Original Article

Gender Differences in Chronic Kidney Disease. Findings from a Two Center Study in Nigeria

Peter Kehinde Uduagbamen[1,2]*, Abdallah Olukayode AdebolaYusuf[3], Sule Ilegieuno Ahmed[4], Mary Umoh Thompson[3], Boladale Ajani Alalade[5], Marion Itohan Ogunmola[1], Tolulope Esther Falana[1], Olutomiwa Ayoola Omokore[1], Chibuike Christian Emmanuel[1]

[1]Division of Nephrology and Hypertension, Department of Internal Medicine, Ben Carson (Snr) School of Medicine, Babcock University/Babcock University Teaching Hospital, Ilishan-Remo, Nigeria. [2]Nephrology Unit, Department of Internal Medicine, Federal Medical Centre, Abeokuta, Nigeria. [3]Division of Radiodiagnosis, Department of Surgery, Ben Carson (Snr) School of Medicine, Babcock University/Babcock University Teaching Hospital, Ilishan-Remo, Nigeria. [4]Orthopedic and Trauma Unit, Department of Surgery, Asokoro District Hospital, HMB, FCT, Abuja, Nigeria. [5]Endocrine, Diabetes and Metabolism Unit, Department of Internal Medicine, Federal Medical Centre, Abeokuta, Nigeria.

Abstract

Gender differences have been known to exist both in physiologic and pathological states including kidney disease. There is a need to be well acquitted with these differences to enhance preventive and curative strategies for kidney diseases. One hundred and forty-four participants with chronic kidney disease, stage 3 to non-dialytic 5 had urine, blood, and radiological investigations to assess albuminuria, kidney function, and sizes. The findings were compared on a gender basis. Eighty-two males and 62 females participated. The mean age of the males and females were 47.9 ± 16.8 years and 50.5 ± 14.73 years respectively. A greater proportion of participants 65 years and older were females. Chronic interstitial nephritis was more common in females while chronic glomerulonephritis was more common in males. Hyponatremia, metabolic acidosis, and hyperphosphatemia were more common in females. Men used vitamin D analogs and erythropoietin more than women while women used sodium bicarbonate and phosphate binders more than men. Aging (OR-3.28, CI-2.69-387), hyponatremia (OR-4.74, CI-2.10-6.33), hypoalbuminemia ((OR-4.56, CI-3.45-7.49)), and metabolic acidosis (OR-4.14, CI-1.46-4.92) were independently associated with the female gender. Gender differences exist in the risk profile, epidemiology, laboratory findings, and response to treatment of CKD sufferers. Women had more hyponatremia and hyperphosphatemia while men had higher albumin and kidney sizes. Gender partitioned median range cut-offs of some variables would be needed for effective prevention, treatment, and follow-up of CKD sufferers.

Keywords: Gender differences, Chronic kidney disease, Hyponatremia, Metabolic acidosis, Phosphate binders, Erythropoietin

Introduction

Many diseases including chronic kidney disease (CKD) exhibit gender differences in risk profile, pathophysiologic mechanisms, symptomatology, and response to treatment [1]. During the reproductive years, estrogens mediate prostaglandin-induced vasodilatation, higher serum potassium, suppressed renin-angiotensin-aldosterone system (RAAS), and sympathetic activity in females [2, 3] while testosterone is toxic to the renal tubules [3]. In the first post-menopausal decade, there is equilibration between the risk of and protection from CKD in both genders. Thereafter, the cardiovascular risk associated with CKD is higher in females than males [1-4].

During acute inflammatory states, women mount greater responses than men, and in the process, suffer greater tissue injuries but recover better compared to men [5, 6]. In chronic inflammatory conditions, females mount lesser responses, comparably suffering mild cellular destruction but with poorer recovery, except, in connective tissue diseases [5]. Chronic kidney disease is commonly associated with cardiovascular disease, acid-base imbalance, extracellular volume (ECV) expansion, proteinuria, dyslipidemia, anemia, increased morbidity, and mortality. The prevalence of CKD in the United States is higher in females while the incidence of end-stage kidney disease (ESKD) is higher in males [1].

Worldwide, females are less likely to seek medical treatment for illnesses, a bias that is heightened in low-income nations

Address for correspondence: Peter Kehinde Uduagbamen, Division of Nephrology and Hypertension, Department of Internal Medicine, Ben Carson (Snr) School of Medicine, Babcock University/Babcock University Teaching Hospital, Ilishan-Remo, Nigeria.
petr.uduagbamen@gmail.com

How to cite this article: Uduagbamen PK, AdebolaYusuf AO, Ahmed SI, Thompson MU, Alalade BA, Ogunmola MI, et al. Gender Differences in Chronic Kidney Disease. Findings from a Two Center Study in Nigeria. Arch Pharm Pract. 2022;13(2):69-77. https://doi.org/10.51847/EOLTIdNXtq

(LINs) particularly in sub-Saharan Africa, occasioned by socioeconomic differences, ethnic, and cultural practices. These cultural imbalances favor men's higher educational attainment, better employment opportunities, and capability to fund treatment during illnesses [7-9]. Women are known to commence maintenance hemodialysis (MHD) later than men, and the mortality rate in CKD is reported to be higher in them [6]. Women possess greater sodium chloride co-transporters (NCC) receptor activity that could impact the treatment outcome in CKD significantly [10, 11].

