author also documented that adequate moderation and food restriction slows progression of ADPKD. [18] A larger cohort study in the study environment is highly advocated to ascertain the relationship between BMI and ADPKD progression.

The mean eGFR was significantly lower in hypertensive subject than in control group. Decline in eGFR in hypertensive as well as in patients with CKD, ESRD and ADPKD have been previously reported. [15]As in our study, patients may not develop notable renal insufficiency until 30s or later, after which the GFR rate declines at an average of 4.4 to 5.9ml per minute per year. [1, 19] Our participants are newly diagnosed hypertensive though with lower eGFR than control, it is still within the normal range. Under gender comparison, mean eGFR was significantly lower in female hypertensive subjects when compared with male hypertensive subjects. Decline in eGFR caused by PKD has previously been shown to be higher in men than in women.[1, 19] This can be as a result of renal function being more impaired in female due to adverse renal complications. GFR has been shown to maintain the normal range as a result of compensatory hyper filtration, even when cysts develop progressively.[3] Additionally, ADPKD genotype enhances disease progression to ESRD in Patients with a truncated *PKD1* mutation, compared to patients with a *PKD2* mutation.

The mean creatinine and urea were significantly raised in the hypertensive subjects compared with control. The results were in agreement with the reports of Vaidya et al. [15] Based on gender, the mean creatinine was significantly increased in female and male hypertensive compared with their corresponding controls. Most patients suffering from PKD die as a result of ureamia.

Increased serum creatinine and urea suggests abnormal kidney function which indicates early signs of ADPKD and may subsequently lead to disease severity.

Sodium (Na^+) and Chloride (Cl^-) were also found to be significantly higher in the hypertensive subjects including female and male hypertensive compared with their control counterparts. The result for sodium (Na^+) is consistent with the previous report by [3] which reported increases in sodium retention, reabsorption and thus increased serum sodium level. Increased urinary sodium excretion has been associated with increased total kidney volume hence, the implication in progression of ADPKD. The association between increased kidney volume and the risk factors of ADPKD has also been reported. However; dietary sodium restriction is highly beneficial in the prognostic management of ADPKD. [19]

The significant increase in mean Chloride can be as a result of chloride shift which usually happens when renal function and acid-base balance of the body are impaired. Cystic fibrosis transmembrane conductance regulator (CFTR)-mediated chloride transport has been strongly implicated in progressive renal cyst development and as an important inducer of cAMP transmembrane fluid secretion in ADPKD. [20] It has been shown that the force of active chloride excretion in PKD is enhanced by the basolateral sodium-potassium ATPase producing a chemical gradient driving the influx of potassium and chloride through basolateral sodium, potassium and chloride (Na^+- K^+-$2Cl^-$) co-transporters and the significant accumulation of sodium and chloride in lumen results in water secretion by osmotic forces in PKD. [21] The inhibition of Na^+, K^+-ATPase, Na^+- and K^+-$2Cl^-$ co-transporters and potassium transporters in the basolateral membrane on the other hand, would absolutely prevents the chloride secretion and progressive cyst development. [21] Additionally, previous researches have demonstrated that the V2 receptor of arginine vasopressin (AVP) which stimulates cAMP production through adenylyl cyclase 6 as well as calcium activated chloride channel (CaCC) are critical factors for chloride-driven fluid secretion in PKD. [19] Blocking of the V2 receptor with different antagonists or reduction in the plasma level of AVP by increasing water intake grossly decreases renal cAMP levels and inhibits development of cyst in PKD and ADPKD.[19, 22] More longitudinal study on the mechanism of ATP-driven chloride transport and intracellular calcium contents in cells are still needed.

The mean values of systolic blood pressure (SBP) and diastolic blood pressure (DBP) were significantly higher in hypertensive groups (including male and female) compared with control group, of course this result was expected because the test subjects were newly diagnosed hypertensive and have not been placed on medication prior to this study. Hypertension is the most common early manifestation of PKD and contributes to renal dysfunction and cardiovascular complications, which are the most common causes of death in those with PKD. [23]

Conclusions

The presence of multiple signs and symptoms with evidence of some significant laboratory findings in the hypertensive patients strictly indicates high risk factors of ADPKD. Also, more longitudinal study with more sensitive biomarkers and predictors of ADPKD including ultrasound imaging is recommended to establish the prevalence of ADPKD in the study environment. Routine screening of family members with hypertension and symptomatic cases of hypertension for PKD is also strongly recommended.

Consent for Publication

All authors declare that 'written and informed consent was obtained from patients for publication of this study.

Ethics Approval and Consent to Participate

" All authors hereby declare that all experiments have been examined and approved by the board of ethics committee of Nnamdi Azikiwe University Teaching Hospital, Nnewi, Anambra State, Nigeria with ref no: NAUTH/CS/66B/VOL.2/011 in accordance with the ethical standards laid down in 1964 Declaration of Helsinki"

COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we

do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

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