ORIGINAL ARTICLE

GENDER DISPARITY IN RISK FACTORS FOR CHRONIC KIDNEY DISEASE IN A RURAL COMMUNITY IN SOUTHERN NIGERIA

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ABSTRACT

Background: : The evidence for gender disparity in prevalence of CKD is conflicting; while some studies report male preponderance, others have report female preponderance or no difference. Reasons for gender disparities in CKD prevalence may be related to differences in the occurrence of risk factors across the gender, amongst other factors. This study was to determine gender disparities in the risk factors for CKD. Method: This study is based on data from a community based cross-sectional study carried out in Ogbona, a rural community in Southern Nigeria. The WHO STEPS for surveillance of chronic diseases risk factors and chronic disease-specific morbidity and mortality questionnaire was adapted for this study. Four hundred and seventy-six participants were selected from 142 housing units in the community using multi-stage cluster sampling. Clinical examinations and laboratory investigations including serum creatinine, and urinalysis were performed. Results: Majority of participants were females (66.2%). CKD was commoner in females compared to males (14.3% vs. 12.7%, *P= 0.06*). More females than males had high body fat percentages (65.7% vs. 40.9%, *P=<0.0001*), high waist-hip ratio (99.7% vs 73.3%, *P=<0.0001*) and central obesity (43.1% and 4.3% *P=<0.0001*). More males compared to females used alcohol (56% vs. 9.2%, *P=<0.0001*), were overweight (42.2% vs 28.9%, *P=0.004*), and had proteinuria (6.2% vs 2.5%, *P=0.054*). The odds of females having central obesity are 16.7 times the odds of males having central obesity; similarly, the odds of females having high BF are 2.7 times the odds of males having high BF. Females had 122-fold the odds of men having high WHR. The odds of drinking alcohol are 92% less compared to males. There were no statistically significant gender differences regarding hypertension, diabetes mellitus, and use of nephrotoxins (NSAIDS, skin lightening agents, herbal medications). No female smoked cigarettes. Conclusion: This study shows that there is no statistically significant gender difference as regards prevalence of CKD, however several risk factors of CKD show gender disparity. The odds for central obesity, high WHR, high body fat percentages are significantly greater in females; while smoking, alcohol use, and over weightness, are commoner in males. There were no statistically significant gender differences regarding hypertension, diabetes mellitus, and use of nephrotoxins (NSAIDS, skin lightening agents, herbal medications).

KEY WORDS: Gender disparities, Chronic kidney disease, Risk factors, Southern Nigeria

Access this article online

Quick Access Code

WEBSITE: www.kjmsmedicaljournal.com

DOI: 10.36020/kjms.2020.1401.009

INTRODUCTION

Chronic kidney disease (CKD) is one of the major non-communicable diseases contributing to significant morbidity and mortality globally. A systematic analysis for the Global Burden of Disease Study 2017 reports that the global all-age mortality rate from chronic kidney disease increased 41.5% from 1990-2017.[1] The epidemiology of CKD varies from country to

country, however the global prevalence of all-stages of CKD is 9%, with all-age prevalence increasing by 29.3% from 1990 to 2017. [1]The common risk factors for development of CKD include hypertension, diabetes mellitus, glomerulonephritis, autoimmune diseases, urinary tract infections, urinary stones, nephrotoxins and lower urinary tract obstruction. Sub-Saharan Africa is one the regions with the highest burdens of CKD, and this has been associated with socio-economic factors as well as peculiar risk factors of CKD such as infections and exposure to toxins amongst others. [2,3]

The evidence for gender disparity in prevalence of CKD is conflicting, reasons for this variability in reports may be attributable to socio-demographics of study population, and methodology. Some studies have reported a male preponderance; [1,4] and this may be related to the higher prevalence of some risk factors for CKD in the males compared to females, a possible hormonal protection in females, genetic, geographical, and lifestyle factors. The Global Burden of Disease Study 2017 reported that age-standardised prevalence of CKD stages 1-3 was 1.29 times higher in females compared to males, while age-standardised CKD mortality was higher in males.[1] Other studies generally report no significant gender predilection in CKD [5,6], while the NHANES and Global Burden of Disease 2016 studies reported a female preponderance.[7,8] Aside from common traditional risk factors for CKD like hypertension and diabetes, pregnancy related AKI (preeclampsia, septic abortion, post-partum haemorrhage) is a major contributor to morbidity and mortality among women of childbearing age, and increases the risk for CKD in survivors. [9] Some aetiologies of CKD (e.g. autoimmune disorders) are also commoner in females. The variability of age distribution across studies may influence the gender distribution. Studies in which middle and older age groups predominate may observe more females than males, given that females have a longer life span.[10]

Studies have consistently shown that males predominate in the ESRD population in most countries and are at a higher risk of progressive CKD.[11-14] The preponderance of certain CKD progressive risk factors in males, and differential accessibility to health care, may contribute to higher prevalence of ESRD in males compared to females. Smoking and alcohol use, which are significant risk factors for CKD progression and cardiovascular disease are more common among males compared to females.[15,16] Hypertension, which is one of the commonest predisposing factors for CKD, is said to be more prevalent in men compared to women until after menopause, when it's prevalence either equals that of men, or becomes higher in women. [17,18] The reason for this trend is multifactorial, including neuro-hormonal and psychologic factors. [19] Concerning obesity, the evidence is inconsistent; some studies have reported obesity as a risk for CKD in females but not in males [20,21]; while others studies have reported the opposite. [22,23]

Gender differences in the risk factors of CKD, cannot be generalized due to ethnic, genetic, socio-cultural and environmental differences from one country to another. The aim of this study was to determine gender disparities in the risk factors for CKD in a rural population in Sub-Saharan Africa.

