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Research Article

Risk factors for Undiagnosed Kidney Disease among Stable First-Degree Relatives of Chronic Kidney Disease Patients at Nnamdi Azikiwe University Teaching Hospital, Nnewi, South Eastern Nigeria

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Abstract

Background: Chronic kidney disease (CKD) is a global public health problem and has a major impact on health and cost of health care. In Nigeria, renal replacement therapy (RRT) is funded out of pockets by patients and their relatives unlike in most developed countries. There is a high clustering of the risk factors for CKD in FDRs of CKD patients, making then an ideal population for the screening for and the reversal of the modifiable risk factors that predispose to CKD.

Objective: This study determined the risk factors for CKD in the FDRs of patients with CKD in South Eastern Nigeria.

Methodology: This was a hospital based prospective study involving 300 subjects: 150 FDRs of CKD patients and 150 control subjects without personal or family history of CKD. The study and control subjects were screened for CKD using urine albumin creatinine ratio (uACR) and estimated glomerular filtration rate (eGFR). Prevalence rate of the risk factors for CKD such as hypertension, diabetes mellitus, obesity, dyslipidaemia, hyperuricaemia and life style practices like significant smoking and heavy alcohol consumption were determined for both the FDRs and the control subjects. Data was analyzed with SPSS version 21.0. Mann-Whitney U test was used for comparing the variables between the two study groups for continuous variables that were not normally distributed and Chi square tests for categorical variables.

Results: The prevalence rate of dyslipidaemia and hyperuricaemia was significantly higher among the FDRs of CKD patients compared with the control subjects (26% versus 12%; P = 0.003) and (20.7% versus 7.3%; P = 0.001) respectively. The other risk factors for CKD that included hypertension, diabetes mellitus, obesity, significant cigarette smoking, heavy alcohol consumption and herbal medication use were equally more among the FDRs of CKD patients compared with the controls, although not statistically significant.

Conclusion: The risk factors for CKD were common among FDRs of CKD patients. Screening for these risk factors at the earliest possible contact with the FDRs of CKD patients and taking appropriate actions to tackle the modifiable ones will prevent the development of CKD and retard the progression of the already existing disease, reduce the alarming global burden of CKD.

Keywords: Chronic kidney disease. First degree relatives. Nigeria. Risk factors, Undiagnosed.

1. INTRODUCTION

Chronic kidney disease (CKD) is a global public health problem and has a major impact on health and cost of health care[1]. For individuals with CKD, the burden of the risks leads to higher rates of hospitalization and accounts for a large fraction of health care costs associated with CKD[2,3]. In most developed countries, renal replacement therapy (RRT) is funded by government and insurance schemes but in Nigeria, RRT is funded out of pockets by patients and their relatives[4]. Fortunately, though, chronic kidney disease (CKD) is a preventable condition with risk factors that are non-modifiable or modifiable. The non-modifiable risk factors are older age, male sex, African origin, and family history of CKD[5]. The modifiable risk factors are diabetes mellitus, hypertension, proteinuria, obesity, dyslipidaemia, hyperuricaemia and prolonged use of non-steroidal anti-inflammatory drugs[5].

Family history of kidney disease is an important risk factor for CKD[6]. There is higher risk of CKD in FDRs of CKD patients, making then an ideal population for the screening for and the reversal of the modifiable risk factors that predispose to CKD[7]. First degree relatives of CKD patients have increased risk of CKD due to genetic link and environmental exposure[8,9]. The prevalence of CKD among FDRs of CKD patients in a Nigerian study was 37.4%[10]. There is higher prevalence of CKD, history

of hypertension and diabetes mellitus in first degree relatives of patients with CKD as compared with first degree relatives of the general population[11].

Several studies have shown that kidney disease and by extension its risk factors are prevalent in first degree relatives (parents, siblings and children) of CKD subjects, especially in Africans and African Americans and a key public health strategy in CKD prevention and management is the screening of this high risk populations for the risk factors of CKD[5,7,12,13]. The rate of CKD progression is determined by the underlying a etiology of CKD, associated co-morbidities and availability of treatment options[14].

Worldwide, the common causes of CKD are hypertension, diabetes mellitus, chronic glomerulonephritis (CGN), analgesic nephropathy, obstructive uropathy, polycystic kidney disease, and others[15]. In Unites States of America, diabetic nephropathy and hypertension are the major causes of CKD, while chronic glomerulonephritis (CGN) and hypertension are the major causes of CKD in sub-Saharan Africa[16]. In Nigeria, the common causes of CKD are CGN, hypertension and diabetes mellitus[16].

The incidence, prevalence and progression of CKD are influenced by gender[17]. Some studies have observed higher incidence and prevalence rate of CKD in males than females whereas the opposite have been documented by other studies[17].