Renal function decline with aging and gender differences in CKD progression rate could also depend on body weight with obesity, known to impact positively during kidney functional decline, reported to be more common in women with CKD [12]. Thiazides, commonly used in controlling the blood pressure and the expanded ECV, exert greater diuresis in females from differential NCC activity [9]. Gender differences in the cut-off values of markers of kidney dysfunction don't commonly have universal application, hence, males' serum levels of creatinine, potassium, and anion gap in CKD could be deleterious for females, as saturation percent (SPO_2), serum bicarbonate concentration (SBC), hematocrit (HCT) and albumin that are adequate for females may increase CKD progression rate in males [13].

Much literature on gender differences in CKD is available in developed nations but in LINs, even with greater socioeconomic and cultural differences, literature is scarce. We studied the risk profile, epidemiologic, clinical, radiological, and laboratory findings, and response to drug treatment in CKD cohorts in Nigeria, and explore gender differences.

Materials and Methods

This was a hospital-based comparative study conducted at the Nephrology and hypertension clinics of Babcock University Teaching Hospital, Ilishan-Remo, Nigeria, from August 2019 to July 2021. Eighty-two males and sixty-two females who were receiving treatment at Babcock University Teaching Hospital, Ilishan-Remo, met the kidney disease outcome quality initiative (KDOQI) 2012 diagnostic criteria [14], were 16 years or older, gave informed consent, and were studied. Participants with infections, kidney transplants, liver disease, and malignancy were excluded. Participants' data were taken from an interviewer-administered questionnaire, history, physical examination, laboratory results, and the participants' case files, from where, their age, gender, family history, and the etiology, type, and duration of CKD were retrieved

The height (meters) and weight (kilogram) were measured according to standardized protocols and the body mass index (BMI) was calculated in kg/m^2. The blood pressure was taken at rest with the participants' back and arms rested on support. Two on-the-spot urine samples were taken for a dip strip urinalysis to determine specific gravity (SG), pH, and proteinuria, and a Micra Albustic test to determine urine albumin creatinine ratio (UACR). The Micra strip was taken from its container (immediately closed) and the paddy strip end was completely immersed in the urine covering the full length of the pads for 50 seconds. Removal of the strip was done by rolling it against the edge of the universal bottle to remove any excess urine. The strip pad color was matched against the "strip pad color" inscribed on the strip container and the results were documented. The combi 10 dip strip was taken from the container and the end containing the pad was immersed into the urine to cover the strip pad and removed after 60 seconds by rolling it against the edge of the universal bottle to remove excess urine. The result based on the matching color was documented.

Blood was taken from a peripheral vein into a Lithium heparin bottle to determine the serum electrolytes, urea, creatinine, and uric acid using an autoanalyzer (Roche Diagnostics GmbH, Mannheim Germany). The Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula [15] was used to calculate the creatinine-based glomerular filtration rate (GFR). About 1-2 mL of blood was taken into a micropipette for determination of the hematocrit using a hematocrit centrifuge.

Data was analyzed using SSPS 22. Continuous variables, as mean with standard deviation, were compared using paired student's t-test while categorical variables, as proportions and frequencies, were compared using Chi-square or fisher's exact test, P-value <0.05 was considered statistically significant. Variables with $P < 0.025$ from the univariate model were entered as adjustment variables in multivariate analyses to determine independent associates of the female gender [16].

This study was approved by the Babcock University Human Research Ethics Committee (NHREC/24/01/2018 and BUHREC501/19).

Definitions

In this study, we did not use kidney biopsy in classifying CKD by etiology.

Hypertension-Associated CKD (HACKD): kidney disease arising from long-standing hypertension, prevalent in the elderly and late middle age.

Chronic Glomerulonephritis: kidney disease that leads to hypertension, common in the young and early middle age with or without a preceding history of pharyngitis or skin sepsis

Chronic Interstitial Nephritis: kidney disease arising from significant exposure to exogenous nephrotoxins after ruling out other risk factors/causes of CKD.

Hypertension: BP $\geq$140/90 mmHg [17].

Diabetes: Fasting blood sugar ≥126mg/dL or diagnosis or use of antidiabetic drugs [18].

Proteinuria: dip strip protein ≥1+ [19].

Microalbuminuria: Urine albumin creatinine ratio >30mg/g (3.4mg/mmoL) [20].

Anemia: Hematocrit <39% [21].

Hypoalbuminemia: Serum albumin <35mg/dL [22].

Hyperuricemia: Males >0.42mmol/L, Females >0.36mmol/L [23].

