Society of Medical Education & Research

2022, Volume 2, Page No: 57-67

International Journal of Social and Psychological Aspects of Healthcare

Gender-Based Disparities in Chronic Kidney Disease: Insights from a Dual-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.

***E-mail** ✉ petr.uduagbamen@gmail.com

Abstract

There are well-documented gender differences in both the physiological and pathological aspects of various health conditions, including kidney disease. These differences must be understood to improve strategies for the prevention and treatment of kidney diseases. In this study, we examined the risk factors, epidemiological trends, clinical and radiological findings, laboratory results, and responses to pharmacological treatment in CKD patients in Nigeria, focusing on gender-based differences. A study was conducted with 144 individuals diagnosed with chronic kidney disease, ranging from stage 3 to non-dialytic stage 5. Participants underwent blood, urine, and radiological tests to assess albuminuria, kidney function, and size. Results were analyzed by gender, with 82 male and 62 female participants. The mean age of males was 47.9 ± 16.8 years, and for females was 50.5 ± 14.73 years. The study showed that a higher proportion of participants aged 65 years and above were females. Chronic interstitial nephritis was more common in women, whereas men were more likely to have chronic glomerulonephritis. Women were also more prone to metabolic acidosis, hyponatremia, and hyperphosphatemia. In contrast, men were more frequently treated with vitamin D analogs and erythropoietin, while women tended to use sodium bicarbonate and phosphate binders more often. Certain factors such as increasing age (OR-3.28, CI-2.69-3.87), 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 more strongly associated with females. Gender differences were evident in the epidemiology, laboratory findings, and response to treatments in patients with chronic kidney disease. Women had higher levels of hyponatremia and hyperphosphatemia, while men showed higher albumin levels and larger kidney sizes. Gender-based median range cut-offs for several clinical parameters would improve prevention, treatment, and follow-up care for individuals with chronic kidney disease.

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

Introduction

There are notable gender-based differences in the risk factors, mechanisms, symptoms, and responses to treatment across various diseases, including chronic kidney disease (CKD) [1]. In women, estrogens contribute to physiological processes like vasodilation through prostaglandins, increased serum potassium, and the suppression of the renin-angiotensin-aldosterone system (RAAS), as well as reduced sympathetic nervous system activity during their reproductive years [2, 3]. Conversely, testosterone has a detrimental effect on renal tubules [3]. Following menopause, the risk of CKD in women becomes more similar to that of men for the first

Access this article online

Website: https://smerpub.com/ **E-ISSN: 3108-4818**

Received: 03June 2022; **Revised:** 14 September 2022; **Accepted:** 16 September 2022

How to cite this article: Uduagbamen PK, AdebolaYusuf AO, Ahmed SI, Thompson MU, Alalade BA, Ogunmola MI, et al. Gender-Based Disparities in Chronic Kidney Disease: Insights from a Dual-Center Study in Nigeria. Int J Soc Psychol Asp Healthc. 2022;2:57-67. https://doi.org/10.51847/V9S94I0APL

decade, after which cardiovascular risks associated with CKD are greater in women than in men [1-4].

Women generally exhibit a stronger inflammatory response than men in acute conditions, leading to greater tissue damage but more effective recovery [5, 6]. In chronic inflammation, however, women's responses are often milder, leading to less cellular damage but slower recovery, except in connective tissue disorders [5]. CKD is commonly accompanied by cardiovascular issues, imbalances in acid-base levels, extracellular fluid expansion, proteinuria, lipid disturbances, anemia, and higher rates of morbidity and mortality. Although CKD is more prevalent in women in the U.S., men have a higher incidence of end-stage kidney disease (ESKD) [1]. Across the globe, women tend to delay seeking medical treatment for illnesses, and this gap is more pronounced in low-income nations (LINs), particularly in sub-Saharan Africa, where cultural practices and socioeconomic disparities contribute to men having better educational opportunities, employment prospects, and the financial ability to afford healthcare [7-9]. Women with CKD often start maintenance hemodialysis (MHD) later than men, with higher mortality rates among women [6].

The greater activity of sodium chloride co-transporters (NCC) in women may impact CKD treatment outcomes significantly [10, 11]. The rate of kidney function decline with age and gender differences in CKD progression can also be influenced by body weight, as obesity, more common in women with CKD, accelerates kidney dysfunction [12]. The use of thiazide diuretics, which are often prescribed for controlling blood pressure and extracellular volume expansion, leads to stronger diuretic effects in women, due to their distinct NCC activity [9].