Hypertension is an important risk factor for CKD development and progression[18]. Hypertension in the adult population is very common world-wide with an estimated prevalence rate of 26.4% in 2000 and this was estimated to rise to 29.2% by 2025[19]. The prevalence of hypertension increases with decline in kidney function and it can be a cause and a consequence of CKD, with associated unfavorable outcome such as development of cardiovascular disease[18]. In Nigeria, hypertension as a primary diagnosis has been reported among end stage renal disease (ESRD) patients to be 17.2%, 26.1% and 31.1%[20-22]. Among relatives of CKD and ESRD patients, the prevalence rate of hypertension as reported in various studies were 41.8% in Argentina, 53% in Taiwan, 26.3% in China, 29.7% in India, 24.3% in Nigeria and 31.7% in Cameroon[23-28,8].

Diabetes mellitus (DM) is both a risk factor and a cause of CKD and ESRD and has had an astronomical rise in its prevalence rate globally, from 8.8% in 2017 to an estimated 9.9% by 2045[5,28]. Worldwide, diabetic nephropathy (DN) is a major cause of ESED and this is due to the increasing prevalence rate of diabetes mellitus[29]. DN occurs in about 30% and 40% of patients with type 1 and 2 DM respectively[29]. About 37.3% of haemodialysis patients in Turkey were diabetic[5]. In United States, half of new ESRD patients had DN[5]. In Nigeria several studies reported that 11.8% 3.7% and 13.1% of cases of ESRD were caused primarily by diabetes mellitus[20,22,30]. FDRs of DM patients with DN have increased risk for developing DN than those without an affected relative[31]. Among FDRs of CKD and ESRD patients, the prevalence of the DM as reported by different studies were 4.9% in Cameroon, 9% in Taiwan, 10.3% in China, 3.6% in India and 8.7% in Nigeria[8,24-27].

Long-term intensive glycaemic control has been shown to reduce the risk of development and progression of DN[29]. Furthermore, optimal blood pressure control with ACE inhibitors and ARBs have been shown to reduce the risk of development and progression of CKD in people with DM[32].

The association between dyslipidaemia and the development of CKD remains unclear[33]. Some studies have documented that lipid abnormalities might be an independent risk factor for CKD[34]. There is evidence from animal models that lipid abnormalities lead to glomerular injury and glomerulosclerosis[33]. Similar studies in humans are scanty[33]. However, Schaeffner *et al*, reported that elevated total cholesterol (TC), a high ratio of total cholesterol/high density lipoprotein (TC/HDL) and low HDL were significantly associated with increased risk of developing renal dysfunction in apparently healthy men[33]. Another study found a significant association between low levels of HDL and the risk of developing CKD and CKD progression[35]. Lipid abnormalities have been observed among FDRs of ESRD patients. Kong *et al* observed that 45.2% of FDRs of haemodialysis patients had dyslipdaemia, while Inserra *et al* found that 42.9% of FDRs of ESRD patients had hypercholesterolaemia[25,23].

Effective treatment of dyslipidaemia with lipid lowering therapy may reduce the development and progression of CKD. Clinical trials have shown that lipid lowering therapy were associated with a decline in the rate of CKD progression[36].

Cigarette smoking is an independent risk factor for development and progression of CKD[37]. It is a strong predictor of increased urine albumin excretion in diabetics and hypertensive patients[38]. Cigarette smoking has also been shown to promote the progression of DN[38]. Smoking increases CKD risk through endothelial dysfunction, glomerulosclerosis and tubular atrophy[5]. Smoking of > 20 sticks of cigarettes per day increased the risk of CKD in non-diabetic cohorts[5].

Cessation of smoking has been found beneficial in retarding the rate of decline in renal function[38].

The role of heavy alcohol consumption as a risk factor and a cause of renal damage is controversial[39]. Although, some studies had shown that heavy alcohol consumption was associated with CKD, ESRD and proteinuria, others had demonstrated no association between heavy alcohol drinking and CKD[39]. In Nigeria, Ogiator *et al* reported that 18% of FDRs of CKD patients with advanced renal disease had history of alcohol use[9]. A study in the American population showed an increased risk of ESRD in people with high alcohol consumption of more than two drinks per day[39].

Similarly, studies have documented an association between regular analgesic use such as acetaminophen, aspirin and non-steroidal anti-inflammatory drugs (NSAIDs) and CKD[40]. A case control study showed a twofold increased risk of ESRD in people with lifetime use of greater than 1000 pills of acetaminophen and an eightfold increased risk in those with a lifetime cumulative dose of greater than 5000 pills of NSAIDs[40].

Education on the rational use of analgesics may modify the risk of kidney disease associated with analgesic abuse. Furthermore, early CKD detection among analgesics users and subsequent withdrawal of the analgesics may reduce the burden of CKD associated with analgesic abuse[41].

Overall, FDRs of CKD patients have a greater prevalence of CKD risk factors than the general population and therefore should be screened for the presence of kidney disease[6].