Results and Discussion

A total of 144 (82 males and 62 females) participants were studied. The mean ages of the population, males, and females were 48.8 ± 15.9 years, 47.9 ± 16.8 years, and 50.5 ± 14.73 years respectively. Seven percent of males but 11.1% of females were ≥60 years, P=0.003. The mean BMI of males and females was 26.6 ± 4.3 kg/m^2 and 26.5 ± 4.8 kg/m^2 respectively, P=0.8. The BMI, systolic and diastolic BP **(Table 1)** were higher in males than females, P=0.04, P=0.001, and P=0.002 respectively.

Table 1. Sociodemographic, and clinical characteristics of participants

Variables	All participants	Males	Females	P-value
	N=144 (%)	N=82 (%)	N=62 (%)	
Age, years				
16-39	31 (21.5)	20 (24.4)	11 (17.7)	
40-64	94 (65.3)	56 (68.3)	38 (61.3)	0.002
≥65	19 (13.2)	6 (7.3)	13 (21.0)	
BMI, kg/m^2				
<25.0	58 (40.3)	31 (37.8)	27 (43.6)	0.04
≥25.0	86 (59.7)	51 (62.2)	35 (56.4)	
Systolic BP, mmHg				
<140	89 (61.8)	45 (54.9)	44 (71.0)	0.001
≥140	55 (38.2)	37 (45.1)	18 (29.0)	
Diastolic BP, mmHg				
<90	106 (73.6)	56(68.3)	50 (80.8)	0.002
≥90	38 (26.4)	26 (31.7)	12 (19.2)	

BMI-body mass index, SBP-systolic blood pressure, DBP-diastolic blood pressure

A greater proportion of the cohorts had HACKD (44.4%), jointly followed by CGN (19.4%) and CIN (19.4%) **(Table 2)**, 6.9% had obstructive uropathy and 9.7% had other causes. The proportion of men with CGN was higher than females while the proportion of women with CIN was higher than men.

Table 2. Etiology of Chronic kidney disease in cohorts

Variables	All cohorts	Frequency (%)		P-value
		Males	Females	
	N=144 (%)	N=82 (%)	N=62 (%)	
Chronic glomerulonephritis	28 (19.4)	17 (20.7)	11 (17.7)	
Hypertension	64 (44.5)	36 (43.9)	28 (45.2)	
Chronic tubulointerstitial nephritis	28 (19.4)	13 (15.9)	15 (24.2)	0.03
Obstructive uropathy	10 (7.0)	7 (8.5)	3 (4.8)	
Others	14 (9.7)	9 (11.0)	5 (8.1)	

The proportion of men that took RAAS inhibitors, erythropoietin, and vitamin D analogs was higher than females, P<0.001, P=0.02, and P=0.003 respectively **(Table 3)**. The proportion of women that took calcium channel blockers (CCBs), sodium bicarbonate, and phosphate binders were higher than men, P=0.001, P=0.001, and P<0.001 respectively.

Table 3. Drug history of participants

Variables	All participants N=144 (%)	Males N=82 (%)	Females N=62 (%)	P-value
Diuretics				
Yes	126 (87.5)	72 (87.8)	54 (87.1)	0.8
No	18 (12.5)	10 (12.2)	8 (12.9)	
Calcium channel blockers				
Yes	134 (93.0)	74 (90.2)	60 (96.8)	0.001
No	10 (7.0)	8 (19.8)	2 (3.2)	
RAASIs (ACEIs/ARBs)				
Yes	88 (61.1)	57 (69.5)	31 (50.0)	<0.001
No	56 (38.9)	25 (30.5)	31 (50.0)	
Other antihypertensives				
Yes	68 (47.2)	37 (45.1)	31 (50.0)	0.04
No	76 (52.8)	45 (54.9)	31 (50.0)	
Erythropoietin				
Yes	22 (15.3)	14 (17.1)	8 (12.9)	0.02
No	122 (84.7)	68 (82.9)	54 (87.1)	
Vitamin D analogs				
Yes	90 (63.5)	53 (64.6)	37 (59.7)	0.003
No	54 (36.5)	29 (35.4)	25 (40.3)	
Sodium Bicarbonate				
Yes	64 (44.4)	32 (39.0)	32 (51.6)	0.001
No	80 (55.6)	50 (61.0)	30 (48.4)	
Phosphate binders				
Yes	93 (64.6)	48 (58.5)	45 (72.6)	<0.001
No	51 (35.4)	34 (41.5)	17 (27.4)	
Intravenous Iron				
Yes	20 (13.9)	12 (14.6)	8 (12.9)	0.05
No	124 (86.1)	70 (85.4)	54 (87.1)	

RAASIs-renin-angiotensin aldosterone system inhibitors, ACEIs-angiotensin-converting enzymes inhibitors, ARBs-angiotensin receptors blockers

As CKD worsened down the stages, the percentage of affected women increased **(Table 4)**. The mean age, BMI, systolic and diastolic BP were 48.8 ± 15.9 years, 26.53 ± 4.51 kg/m^2, 146.8 ± 10.2 mmHg, and 93.7 mmHg respectively. The mean serum sodium, potassium, bicarbonate, and anion gap of the cohorts were 136.7mmol/L, 4.1mmol/L, 21.2mmol/L, and 15.7mEq respectively. The mean creatinine, GFR hematocrit, and serum albumin were 179.1 ± 14.2 umol/L, 37.2 ± 7.4 ml/min, 32.7 ± 4.4%, and 44.1 ± 8.6 g/dL respectively.