Gender-specific reference values for kidney function markers are not universally applicable. For instance, the serum levels of creatinine, potassium, and anion gap in males may negatively impact females, while values like saturation percentage (SpO2), serum bicarbonate concentration (SBC), hematocrit (HCT), and albumin, which are normal for women, might lead to faster CKD progression in men [13].

Although extensive research on gender disparities in chronic kidney disease (CKD) exists in developed countries, there is a notable lack of studies in low-income nations (LINs), where socioeconomic and cultural factors may present even greater differences. In this study, we examined the risk factors, epidemiological trends, clinical and radiological findings, laboratory results, and responses to pharmacological treatment in CKD patients in Nigeria, focusing on gender-based differences.

Materials and Methods

This hospital-based comparative study was carried out at the Nephrology and Hypertension Clinics of Babcock University Teaching Hospital in Ilishan-Remo, Nigeria, spanning from August 2019 to July 2021. A total of 82 male and 62 female participants, all meeting the diagnostic criteria for kidney disease set by the Kidney Disease Outcome Quality Initiative (KDOQI) [14], and aged sixteen years or older, were included in the study following informed consent. Individuals with conditions like infections, previous kidney transplants, liver disorders, or malignancies were excluded. Data were gathered through structured questionnaires, medical histories, physical exams, lab results, and the participants' case records, which provided information on their gender, age, and family history, as well as the type, cause, and duration of chronic kidney disease (CKD).

Height (in meters) and weight (in kilograms) were measured according to established protocols, and body mass index (BMI) was calculated. Blood pressure was taken while the participant was seated with their back and arms properly supported. Two urine samples were collected for dipstrip analysis, which tested for specific gravity (SG), proteinuria, and pH. Additionally, the Micra Albustic test was used to evaluate the urine albumin-to-creatinine ratio (UACR). The test strip was immersed in urine for 50 seconds, excess urine was removed by rolling the strip against the bottle's edge, and the results were recorded by matching the color of the strip to a reference chart. A Combi 10 dipstrip was used similarly, and the outcomes were recorded based on the color match.

Peripheral blood samples were drawn into lithium heparin tubes to determine serum electrolytes, creatinine, urea, and uric acid levels using an autoanalyzer (Roche Diagnostics GmbH, Mannheim, Germany). The glomerular filtration rate (GFR) was calculated using the CKD-EPI formula [15]. Hematocrit levels were measured using a hematocrit centrifuge after collecting 1-2 milliliters of blood.

Statistical analysis was performed using SPSS version 22. Continuous variables were compared using paired student's t-test, while categorical variables were assessed with Chi-square or Fisher's exact tests. A P-value of less than 0.05 was considered statistically important.

Variables that showed a P-value of less than 0.025 in univariate analysis were included in the multivariate model to identify independent associations with the female gender [16].

Ethical approval for the study was granted by the Babcock University Human Research Ethics Committee (NHREC/24/01/2018 and BUHREC501/19).

Definitions

For this study, kidney biopsy was not employed to determine the cause of chronic kidney disease (CKD).

Hypertension-Related CKD (HACKD): Kidney damage resulting from chronic hypertension, most often observed in older adults and those in their late middle age.

Chronic Glomerulonephritis: A kidney condition that leads to elevated blood pressure, generally seen in younger individuals and early middle-aged people, sometimes following a history of throat or skin infections.

Chronic Interstitial Nephritis: Kidney disease linked to substantial exposure to external nephrotoxins, once other potential causes or risk factors for CKD have been ruled out.

Hypertension: Blood pressure readings above 140/90 mmHg [17].

Diabetes: Fasting blood sugar exceeding 126 mg/dL, or the use of medications for controlling blood sugar levels [18].

Proteinuria: Dipstick test result showing more than 1+ protein presence [19].

Microalbuminuria: Urine albumin-to-creatinine ratio greater than 30 mg/g (3.4 mg/mmol) [20].

Anemia: Hematocrit levels falling below 39% [21].

Hypoalbuminemia: Serum albumin concentration lower than 35 mg/dL [22].

Hyperuricemia: Elevated uric acid levels, above 0.42 mmol/L in men and 0.36 mmol/L in women [23].