In developing countries like Nigeria, there is shortage of dialysis and renal transplant facilities which are the treatment options for ESRD. Therefore, early detection, reversal or prevention of the modifiable risk factors of CKD and treatment of CKD in FDRs of CKD patients are essential for decreasing the economic and personal burdens of CKD in Nigeria and delaying the progression to advanced stages. FDRs of CKD patients can easily be accessed as they often serve as care givers to their relatives with CKD and most times accompany them to hospitals where they receive treatment.

There is however a paucity of data on risk factors of CKD in FDRs of CKD patients in Nigeria. This study sets out to answer the following research questions: what are the risk factors for

CKD in FDRs of CKD patients in Nigeria? Is there a difference in the prevalence rate of risk factors for CKD in FDRs of CKD patients in Nigeria compared with a healthy control group?

This study aims to bridge these gaps in knowledge and add to the existing local literature.

2. MATERIALS AND METHOD

This was a hospital based prospective study carried out at the Nephrology Outpatient Clinic and the Haemodialysis Unit of Nnamdi Azikiwe University Teaching Hospital (NAUTH), Nnewi in Anambra State, Nigeria. The study was done from September 2018 to August 2019. The study participants comprised two groups: the subjects, who were the first-degree relatives (FDRs) that included the parents, siblings and children of CKD patients attending the outpatient clinic and those on maintenance haemodialysis. The second was a control group that was age and sex matched with the subjects and were drawn from the General Outpatient Department (GOPD), hospital staff and medical and paramedical students of NAUTH.

54 CKD patients were consecutively selected as they were seen at the Nephrology Clinic and the haemodialysis center after providing an informed written consent. A pool of the names of the FDRs of these CKD probands was made and a possible 3 selected by balloting, giving a total of 162 study subjects. In the families of CKD patients with less than 4 FDRs, all members were selected. FDRs of CKD patients that withheld their consent to participate in the study were replaced from the pool. The selected FDRs were invited to participate in the study by their CKD relatives. 162 FDRs commenced the study, 150 completed the study while 12 were lost to follow up.

Similarly, 152 consenting control subjects were randomly selected from the patients attending the GOPD, hospital staff and the medical and paramedical students of NAUTH. 150 of these control subjects completed the study while 2 were excluded on account of a positive retroviral screening test results. The 150 control subjects were individually age and gender matched with the study subjects.

Inclusion criteria for both the study subjects and control subjects were: provision of a written informed consent and age of 18 years and above.

The study subjects were excluded from the study if they had febrile illness, urinary tract infection, heart failure, retroviral disease or were pregnant.

The control subjects were excluded from the study if they had personal or family history of CKD, had febrile illness, urinary tract infection, heart failure, retroviral disease or were pregnant.

Three hundred (300) participants that comprised 150 subjects and 150 controls completed the study and their data were analyzed. They were seen at 2 separate visits: the baseline and the follow-up visits. At the baseline visit the researcher structured and administered pretested questionnaire was filled out for the collection of the medical, life style and demographic data. Anthropometric and blood pressure measurements were done and blood and urine samples collected for laboratory tests.

The follow up visit at 3 months later was for the study and control subjects that had estimated GFR < 60ml/min/1.73m^2 and or urine albumin creatinine ratio (ACR) ≥ 30mg/g at the baseline visit. At this visit follow up laboratory tests that included serum creatinine and urine ACR were done.

Sample collection for the laboratory tests were done after an overnight fast as the participants were instructed, 6mls of blood was collected from each study and control subjects. 1 ml of blood was dispensed into a fluoride oxalate container for fasting plasma glucose analysis. The remaining 5 ml of blood was dispensed into a sterile plain container and allowed to clot and retracted. The blood was centrifuged at 3000 rpm for 10 minutes and the serum separated into two aliquots and stored at -20 °C. The analysis of all the biochemical parameters was done within one month of collection. The biochemical parameters analyzed were serum creatinine, serum uric acid, fasting lipid profile (triglyceride, total cholesterol, high density lipoprotein and low density lipoprotein cholesterol) and retroviral screening. All the samples were analyzed at the laboratory of Nnamdi Azikiwe University Teaching Hospital, Nnewi.

The serum creatinine was determined using Jaffe method[42]. Serum uric acid was determined using colorimetric method[43]. Fasting plasma glucose was assayed colorimetrically using glucose oxidase method[44].

Urine samples were collected between 7am and 10am in the morning. Urinalysis was done using Combi 10 dipsticks to check for proteinuria and infection. Positive nitrite or leucocyte test indicated presence of urinary tract infection.

Retroviral screening was done using Determine kit (Alere Determine™ HIV- 1/2, LOT 87029K100A, Japan).