Table 4. Relationship between kidney function and participants' characteristics

Variables	Stage 3a N=33 (%) Mean ± SD	Stage 3b N=42 (%) Mean ± SD	Stage 4 N=47 (%) Mean ± SD	ND Stage 5 N=22 (%) Mean ± SD	P-value
Sex					
Males	21 (63.6)	25 (59.5)	27 (54.4)	9 (40.9)	0.03
Females	12 (36.4)	17 (40.5)	20 (45.6)	13 (59.1)	

Age, years (mean)	46.6 ± 5.5	47.8 ± 6.7	49.7 ± 8.9	52.1 ± 14.8.6	<0.001
BMI, kg/m^2	25.7 ± 3.6	26.5 ± 5.4	26.8 ± 4.3	26.8 ± 7.7	0.06
Systolic BP mmHg	142.4 ± 8.6	142.9 ± 5.5	147.4 ± 8.2	151.5 ± 9.3	0.01
Diastolic BP, mmHg	93.1 ± 7.1	93.7 ± 3.8	92.6 ± 6.7	96.4 ± 9.1	0.05
Sodium, mmol/L	139.2 ± 12.8	138.7 ± 7.4	136.9 ± 10.8	130.6 ± 11.4	0.001
Potassium, mmol/L	3.5 ± 2.1	3.7 ± 2.8	4.2 ± 2.6	4.8 ± 2.9	0.02
Bicarbonate, mmol/L	22.2 ± 4.3	21.8 ± 5.3	20.8 ± 4.2	19.3 ± 5.4	0.04
Anion gap, mEq	14.2 ± 7.8	15.6 ± 5.7	16.1 ± 6.2	17.2 ± 8.6	0.04
Creatinine, umol/L	110.6 ± 9.4	167.2 ± 6.4	209.2 ± 6.6	268.7 ± 11.5	<0.001
eGFR, (mean)	56.2 ± 6.8	44.6 ± 8.0	28.1 ± 7.3	13.8 ± 3.3	<0.001
Hematocrit, (mean)	38.6 ± 5.5	34.0 ± 6.4	30.6 ± 3.8	25.7 ± 3.3	<0.001
Albumin, (mean)	49.5 ± 8.2	46.8 ±5.7	41.2 ± 5.5	36.4 ± 4.9	<0.001

BMI-body mass index, BP-blood pressure, eGFR-estimated glomerular filtration rate

The men, compared with women, were more likely to use erythropoietin and be hypertensive, P=0.04 and P=0.03 respectively **(Table 5)**. Hyponatremia, MA elevated AG and microalbuminuria were more common in women than in men, P=0.001, P<0.001, 0.004, and 0.04 respectively. The cortical thickness and kidney volumes were lower in women than men, P=0.02 and P=0.03 respectively.

Table 5. Relationship between gender and participants' characteristics

Variables	Males N=82 (%)	Females N=62 (%)	OR	95% CI	P-value
Age, yrs					
<65	76 (60.8)	49 (39.2)	3.66	1.97-4.53	0.002
≥65	6 (31.6)	13 (68.4)			
Etiologic factors					
Chronic TIN	14 (50.0)	14 (50.0)	2.97	2.04-4.13	0.03
Others	68 (58.9)	48 (41.1)			
Erythropoietin					
Yes	12 (63.2)	7 (36.8)	2.44	1.32-2.87	0.04
No	70 (56.0)	55 (44.0)			
BMI, kg/m^2					
<25.0	31 (53.4)	27 (46.6)	1.78	0.98-1.99	0.05
≥25.0	51 (59.3)	35 (40.7)			
Systolic BP, mmHg					
<140	45 (50.6)	44 (49.4)	2.16	2.74-3.77	0.04
≥140	37 (67.3)	18 (32.7)			
Diastolic BP, mmHg					
<90	56 (52.8)	50 (47.2)	2.32	2.90-4.96	0.03
≥90	26 (68.4)	12 (31.6)			
Serum sodium, mmol/L					
<135	21 (42.0)	29 (58.0)	3.96	2.44-5.54	0.001
≥135	61 (64.9)	33 (35.1)			
Potassium, mmol/L					
<5.5	76 (56.7)	58 (43.3)	1.22	1.02-1.87	0.07
≥5.5	6 (60.0)	4 (40.0)			
Bicarbonate, mmol/L					