Results and Discussion

A total of 144 participants were included in the study, comprising 82 males and 62 females. The average age of the entire group, males, and females were 48.8 ± 15.9 years, 47.9 ± 16.8 years, and 50.5 ± 14.73 years, respectively. Among the participants, 7% of the males and 11.1% of the females were aged over 60 years (P = 0.003). The average body mass index (BMI) for males and females was 26.6 ± 4.3 kg/m² and 26.5 ± 4.8 kg/m², respectively (P = 0.8). Males exhibited higher BMI, and systolic, and diastolic blood pressure compared to females, with P-values of 0.04, 0.001, and 0.002, respectively **(Table 1)**.

Table 1. Sociodemographic, and clinical characteristics of participants

Variables	All participants (n = 144)	Males (n = 82)	Females (n = 62)	P-value
	N (%)	N (%)	N (%)	
Age (years)				
16-39	31 (21.5)	20 (24.4)	11 (17.7)	0.002
40-64	94 (65.3)	56 (68.3)	38 (61.3)	
≥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

The largest group among the cohorts had hypertension-associated chronic kidney disease (HACKD) at 44.4%, followed by chronic glomerulonephritis (CGN) and chronic interstitial nephritis (CIN), each at 19.4% **(Table 2)**. A smaller percentage, 6.9%, had obstructive uropathy, while 9.7% had other causes. The incidence of CGN was

higher in men compared to women, whereas the occurrence of CIN was more prevalent in women than in men.

Table 2. Etiology of chronic kidney disease in cohorts

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

A greater number of men used RAAS inhibitors, erythropoietin, and vitamin D analogs compared to women, with significant differences observed at P < 0.001, P = 0.02, and P = 0.003, respectively **(Table 3)**. On the other hand, women were more likely to take calcium channel blockers (CCBs), sodium bicarbonate, and phosphate binders than men, with P-values of 0.001, 0.001, and < 0.001, respectively.

Table 3. Drug history of participants

Variables	All participants (n = 144)	Males (n = 82)	Females (n = 62)	P-value
	N (%)	N (%)	N (%)	
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 the severity of chronic kidney disease (CKD) advanced, a higher proportion of women were affected **(Table 4)**. The average age, body mass index (BMI), systolic blood pressure, and diastolic blood pressure of the participants were 48.8 ± 15.9 years, 26.53 ± 4.51 kg/m², 146.8 ± 10.2 mmHg, and 93.7 mmHg, respectively. The cohort's mean serum levels of sodium, potassium, bicarbonate, and anion gap were 136.7 mmol/L, 4.1 mmol/L, 21.2 mmol/L, and 15.7 mEq, respectively. Serum creatinine, glomerular filtration rate (GFR), hematocrit, and albumin had mean values of 179.1 ± 14.2 µmol/L, 37.2 ± 7.4 milliliters per minute, 32.7 ± 4.4%, and 44.1 ± 8.6 grams per deciliter, respectively.

Table 4. Relationship between kidney function and participants' characteristics

Variables	Stage 3a (n = 33)	Stage 3b (n = 42)	Stage 4 (n = 47)	ND Stage 5 (n = 22)	P-value
Sex					
Males (N (%))	21 (63.6)	25 (59.5)	27 (54.4)	9 (40.9)	0.03
Females (N (%))	12 (36.4)	17 (40.5)	20 (45.6)	13 (59.1)	
Age (years, mean ± SD)	46.6 ± 5.5	47.8 ± 6.7	49.7 ± 8.9	52.1 ± 14.8.6	< 0.001
BMI (kg/m^2, mean ± SD)	25.7 ± 3.6	26.5 ± 5.4	26.8 ± 4.3	26.8 ± 7.7	0.06
Systolic BP (mmHg, mean ± SD)	142.4 ± 8.6	142.9 ± 5.5	147.4 ± 8.2	151.5 ± 9.3	0.01
Diastolic BP (mmHg, mean ± SD)	93.1 ± 7.1	93.7 ± 3.8	92.6 ± 6.7	96.4 ± 9.1	0.05
Sodium (mmol/L, mean ± SD)	139.2 ± 12.8	138.7 ± 7.4	136.9 ± 10.8	130.6 ± 11.4	0.001
Potassium (mmol/L, mean ± SD)	3.5 ± 2.1	3.7 ± 2.8	4.2 ± 2.6	4.8 ± 2.9	0.02
Bicarbonate (mmol/L, mean ± SD)	22.2 ± 4.3	21.8 ± 5.3	20.8 ± 4.2	19.3 ± 5.4	0.04
Anion gap (mEq, mean ± SD)	14.2 ± 7.8	15.6 ± 5.7	16.1 ± 6.2	17.2 ± 8.6	0.04
Creatinine (umol/L, mean ± SD)	110.6 ± 9.4	167.2 ± 6.4	209.2 ± 6.6	268.7 ± 11.5	< 0.001
eGFR (mean ± SD)	56.2 ± 6.8	44.6 ± 8.0	28.1 ± 7.3	13.8 ± 3.3	< 0.001
Hematocrit (mean ± SD)	38.6 ± 5.5	34.0 ± 6.4	30.6 ± 3.8	25.7 ± 3.3	< 0.001
Albumin (mean ± SD)	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