Urinary albumin was estimated using turbidimetric immunoassay method (Lot No 30030164, AGAPEpeagent, Switzerland). Urinary creatinine was measured using Jaffe method[42]. Urinary albumin-creatinine ratio was calculated in milligram of albumin per gram of creatinine and results were interpreted as follows: less than 30mg/g was regarded as normal, between 30-300mg/g was regarded as moderately increased and greater than 300mg/g was regarded as severely increased[45].

The estimated glomerular filtration rate (eGFR) was calculated using the Modification of Diet in Renal Disease (MDRD) formula. This is available online at: www.kidney.org/kls/professionals/gfr/calculator.cfm. The equation is stated below:

186 x (serum creatinine in mg/dl) $^{-1.154}$ x (age in years) x 0.742 (for female) x 1.210 (for blacks)[46].

The height and weight were measured using a stadiometer. Body mass index (BMI) was calculated as weight (in Kg) divided by square of the height (in meters)[47].

Waist circumference (WC) was measured with a non-stretch metric tape while the subjects were standing[48].

Blood pressure was measured using Accoson mercury sphygmomanometer (Dekamet England)[49].

2.1 DATA ANALYSIS

Data was analyzed using Statistical Package for Social Sciences (SPSS) version 21.0 (IBM Software Group, 200W. Madison St., Chicago, IL; 60606 USA). Categorical data were presented as frequencies and percentages. Differences in variables between the two groups (FDRs and control subjects) were statistically compared using Mann-Whitney U test for continuous variables that were not normally distributed and Chi square tests for categorical variables. P value < 0.05 was considered statistically significant.

2.2 DEFINITION OF OPERATIONAL TERMS

1. Chronic kidney disease was defined as estimated GFR < 60ml/min/1.73m^2 for > 3 months with or without evidence of kidney damage or if there was an indicator of kidney damage like albuminuria – in this study

albuminuria was defined as urine albumin creatinine ratio (ACR) ≥ 30mg/g for > 3months[45].

2. Hypercholesterolaemia – total cholesterol ≥ 5.2 mmol/l[50].
3. Dyslipidaemia – total cholesterol/HDL ratio ≥ 5[50].
4. Hyperuricaemia – serum uric acid ≥ 420µmol/l (7.0 mg/dl)[51].
5. Diabetes mellitus – defined as fasting plasma glucose of ≥ 7.0mmol/l (126mg/dl) or previous diagnosis of diabetes mellitus or individuals taking anti-diabetic agents[52].
6. Significant cigarette smoking – defined as smoking 20 cigarettes daily for more than one year[53].
7. Heavy alcohol consumption – defined as consumption of >210grams of alcohol per week[54].
8. Analgesic abuse – defined as cumulative lifetime use of more than 5000 pills of analgesics[55]. This will be calculated from multiplying the average number of pills consumed in a week by the duration of use in years[55].
9. Proband: refers to a person in a family affected with a disease or condition that raises suspicion that other family members may have an increased propensity for the same disease or condition[56].
10. Hypertension was defined as a systolic blood pressure ≥ 140mmHg or diastolic blood pressure ≥ 90mmHg or use of antihypertensive medication for blood pressure control or history of hypertension[49].
11. Underweight was defined as BMI < 18.5, normal weight as BMI of 18.5 – 24.9, overweight as BMI of 25 – 29.9 and obesity as BMI ≥ 30 Kg/m^2 [47].
12. Truncal obesity was defined as WC ≥ 102 cm in males and ≥ 88 cm in females[48].

3. RESULTS

A total of 150 FDRs and control subjects completed the study respectively. The overall prevalence of CKD in FDR and control was 26.7% and 9.3% respectively (p < 0.001) [OR (95% CI) = 3.5 (1.8-6.8)].

Characteristics of the probands/presumed aetiology of CKD

A total of 54 consented probands with CKD participated in the study. They comprised 31 males (57.4%) and 23 females (42.6%) with median age and inter-quartile range of 56.0 (5.50) years.

The presumed aetiology of CKD in these probands were hypertension 22 (40.70%), diabetes mellitus 14 (25.90%), chronic glomerulonephritis 6 (11.10%), obstructive uropathy 5 (9.30%), autosomal dominant polycystic kidney disease 3 (5.60%), lupus nephritis 2 (3.70%), and unknown 2 (3.70%) (details in Figure 1).