<22	23 (44.2)	29 (55.8)	4.08	1.76-5.11	<0.001
≥22	59 (64.1)	33 (35.9)			
Calcium x phosphate, mmol^2/L^2					
<3.4	73 (56.6)	56 (43.4)	1.33	0.95-2.67	0.06
≥3.4	9 (60.0)	6 (40.0)			
Creatinine, umol/L					
M<132; F<106	42 (67.7)	20 (32.3)	3.52	2.20-4.25	0.002
M≥132; F≥106	40 (47.5)	42 (52.5)			
eGFR, ml/min					
<30	37 (49.3)	38 (50.7)	3.77	3.09-6.15	0.001
≥30	45 (65.2)	24 (34.2)			
Anion gap, mEq					
<16	68 (58.6)	48 (41.4)	3.14	2.64-4.79	0.004
≥16	14 (50.0)	14 (50.0)			
Hematocrit, %					
<39	29 (50.9)	28 (49.1)	2.94	1.38-3.95	0.003
≥39	53 (60.9)	34 (39.1)			
Serum albumin, mg/dL					
<35	6 (42.9)	8 (57.1)	5.13	3.58-7.03	<0.001
≥35	56 (50.9)	54 (49.1)			
Urine ACR, mg/mmol					
<3.4	73 (56.6)	56 (43.4)	2.07	1.88-3.62	0.04
≥3.4	11 (45.8)	13 (54.2)			
Kidney cortical thickness, mm					
<7	35 (53.0)	31 (47.0)	2.89	1.28-3.91	0.02
≥7	47 (60.3)	31 (39.7)			
Kidney volume, cm^3					
<50	20 (41.7)	28 (58.3)	2.59	2.48-5.09	0.03
≥50	62 (64.6)	34 (35.4)			

OR-odds ratio, TIN-tubulointerstitial nephritis, BMI-body mass index BP-blood pressure, eGFR-estimated glomerular filtration rate, ACR-albumin creatinine ratio

From the multivariate model, aging (OR-3.28, CI-2.69-387), hyponatremia (OR-4.74, CI-2.10-6.33), MA (OR-4.14, CI-1.46-4.92 **(Table 6)**, elevated creatinine (OR-3.06, CI-2.83-3.99), low eGFR (R-O4.82, CI2.68-4.95) and hypoalbuminemia (OR-4.56, CI-3.45-7.49) were independently associated with the female gender.

Table 6. Multivariate regression analysis showing independent associates of female gender

Variable	aOR	95% CI	P-value
Advancing age	3.28	2.69-387	0.03
Hyponatremia	4.74	2.10-6.33	<0.001
Metabolic acidosis	4.14	1.46-4.92	0.001
Creatinine`	3.06	2.83-3.99	0.04
eGFR	4.82	2.68-4.95	0.001
Anion gap	1.37	0.63-1.54	0.05
Anemia	0.97	0.77-1.94	0.09
Hypoalbuminemia	4.56	3.45-7.49	<0.001
Kidney cortical thinness	1.12	1.03-1.95	0.07

aOR-adjusted odds ratio, CI-95% confidence interval, eGFR-glomerular filtration rate

There were gender differences in the socioeconomic, laboratory, and radiological characteristics of cohorts as the prevalence of CKD was higher in younger males with higher BMI and blood pressure. The female cohorts had more hyponatremia, metabolic acidosis, hyperphosphatemia, anemia, hypoalbuminemia, higher UACR, and lower kidney sizes. The male preponderance mirrors earlier studies in our setting and some foreign studies [24-26]. The higher prevalence of CKD in males could involve genetic, hormonal, socioeconomic, and clinical factors. An absence of the renal and cardiovascular protective effects of estrogens in men coupled with the anti-apoptotic actions of testosterone in the renal tubules increases the risk of kidney damage in them [2, 3]. Males respond more to sympathetic stimulation than females and, with the use of the RAAS inhibitors to treat hypertension, proteinuria, and CKD, males manifest a lower response to these drugs, particularly after 8 weeks of use [27]. This entails a poorer blood pressure control in males and a faster progression rate from pre-CKD to CKD, and end-stage kidney disease [6, 28-30]. Our finding however disagrees with findings by Ricardo *et al*. who reported higher CKD prevalence in women in the US [1].

The later presentation of females could arise from the mitigating effects of estrogens on kidney function and, socioeconomic, educational, and cultural biases against women [2, 5]. Higher blood pressures in males, with or without metabolic syndrome, could further worsen CKD outcomes in males [31]. However, the fairer biochemical findings in men in this study are supportive of studies that found the leveling of the cardiovascular risk between men and women in the first post-menopausal decade, before the reported relative increase in female CVS risk profile afterward [4, 32, 33].

We found CIN to be more common in females mirroring studies that reported a higher incidence of kidney dysfunction from the use of non-steroidal anti-inflammatory drugs (NSAIDs) and other nephrotoxins, particularly weight-losing herbal remedies, in females [34-36] Likewise, the higher prevalence of CGN in young men is in agreement with previous studies in Nigeria and many LINs that reported a relatively large proportion of CGN among its CKD population, mostly from infective causes [36, 37]

The higher incidence of hyponatremia in women is in agreement with earlier studies that found hyponatremia and its related complication of central pontine myelinolysis to be more common in women [38]. Diuretics particularly thiazides are commonly used in treating hypertension and CKD. The higher quantity and affinity of sodium chloride co-transporters (NCC) receptors in women, therefore, entailing greater response to thiazide in females than in males, increasing their risk of hyponatremia [39]. The higher incidence of hyperphosphatemia in females mirrors findings by Deepak *et al*. [40] who found an inverse relationship between the body weight and serum phosphate levels, but is not in agreement with findings by Barreto *et al*. [41]. In our clime, men are involved more in higher meat and alcohol intake, as well as other risk factors for hyperphosphatemia [7]. Estrogens stimulate the reabsorption of phosphate in the proximal and distal renal tubules through the activities of the brush border sodium-potassium ATPase-dependent sodium phosphorus co-transporter (NPT) [42]. This also agrees with suggestions that hyperphosphatemia is more commonly from reduced excretion than from excessive intake.