Men were more likely to use erythropoietin and had a higher prevalence of hypertension compared to women, with P-values of 0.04 and 0.03, respectively **(Table 5)**. In contrast, women exhibited a higher occurrence of hyponatremia, metabolic acidosis, elevated anion gap, and microalbuminuria than men, with P-values of 0.001, < 0.001, 0.004, and 0.04, respectively. Additionally, women had lower cortical thickness and kidney volumes compared to men, with P-values of 0.02 and 0.03, respectively.

Table 5. Relationship between gender and participants' characteristics

Variables	Males (n = 82)	Females (n = 62)	OR	95% CI	P-value
	N (%)	N (%)			
Age (years)					
< 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 results of the multivariate analysis, several factors were significantly associated with the female gender, including aging (OR-3.28, CI-2.69-3.87), hyponatremia (OR-4.74, CI-2.10-6.33), metabolic acidosis (OR-4.14, CI-1.46-4.92) **(Table 6)**, elevated creatinine levels (OR-3.06, CI-2.83-3.99), reduced estimated glomerular filtration rate (eGFR) (OR-4.82, CI-2.68-4.95), and low serum albumin levels (OR-4.56, CI-3.45-7.49).

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 distinct gender-based differences in the laboratory, socioeconomic, and radiological characteristics of the cohorts. The prevalence of CKD was higher among younger males, who also exhibited elevated blood pressure and BMI. In contrast, females showed higher incidences of hyponatremia, hyperphosphatemia, metabolic acidosis, anemia, hypoalbuminemia, increased UACR, and smaller kidney sizes. The higher rate of CKD in males corresponds with earlier studies both locally and globally [24-26]. This higher prevalence in men could be due to a combination of genetic, hormonal, and clinical factors, as well as socioeconomic aspects. Men lack the renal and cardiovascular protection provided by estrogen, and the presence of testosterone's anti-apoptotic properties in renal tubules may increase their risk of kidney damage [2, 3]. Men also tend to respond more strongly to sympathetic nervous system stimulation, and when treated with RAAS inhibitors for hypertension, proteinuria, and CKD, they show less efficacy with these drugs, especially after eight weeks of treatment [27]. This results in poorer blood pressure control and a quicker progression from pre-CKD to full CKD and end-stage renal disease [6, 28-30]. However, our results are contrary to those of Ricardo et al., who found that CKD was more prevalent in women in the United States [1].

The later onset of CKD in females may be due to the protective effects of estrogen on kidney function, along with societal, cultural, and educational barriers that often disadvantage women [2, 5]. Additionally, higher blood pressure in men, with or without metabolic syndrome, could worsen CKD outcomes in this group [31]. However, the more favorable biochemical findings for men in this research support other research that suggests the cardiovascular risk for both genders is more balanced in the decade following menopause, before women experience an increased risk later in life [4, 32, 33].

Our study also found CIN to be more prevalent in females, mirroring findings from research indicating a greater incidence of kidney dysfunction due to the use of NSAIDs and nephrotoxic substances, such as weight-loss herbal remedies, among women [34-36]. Likewise, the higher frequency of CGN in younger men aligns with studies in Nigeria and other low-income nations (LINs), where a large proportion of CKD cases, especially those caused by infections, are attributed to CGN [36, 37].