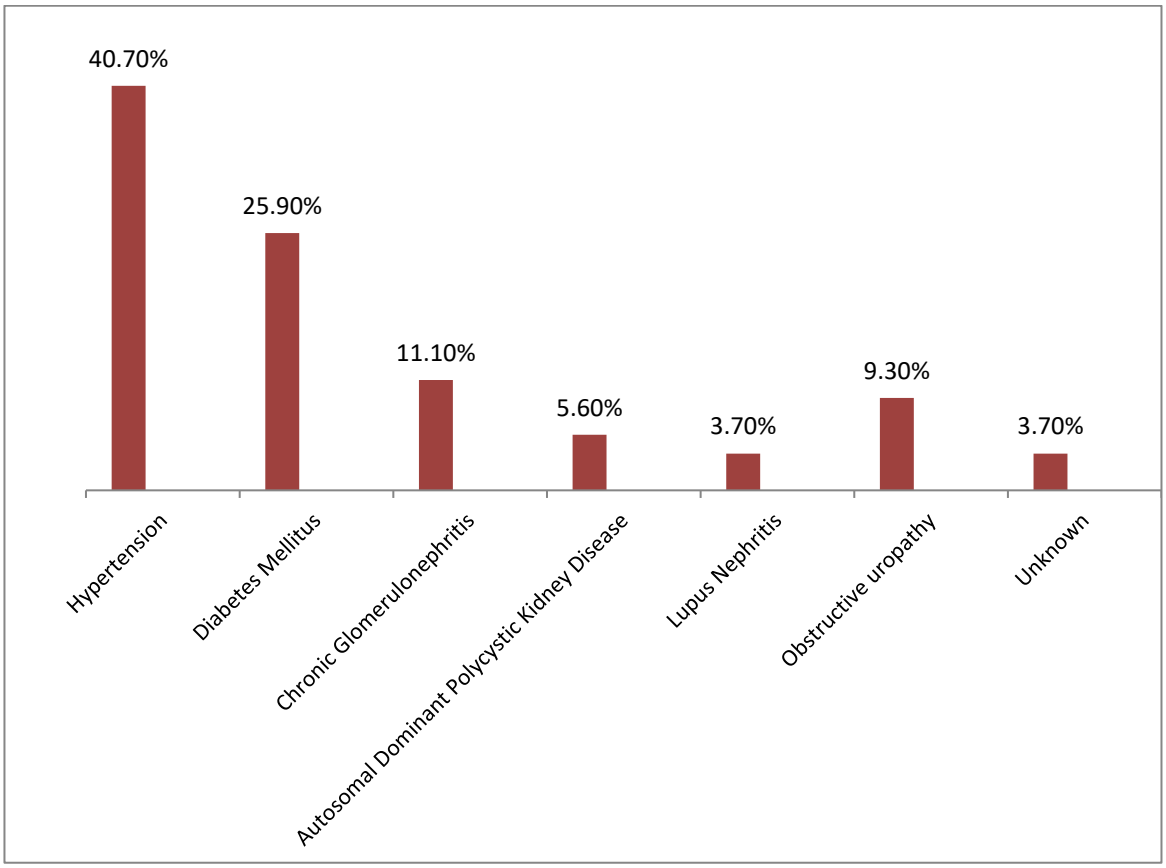

Figure 1: Distribution of the presumed aetiology of CKD among the probands

Comparison of the clinical characteristics of the FDRs and Controls

The clinical characteristics of the two study groups were similar in terms of subjects with hypertension, newly diagnosed hypertension, diabetes mellitus, known DM, newly diagnosed DM, heavy alcohol consumption, cigarette smoking, herbal medication, body mass index, truncal obesity, waist circumference and systolic blood pressure (p > 0.08). However, they differ with regards to their diastolic blood pressure and those that were known hypertensives (p < 0.05) (details in Table 1).

Table 1: Comparison of the clinical characteristics of the FDRs and controls at baseline

Variables		FDR (%) N = 150	Controls (%) N = 150	Test Stat	p-value
Hypertension	Present	34 (22.7)	22 (14.7)	χ^2= 3.162	0.103
	Absent	116 (77.3)	128 (85.3)		
Known Hypertension	Yes	14 (9.3)	4 (2.7)	χ^2= 5.910	**0.026***
	No	136 (90.7)	146 (97.3)		
Newly diagnosed Hypertension	Yes	20 (13.3)	18 (12.0)	χ^2= 0.121	0.862
	No	130 (86.7)	132 (88.0)		
Diabetes Mellitus	Present	19 (12.7)	10 (6.7)	χ^2= 3.092	0.117
	Absent	131 (87.3)	140 (93.3)		
Known Diabetes	Yes	11 (7.3)	3 (2.0)	χ^2= 4.795	0.052
	No	139 (92.7)	147 (98.0)		
Newly diagnosed Diabetes	Yes	8 (5.3)	7 (4.7)	χ^2= 0.070	1.000
	No	142 (94.7)	143 (95.3)		
Heavy alcohol consumption	Present	26 (17.3)	19 (12.7)	χ^2= 1.281	0.332
	Absent	124 (82.7)	131 (87.3)		
Significant cigarette smoking	Present	11 (7.3)	7 (4.7)	χ^2= 0.946	0.467
	Absent	139 (92.7)	143 (95.3)		
Herbal consumption	Present	24 (16.0)	20 (13.3)	χ^2= 0.424	0.625
	Absent	126 (84.0)	130 (86.7)		
BMI	Normal	55 (36.7)	55 (36.7)	χ^2= 4.664	0.097
	Overweight	74 (49.3)	85 (56.7)		
	Obesity	21 (14.0)	10 (6.7)		
Median BMI (IQR) in Kg/m²		26.03 (4.21)	26.04 (3.72)	U = 10841.50	0.587
Truncal Obesity	Present	42 (28.0)	30 (20.0)	χ^2 = 2.632	0.137
	Absent	108 (72.0)	120 (80.0)		
Median WC in cm		83.50 (30.25)	81.70 (23.05)	U = 10911.00	0.652
Median SBP (IQR) in mmHg		130.00 (17.25)	120.00 (20.00)	U = 10091.50	0.116
Median DBP (IQR) in mmHg		80.00 (16.00)	80.00 (10.50)	U = 9794.50	**0.044***