The higher incidence of MA and elevated anion gap in female cohorts are in agreement with findings by Veiras *et al*. [43] who reported that the phosphorylation of the sodium-potassium exchanger isoform 3 (*NHE3*) in the proximal tubules is heightened in females, resulting in reduced bicarbonate absorption, relative hypobicarbonatemia and elevated anion gap in females. We found a higher prevalence of anemia among female cohorts similar to earlier findings. A large proportion of the females in our study were postmenopausal. Except with proteinuria and some other conditions, women within the active reproductive years are not routinely prescribed long-term RAAS inhibitors (inhibitors of erythropoiesis) in our clime [7], one would have expected a corresponding match-up between the hematocrit of males and females. However, the pro erythropoietic actions of androgen coupled with the fact that the women had more severe renal disease could have accounted for the lower hematocrit in them.

Females had worse hypoalbuminemia compared with men. Serum albumin, apart from being an inflammatory marker, its levels in the blood are dependent on positioning, hence all cohorts had their samples taken in the sitting position [22]. The stimulatory effect of hypoalbuminemia on the antidiuretic hormone (ADH) could lead to poor salt water retention that could be complicated by hyponatremia and hemodilution-induced anemia, features that were present among the female cohorts.

The higher volume of albuminuria in the female cohorts is similar to findings by Ahmad *et al*. [44] but disagrees with Park *et al*. [45] who found higher urine ACR in males. We infer that the greater deterioration in kidney function in females, coupled with lesser use of antiproteinuric agents, particularly the RAAS inhibitors in them, accounted for their heavier albuminuria. The renal sizes (cortical thickness and kidney volume) were less in females as previously reported. The reductions in renal sizes in the female cohorts, apart from being secondary to the more severe disease in females, could also be associated with genetically determined smaller kidneys in females [27].

The cross-sectional design of the study impeded us from confirming the chronicity of the disease. Other limitations included incomplete data on lipid profile, hence, was not analyzed. We didn't assess CKD-BMD and the parathyroid hormone in cohorts. The study is strengthened by its involvement of a sizeable proportion of cohorts who had CIN from the use of exogenous substances like weight loss remedies and non-steroidal anti-inflammatory drugs (NSAIDs), a rising trend in our clime, and which may alter the demographics of CKD in the nearest future.

Conclusion

Gender differences exist in the risk profile, epidemiology, symptomatology, and response to the treatment of CKD. The prevalence of CKD was higher in younger males, the majority of cohorts above 60 years were females. HACKD was the commonest cause of CKD, chronic glomerulonephritis was more common in males while CIN was more common in females. Hyponatremia, MA, elevated UACR and hyperphosphatemia were more common in females while hematocrit, albumin, and kidney sizes were higher in men. The use of RAAS inhibitors, erythropoietin, and vitamin D analogs was more common among the men while the use of CCBs, sodium bicarbonate and phosphate binders were more common in females. Advancing age, hyponatremia, MA, and hypoalbuminemia were independently associated with the female gender. Gender partitioned median range cut-offs of some variables would be needed for effective prevention, treatment, and follow-up of sufferers of CKD.

ACKNOWLEDGMENTS: We appreciate the support of the nurses and supporting staff of the Nephrology and Hypertension clinic of Babcock University Teaching Hospital, Ilishan-Remo, Nigeria.

CONFLICT OF INTEREST: None

FINANCIAL SUPPORT: None

ETHICS STATEMENT: This study was approved by the Babcock University Human Research Ethics Committee (NHREC/24/01/2018 and BUHREC501/19).