The increased occurrence of hyponatremia in women aligns with previous research, which has highlighted a higher prevalence of hyponatremia and its associated complication, central pontine myelinolysis, among women [38]. Thiazide diuretics, commonly used for managing hypertension and chronic kidney disease (CKD), have a stronger effect in women due to their higher levels of sodium chloride co-transporters (NCC), making them more susceptible to hyponatremia compared to men [39]. Similarly, the higher frequency of hyperphosphatemia in women is consistent with findings by Deepak *et al*. [40], who observed an inverse correlation between serum phosphate levels and body weight, although this contradicts the results from Barreto *et al*. [41]. In our region, men are more likely to consume higher amounts of meat and alcohol, contributing to a greater risk of hyperphosphatemia [7]. Estrogen has been shown to enhance phosphate reabsorption in both the proximal and distal renal tubules through the action of the sodium-potassium ATPase-dependent sodium-phosphate co-transporter (NPT) in the brush border [42]. This further supports the idea that hyperphosphatemia is typically caused by reduced excretion rather than excessive intake.

The higher occurrence of metabolic acidosis (MA) and an elevated anion gap in women is consistent with findings by Veiras *et al*. [43], who demonstrated that the phosphorylation of sodium-potassium exchanger isoform 3 (NHE3) in the proximal renal tubules is more pronounced in females, leading to decreased bicarbonate absorption, mild hypobicarbonatemia, and a raised anion gap. Anemia was also more prevalent among women, in line with earlier studies, particularly since many of the females in our research were postmenopausal. While women in their reproductive years typically do not receive long-term RAAS inhibitors unless they have proteinuria or other specific conditions [7], one might expect similar hematocrit levels between men and women. However, the erythropoietic effects of androgens, combined with the more advanced renal disease in women, may explain their lower hematocrit levels.

Women also exhibited more severe hypoalbuminemia compared to men. Since serum albumin levels are influenced by position, all participants had their samples collected while seated [22]. Hypoalbuminemia can stimulate the release of antidiuretic hormone (ADH), which may impair salt and water retention, potentially leading to complications like hyponatremia and hemodilution-induced anemia, both observed more frequently in female participants.

In terms of albuminuria, women had higher levels, aligning with Ahmad et al.'s findings [44], although this contrasts with Park et al.'s study [45], which found higher urine albumin-to-creatinine ratios (ACR) in men. We believe that the more significant decline in kidney function in women, along with the reduced use of antiproteinuric agents like RAAS inhibitors, may explain their increased albuminuria. Additionally, women had smaller renal sizes (both cortical thickness and kidney volume), as previously documented. These reductions could be attributed to the more severe nature of kidney disease in women, as well as the possibility of smaller kidneys being genetically determined in females [27].

The study's cross-sectional design limited our ability to determine the chronic nature of the disease. Additional constraints included missing data on lipid profiles, which were not included in the analysis, and the lack of assessment of CKD-BMD and parathyroid hormone levels in the participants. However, the study's strength lies in its inclusion of a significant number of individuals who developed CIN due to the use of exogenous substances such as weight loss products and non-steroidal anti-inflammatory drugs (NSAIDs), a growing issue in our region, which may influence the future demographic trends of CKD.

Conclusion

There are notable gender differences in the epidemiology, risk factors, clinical manifestations, and treatment responses in CKD. CKD was more prevalent in younger men, while the majority of those over 60 years of age were women. HACKD was identified as the most common cause of CKD, with chronic glomerulonephritis more frequently observed in males and CIN being more common among females. Hyponatremia, elevated UACR, metabolic acidosis, and hyperphosphatemia were more prevalent in women, while men had higher levels

of hematocrit, albumin, and larger kidney sizes. Men tended to use erythropoietin, RAAS inhibitors, and vitamin D analogs more often, while females more commonly used calcium channel blockers, sodium bicarbonate, and phosphate binders. Factors like advancing age, hyponatremia, metabolic acidosis, and hypoalbuminemia were independently linked to the female gender. Gender-based adjustments for median range values for specific variables would enhance the management, prevention, and monitoring of CKD patients.

Acknowledgments: We acknowledge the contributions of the supporting staff and nurses at the Nephrology and Hypertension clinic of Babcock University Teaching Hospital, Ilishan-Remo, Nigeria.

Conflict of Interest: None

Financial Support: None

Ethics Statement: Approval for this study was granted 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. 95 p.
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? Semin Hematol. 2015;52(4):261-9. 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):125. 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):421. 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(4):150204. 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(3):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.