IQR = Inter-Quartile Range, U= Mann-Whitney U test used. χ^2 = Chi square. BMI = body mass index, WC= waist circumference, SBP = systolic blood pressure, DBP = diastolic blood pressure, * = statistically significant.

Comparison of the laboratory characteristics of the FDRs and controls

Both study groups were similar in fasting plasma glucose, serum uric acid, high density lipoprotein, low density lipoprotein, triglycerides and haematuria ($p > 0.100$), nevertheless, they differ in urine ACR, serum creatinine, eGFR, hyperuricaemia, total cholesterol, dyslipidaemia, hypercholesterolaemia and proteinuria ($p < 0.001$) (details in Table 2).

Table 2: Comparison of the laboratory characteristics of the FDRs and controls at baseline

Variables		FDR (%) N = 150	Controls (%) N = 150	Test Stat	p-value
Median Fasting plasma glucose (IQR) in mmol/l		5.20 (0.90)	5.15 (0.90)	U = 11117.0	0.859
Median uACR (IQR) in mg/g		14.35(28.93)	7.10(14.68)	U = 5494.0	**< 0.001***
Median serum creatinine (IQR) in µmol/l		84.00(32.60)	80.40(27.28)	U = 9300.5	**0.009***
Median eGFR (IQR) in ml/min		81.50 (38.03)	86.35(34.35)	U = 9268.0	**0.008***
Median Serum uric acid (IQR) in µmol/l		246.00 (174.00)	241.50 (101.00)	U = 10801.0	0.550
Hyperuricaemia	Present	31 (20.7)	11 (7.3)	χ^2= 11.074	**0.001***
	Absent	119 (79.3)	139 (92.7)		
Median TC (IQR) in mmol/l		4.78 (1.40)	4.29 (1.14)	U = 8748.0	**0.001***
Median HDL(IQR) in mmol/l		1.20 (0.37)	1.23 (0.39)	U = 10383.5	0.248
Median LDL(IQR) in mmol/l		3.07 (1.45)	2.72 (1.33)	U = 10364.5	0.238
Median TG(IQR) in mmol/l		1.00 (0.46)	0.98 (0.34)	U = 10616.0	0.399
Dyslipidaemia	Present	39 (26.0)	18 (12.0)	χ^2= 9.552	**0.003***
	Absent	111 (73.3)	132 (88.0)		
Hypercholesterolaemia	Present	40 (26.7)	15 (10.0)	χ^2= 13.915	**< 0.001***
	Absent	110 (73.3)	135 (90.0)		
Proteinuria	Present	29 (19.3)	10 (6.7)	χ^2= 10.640	**0.002***
	Absent	121 (80.7)	140 (93.3)		
Haematuria	Present	11 (7.3%)	3 (2%)	χ^2= 4.795	0.520
	Absent	139 (92.7%)	147 (98%)		

IQR = Inter-Quartile Range, U= Mann-Whitney U test used, χ^2= Chi square, uACR = urine albumin creatinine ratio, eGFR = estimated glomerular filtration rate, TC = Total cholesterol, HDL = High density lipoprotein, LDL = Low density lipoprotein, TG = Triglycerides, *= statistically significant

Prevalence of risk factors for CKD among the FDRs and controls

The risk factors for CKD among FDRs when compared with the controls were similar for hypertension, DM, obesity, cigarette smoking, heavy alcohol consumption and herbal medications ($p > 0.05$). However, both study groups differ in dyslipidaemia and hyperuricaemia ($p < 0.05$) (details in Table 3).