References

1. Ricardo AC, Yang W, Sha D, Appel LJ, Chen J, Krousel-Wood M, et al. Sex-Related Disparities in CKD Progression. J Am Soc Nephrol. 2019;30(1):137-46.
2. Nitsch D. Is there a difference in metabolic burden between men and women?. Nephrol Dial Trans. 2014;29(6):1110-2.
3. Oliva MM, Gambioli R, Forte G, Porcaro G, Aragona C, Unfer V. Unopposed estrogens: current and future perspectives. Eur Rev Med Pharmacol Sci 2022;26(8):2975-89. doi:10.26355/eurrev_202204_28629
4. Verzola D, Gandolfo MT, Salvatore F, Villaggio B, Gianiorio F, Traverso P, et al. Testosterone promotes apoptotic damage in human renal tubular cells. Kidney Int. 2004;65(4):1252-61. doi:10.1111/j.1523-1755.2004.00497.x
5. Casimir GJ, Lefèvre N, Corazza F, Duchateau J, Chamekh M. The acid–base balance and gender in Inflammation: a mini-review. Front Immunol. 2018;9:475. doi:10.3389/fimmu.2018.00475
6. Gao Z, Wang Z, Zhu H, Yuan X, Sun M, Wang J, et al. Hyperinsulinemia contributes to impaired-glucose-tolerance-induced renal injury via mir-7977/SIRT3 signaling. Ther Adv Chronic Dis. 2020;11:2040622320916008. doi:10.1177/204062232091600
7. Uduagbamen PK, Ogunkoya JO, Alalade BA, Oyelese AT, Nwogbe IC, Eigbe SO, et al. Chronic Kidney Disease: Socioeconomic Impact. Findings from a Two Center Study in Southwestern Nigeria. IJHSR. 2021;11(10):336-47.
8. Jafar TH, Schmid CH, Stark PC, Toto R, Remuzzi G, Ruggenenti P, et al. The rate of progression of renal disease may not be slower in women compared with men: a patient-level meta-analysis. Nephrol Dialy Transplant. 2003;18(10):2047-53.
9. Li J, Hatano R, Xu S, Wan L, Yang L, Weinstein AM, et al. Gender difference in kidney electrolyte transport. I. Role of AT1a receptor in thiazide-sensitive Na+-Cl− cotransporter activity and expression in male and female mice. Am J Physiol-Renal Physiol. 2017;313(2):F505-13. doi:10.1152/ajprenal.00087.2017
10. Yang CH, Moi SH, Chuang LY, Chen JB. Higher-order clinical risk factor interaction analysis for overall mortality in maintenance hemodialysis patients. Ther Adv Chronic Dis. 2020;11:2040622320949060. doi:10.1177/2040622320949060
11. Graziani M, Nisticò R. Gender differences in pharmacokinetics and pharmacodynamics of methadone substitution therapy. Front Pharmacol. 2015;6:122. doi:10.3389/fphar.2015.00122
12. Raphael KL, Murphy RA, Shlipak MG, Satterfield S, Huston HK, Sebastian A, et al. Bicarbonate Concentration, Acid-Base Status, and Mortality in the Health, Aging, and Body Composition Study. Clin J Am Soc Nephrol. 2016;11(2):308-16.
13. Hansen SI, Petersen PH, Lund F, Fraser CG, Sölétormos G. Gender-partitioned patient medians of serum albumin requested by general practitioners for the assessment of analytical stability. Clin Chem Lab Med. 2018;56(5):843-50. doi:10.1515/cclm-2017-0771
14. National Kidney Foundation. KDOQI Clinical Practice Guideline for Diabetes and CKD: 2012 update. Am J Kidney Dis. 2012;60(5):850-86.
15. Levey AS, Stevens LA, Schmid CH, Zhang Y, Castro III AF, Feldman HI, et al. A new equation to estimate glomerular filtration rate. Ann Intern Med. 2009;150(9):604-12. doi:10.7326/0003-4819-150-9-200905050-00006
16. Hosmer DW, Lameshow S. Applied Logistic Regression. 2nd ed. Wiley: New York N.Y.; 2000. p. 95.
17. Hermida RC, Ayala DE, Fernandez JR, Mojon A, Smolensky MH. Hypertension: New perspective on its definition and clinical management by bedtime therapy substantially reduces cardiovascular disease risk. Eur J Clin Investig. 2018;48(5):e12909. doi:10.1111/eci.12909
18. Kharroubi AT, Darwish HM. Diabetes mellitus: The epidemic of the century. World J Diabetes. 2015;6(6):850-67. doi:10.4239/wjd.v6.i6.850
19. Lamb, EJ, MacKenzie F, Stevens PE. How should proteinuria be detected and measured?. Ann Clin Biochem. 2009;46(3):205-17. doi:10.1258/acb.2009.009007.
20. Medina-Rosas J, Gladman DD, Su J, Sabapathy A, Urowitz MB, Touma Z. Utility of untimed single urine protein/creatinine ratio as a substitute for 24-h proteinuria for assessment of proteinuria in systemic lupus erythematosus. Arthritis Res Ther. 2015;17(1):1-9.
21. Cappellini MD, Motta I. Anemia in clinical practice—definition and classification: does hemoglobin change with aging?. InSeminars in hematology 2015 Oct 1 (Vol. 52, No. 4, pp. 261-269). WB Saunders. doi:10.1053/j.seminhematol.2015.07.006
22. Weaving G, Batstone GF, Jones RG. Age and sex variation in serum albumin concentration: an observational study. Ann Clin Biochem. 2016;53(1):106-11. doi:10.1177/0004563215593561
23. Tsai CW, Lin SY, Kuo CC, Huang CC. Serum uric acid and progression of kidney disease: a longitudinal analysis and mini-review. PloS one. 2017;12(1):e0170393.
24. Unuigbe E. Funding renal care in Nigeria: a critical appraisal. Trop J Nephrol. 2006;1(1):33-8.
25. Arogundade FA, Barsoum RS. CKD prevention in Sub-Saharan Africa: a call for governmental, nongovernmental, and community support. Am J Kidney Dis. 2008;51(3):515-23.
26. Ponte B, Pruijm M, Marques-Vidal P, Martin PY, Burnier M, Paccaud F, et al. Determinants and burden of chronic kidney disease in the

population-based CoLaus study: a cross-sectional analysis. Nephrol Dial Transplant. 2013;28(9):2329-39. doi:10.1093/ndt/gft206.
27. Miller JA, Cherney DZ, Duncan JA, Lai V, Burns KD, Kennedy CR, et al. Gender differences in the renal response to renin-angiotensin system blockade. J Am Soc Nephrol. 2006;17(9):2554-60. doi:10.1681/ASN.2005101095
28. Kaze AD, Ilori T, Jaar BG, Echouffo-Tcheugui JB. Burden of chronic kidney disease on the African continent: a systematic review and meta-analysis. BMC Nephrol. 2018;19(1):1-1. doi:10.1186/s12882-018-0930-5
29. Farron MR, Kabeto MU, Levine DA, Wixom CR, Langa KM. Blood pressure and cognitive function among older adults in India. J Int Med Res. 2022;50(1):03000605211068720.
30. Ulasi I. Gender bias in access to healthcare in Nigeria: a study of end-stage renal disease. Trop Doct. 2008;38(1):50-2.
31. Sarfo FS, Mobula LM, Burnham G, Ansong D, Plange-Rhule J, Sarfo-Kantanka O, et al. Factors associated with uncontrolled blood pressure among Ghanaians: evidence from a multicenter hospital-based study. PloS one. 2018;13(3):e0193494.
32. Iseki F. Gender differences in CKD. Kidney Int. 2008;74(4):415-7. doi:10.1038/ki2008.261
33. Wu Y, Huang B, Zhang W, Farhan KAA, Ge S, Wang M, et al. The interaction analysis between advanced age and longer dialysis vintage on the survival of patients receiving maintenance hemodialysis. J Int Med Res. 2020;50(4):1-12. doi:10.1177/03000605221088557
34. Uduagbamen PK, Salako BL, Hamzat MA, Kadiri S, Arogundade FA. Kidney Function in Frequent Users of Non-steroidal anti-inflammatory Drugs (NSAIDs). Open J Int Med. 2020;10(1):69-82.
35. Ezzat M, Abd Razik B. Molecular Drug Design and Docking Study of Novel N-substituted Celecoxib Derivatives as Selective Cyclooxygenase-2 Inhibitors. Acta Pharm Sci. 2020;58(4). doi:10.23893/1307-2080.APS.05823
36. Akpan EE, Ekrikpo UE. Acute renal failure induced by Chinese herbal medication in Nigeria. Case Rep Med. 2015;2015. doi:10.1155/2015/150204
37. Okaka EI, Okwuonu CG. Blood pressure variation and its correlates among patients undergoing hemodialysis for renal failure in Benin City, Nigeria. Ann Afr Med. 2017;16(2):65-9.
38. Alemu H, Hailu W, Adane A. Prevalence of chronic kidney disease and associated factors among patients with diabetes in northwest Ethiopia: a hospital-based cross-sectional study. Curr Ther Res. 2020;92:100578.
39. Tseng CK, Lin CH, Hsu HS, Ho CT, Huang HY, Liu CS, et al. In addition to malnutrition and renal function impairment, anemia is associated with hyponatremia in the elderly. Arch Gerontol Geriatr. 2012;55(1):77-81.
40. Deepak P, Ehrenpreis ED. Lower body weight and female gender: Hyperphosphatemia risk factors after sodium phosphate preparations. World J Gastroenterol. 2011;17(21):2681-2. doi:10.3748/wjg.v17.i21.2681
41. Barreto FC, Barreto DV, Massy ZA, Drüeke TB. Strategies for phosphate control in patients with CKD. Kidney Int Rep. 2019;4(8):1043-56.
42. Onufrak SJ, Bellasi A, Cardarelli F, Vaccarino V, Muntner P, Shaw LJ, et al. Investigation of gender heterogeneity in the associations of serum phosphorus with incident coronary artery disease and all-cause mortality. Am J Epidemiol. 2009;169(1):67-77. doi:10.1093/aje/kwn285
43. Veiras LC, Girardi AC, Curry J, Pei L, Ralph DL, Tran A, et al. Sexual dimorphic pattern of renal transporters and electrolyte homeostasis. J Am Soc Nephrol. 2017;28(12):3504-17. doi:10.1681/ASN.2017030295
44. Ahmed S, Ahmad SA. Gender difference and relationship of insulin resistance with microalbuminuria type-2 diabetes. J Coll Physicians Surg Pak. 2010;20(1):26-32.
45. Park JB, Kim SA, Sung KC, Kim JY. Gender-specific differences in the incidence of microalbuminuria in metabolic syndrome patients after treatment with fimasartan: The K-MetS study. Plos one. 2017;12(12):e0189342.