Table 3: Prevalence of risk factors for CKD among the FDRs and controls at baseline

Variables		FDR (%) N = 150	Controls (%) N = 150	χ^2	p-value
Hypertension	Present	34 (22.7)	22 (14.7)	3.162	0.103
	Absent	116 (77.3)	128 (85.3)		
Diabetes Mellitus	Present	19 (12.7)	10 (6.7)	3.092	0.117
	Absent	131 (87.3)	140 (93.3)		
Obesity	Present	21 (14.0)	10 (6.7)	4.353	0.056
	Absent	129 (86.0)	140 (93.3)		
Significant cigarette smoking	Present	11 (7.3)	7 (4.7)	0.946	0.467
	Absent	139 (92.7)	143 (95.3)		
Heavy alcohol consumption	Present	26 (17.3)	19 (12.7)	1.281	0.332
	Absent	124 (82.7)	131 (87.3)		
Herbal medication	Present	24 (16.0)	20 (13.3)	0.424	0.625
	Absent	126 (84.0)	130 (86.7)		
Dyslipidaemia	Present	39 (26.0)	18 (12.0)	9.552	**0.003***
	Absent	111 (73.3)	132 (88.0)		
Hyperuricaemia	Present	31 (20.7)	11 (7.3)	11.074	**0.001***
	Absent	119 (79.3)	139 (92.7)		

χ^2= Chi square, * = statistically significant

4. DISCUSSION

In this study, FDRs of CKD patients were screened for CKD and its risk factors using clinical and laboratory parameters. The findings from this work supported familial clustering of CKD and its risk factors. The prevalence of CKD was high in the FDRs. Common risk factors for CKD such as hypertension, DM, obesity, dyslipidaemia and hyperuricaemia were more prevalent in FDRs.

Risk factors for CKD in FDRs of CKD patients

The prevalence of risk factors for CKD in this study was higher among the FDRs than in the controls.

The prevalence of hypertension in FDRs was 22.7% and was higher than 14.7% observed in the control group. This prevalence of hypertension was close to 26.3% reported by Kong *et al* in China among FDRs of dialysis patients[25]. This similarity may be explained by the methodology adopted by both studies. The average of multiple blood pressure recordings was used in both studies. However, the prevalence of hypertension in this study was higher than the 14% reported by Ogiator *et al* in Northern Nigeria[9]. The lower prevalence of hypertension in the later study may be due to the smaller sample size of 100 FDRs they studied. On the other hand, the prevalence of hypertension in this study was lower than 41.8% reported by Inserra *et al*, 53% reported by Tsai *et al* and 24.3% reported by Raji *et al*[23,24,27]. The higher prevalence of hypertension reported by Inserra *et al* and Tsai *et al* may be explained by the method of blood pressure measurement used[23,24]. They adopted single blood pressure measurement for defining hypertension as against the average of two blood pressure recordings that is the standard practice and was used in this study. Therefore, the prevalence of

hypertension they obtained may have been overestimated. The accurate method of measuring blood pressure is by at least two different readings taken at an interval of at least one minute apart and the average of the readings should serve as the individual's blood pressure[57]. Measuring blood pressure only once could even label subjects with white coat hypertension hypertensive patients. Furthermore, the higher prevalence of hypertension obtained in Raji *et al* study may be related to differences in the population studied and level of urbanization[27]. They screened 230 FDRs while this study screened 150 FDRs. Also, their study was conducted in an urban center in Nigeria while this study was done in a semi-urban Nigerian city. Urbanization is associated with increased prevalence of hypertension and other cardiovascular risk factors such as obesity and dyslipidaemia[58].

Diabetes mellitus was more common among the FDRs (12.7%) compared with the controls (6.7%). The prevalence rate of DM in this study is comparable to 10.3% found by a similar study in China[25]. Both studies measured fasting plasma glucose via a glucose oxidase method and employed similar definition for DM. On the other hand, the prevalence rate of DM in this study was higher than 9%, 3.6% and 8.7% reported by Tsai *et al,* Bagchi *et al*, and Raji et al respectively[24,26,27]. The lower prevalence of DM in the later studies may be related to the time difference between the studies. Both Tsai *et al* and Bagchi *et al*'s studies were done 10 years earlier, while Raji *et al*'s study was done 6 years earlier than this study[24,26,27]. The prevalence of DM in this study was also higher than 4.7% reported by Iloh *et al* among adults in South-east Nigeria, although, their study was done 6 years earlier[59]. Familial clustering may also explain the higher prevalence of DM obtained in this study. This is because 25.9% of the probands were diabetic. Furthermore, the astronomical rise in the global prevalence of DM as a result of the rising trend in urbanization, adoption of western and sedentary lifestyles may have also contributed to the higher prevalence rate of DM in this study.

Obesity was observed among 14% of FDRs compared with 6.7% of the controls. The prevalence of obesity observed in this study was similar to 14.6% reported in Cameroun by Temgoua *et al*[60]. This similarity may be explained by shared socio-economic factors and lifestyle changes. However, the prevalence of obesity in this study was lower than 62.1%, 26% and 17.4% reported by Inserra *et al*, Bagchi *et al* and Raji *et al* respectively[23,26,27]. The higher prevalence of obesity observed in the later studies may be related to the socio-demographic characteristics of the population studied, including the level of urbanization, lifestyle measures and diets. Obese family relatives of ESRD patients have been reported to have increased risk for developing CKD due to the presence of high ACR and lower eGFR in them[60]. Therefore, obese individuals should be screened for kidney disease because interventions targeted at obesity reduction have been shown to retard CKD progression.

Cigarette smoking was also a risk factor for CKD among FDRs of CKD patients. The prevalence of significant cigarette smoking among FDRs was 7.3% compared with 4.7% in the controls. This finding was lower than prevalence of 23% and 34.8 % reported by Wei *et al* and Inserra *et al* respectively[7,23]. The higher prevalence in these studies may be due to differences in cultural background, climatic conditions and the prevailing social and life style habits. Studies have shown that cigarette smoking is an independent risk factor for development and progression of CKD[34]. It is also a predictor of raised urine-albumin excretion rate in diabetics and hypertensives[35]. Interventions targeted at smoking cessation have been found to be beneficial in reducing the rate of renal function decline[39]. Therefore, FDRs of CKD patients should be properly educated on the deleterious effect of cigarette smoking on the kidneys, having already been genetically predisposed to having kidney disease.

Heavy alcohol consumption was common among FDRs (17.3%) compared with the control subjects (12.7%) in this study, although this was not statistically significant. This is in agreement with findings of Shankar *et al* who reported association of heavy alcohol consumption with CKD[132]. On the other hand, Koning *et al* reported an inverse association between alcohol consumption and risk of developing CKD[54]. The mechanism of alcohol induced kidney injury may be related to oxidative stress via intra-renal renin angiotensin system activation[61].

Herbal medication use was common among FDRs (16%) compared with controls (13.3%). The prevalence of herbal medication use among FDRs was higher than the 5.6% and 8.2% reported by Wei *et al* and Tsai *et al* respectively[7,24]. The higher prevalence of herbal medication use found by this study may not just be related to the attitude and the belief of the population studied regarding health care but also to the prevailing harsh economic conditions locally. Most Nigerians prefer herbal medications and beverages as alternative to orthodox medicines because they are usually cheaper. In Nigeria, the use of medicinal plants for health care need is practiced by majority of people and the reasons were attributed to their affordability and accessibility[62].

Dyslipidaemia was found to be significantly higher among the FDRs (26%) than the controls (12%). This was lower than 45.2% reported by Kong *et al* among FDRs of haemodialysis patients[25]. The differences in prevalence may be due to disparities in lifestyle and socioeconomic status. Kong et al carried out their study in an urban Chinese city with its attendant western lifestyles as opposed to this study that was done in a semi-urban Nigerian city. Similarly, the prevalence of dyslipidaemia in this study was lower than 74.3% observed by Raji *et al* in South Western Nigeria[27]. The difference in the findings is still related to the characteristics of the population studied and the study settings. Urbanization has been shown to be associated with physical inactivity and changes in dietary and lifestyle habits. Sabir *et al*, reported a higher prevalence rate of dyslipidaemia in urban than rural dwellers[63].

Hyperuricaemia was significantly higher among the FDRs (20.7%) than the controls (7.3%) and this finding was similar to 20.5% observed by Makusidi *et al* among inhabitants of Sokoto metropolis in Nigeria[64]. Although they studied the general population, both studies utilized similar definition for hyperuricaemia. Contrastingly, the prevalence of hyperuricaemia in this study was lower than 29% reported by Tsai *et al* in Taiwan[24]. The difference may be partly due to the difference between the dominant local diets of the two population studied. Fish and seafood which are rich in uric acid are central to Taiwanese diets unlike in our environment. Hyperuricaemia has also been reported to be an independent predictor of CKD development in non-CKD individuals[65]. Therefore, individuals with hyperuricaemia should be screened for CKD.

CONCLUSION

Risk factors for CKD were common in FDRs of CKD patients compared with persons without family history of kidney disease. First degree relatives of CKD patients that have any of the risk factors studied should be screened for the presence of CKD as early as possible.

Recommendations

1. Individuals with family history of kidney disease should be screened for the risk factors for CKD at the earliest possible contact with the appropriate health care personnel.
2. Early screening for CKD among FDRs of CKD patients that are found to have the risk factors for CKD is highly advocated based on the finding that there was genetic predisposition and familial clustering of the risk factors of CKD.
3. More local studies on the clustering of the risk factors of CKD among FDRs of CKD patients are needed.

Limitations Of Study

The study was a hospital-based study done in a semi-urban city in South-eastern Nigeria and so the findings may not reflect the true prevalence of the risk factors of CKD among the FDRs of patients with CKD in the general population, especially in the rural settings.

Ethical Clearance

Ethical approval for this study was obtained from the Ethics Committee of NAUTH, Nnewi before the commencement of the study.

Competing Interests

Authors have declared that no competing interest exist.

Authors Contributions

1. Ozuemba BC – conception, design of the research and manuscript writing.
2. Ezeude CM – literature review, manuscript writing, editing and review.
3. Odenigbo CU – final approval of manuscript and general supervision.
4. Ijoma C – critical revision of manuscript and approval.

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