MATERIALS AND METHOD

This study was based on previous data obtained from a large community based cross-sectional study carried out in Ogbona, a rural community in Etsako-central local government area in Edo State. [24] Multi-stage cluster sampling was used to select 476 consenting adults from 142 housing units in the community, after obtaining permission from the Traditional ruler. The community has a total of 570 housing units with assigned primary health care (PHC) numbers, 142 housing units were selected systematically starting with a randomly determined house. Eligible participants per housing unit were estimated from the total adult population of 2405 as follows: 2405 / 570 = 4. Each housing unit served as a cluster, and four consenting eligible participants in each housing unit were randomly recruited to achieve the sample; where a housing unit had 4 adults, all were recruited. Socio-demographic data, relevant health, and behavioural data were collected using an adapted version of the WHO STEPS for surveillance of chronic diseases risk factors and chronic disease-specific morbidity and mortality questionnaire.[25] Anthropometric measurements, clinical examinations, and laboratory

investigations were performed by the researcher and trained assistants. Obesity was determined by measuring the height, weight, waist, hip circumference; and thereafter calculating the body mass index (BMI) and waist-hip ratio. Body fat percentage was calculated using the Deurenberg equation.[26] Obesity was regarded as BMI > 30kg/m^2 or Body fat percentage of > 32%, for females and >25% for males, waist circumference > 102cm in males, 88cm in females, WHR > 0.7 in females and > 0.9 in males. BMI was further classified according to the WHO classification[27] into underweight (BMI<18.5kg/m^2), normal (18.5-24.9kg/m^2), overweight (25-29.9kg/m^2), obesity I (30-34.9 kg/m^2), obesity II (35.9-39.5kg/m^2) and extreme obesity ($\geq$40 kg/m^2).

Laboratory tests included, serum creatinine, and urinalysis. Subjects who had + protein on dipstick urine test were considered to have proteinuria and were re-examined after 3 months to establish persistence. A single measurement of serum creatinine was done due to the financial implications. Glomerular filtration rate (eGFR) was re-calculated using MDRD (the original study[24] that served as data source used the Cockcroft-Gault equation). CKD was defined as eGFR <60ml/min/1.73m^2, and/or the presence of persistent urinary abnormalities (proteinuria). Ethical clearance was obtained from the University of Benin Teaching Hospital Ethical Committee (Protocol number: ADM/E.22A/VOL.VII/163).

DATA ANALYSIS

Data was analyzed using SPSS statistical software package version 22 (IBM Corp., Amonk, NY, USA). Continuous and categorical variables were expressed as mean ± SD and percentages respectively. Age-adjusted gender-specific crude prevalence rates of risk factors of chronic kidney disease, and adjusted prevalence odds ratio (OR) between the exposure variables and gender were determined. All p values < 0.05 were regarded as statistically significant. The exposure variables included age, smoking, family history, use of nephrotoxic agents (such as NSAIDs, skin lightening agents, herbal remedies), proteinuria, obesity, systolic hypertension, diastolic hypertension, and diabetes.

RESULTS

Demographics, Anthropometric and Laboratory measurements

Four hundred and seventy-six individuals were studied; of these 315 (66.2%) were females while male to female ratio was 1:1.9. Overall mean age was 46± 17years, and there was no statistically significant difference between males and females with regards to age (46.4± 19.6years vs. 46.9±16.8years, *P=0.781*). The overall mean serum creatinine concentration was 0.95±0.31mg/dl. Majority of the participants had serum creatinine within normal limits (Fig 1). Overall prevalence of CKD was 14.3%; 12.7% and 6.8% of males and females respectively had eGFR <60ml/min, however this was not statistically significant (X^2= 3.833, *P=0.06*). Table 1 shows the comparison of anthropometric measurements according to gender. Males had a higher mean weight compared to females; while estimated body fat percentage (BF) and waist circumference (WC) were higher in females; these differences were all statistically significant.

Risk Factors of CKD

Table 2 shows comparison of risk factors of CKD according to gender. A significantly higher proportion of females compared to males, had high estimated BF (65.7% vs. 40.9%, *P= <0.0001*); while females were more obese when defined with BMI, but this was not statistically significant (15.9% vs. 10.6%, *P= 0.127*). Although more females were in the Obesity I and II categories i.e. BMI> 30kg/m^2, significantly more males were overweight compared to females (42.2% and 28.9% respectively, *P=0.004*); all extremely obese individuals were females. The prevalence of central obesity was much higher in females than males (43.2% and 4.3%, *P= <0.0001*), and high WHR was more prevalent among women (99.7% vs. 73.3%, *P=<0.0001*). see Table 2.

A higher proportion of females compared to males used skin-lightening agents (7.9% vs. 6.8%, p=0.405). More males than females drank alcohol (56% vs. 9.2%, *P= <0.0001*), and no female smoked. Use of NSAIDs and herbal medications were commoner in females compared to males but did not reach statistical significance. Similarly, systolic

Table 1: Anthropometric Indices of the 476 Subjects According to Gender

	ALL Mean ± SD	MALES Mean ± SD	FEMALES Mean ± SD	Mean Difference 95%CI
Weight (kg)	65.2 ±12.3	68.9 ±11.5	63.3 ± 12.3	5.6 (3.3, 7.9)*
BF (%)	38.6 ± 8.6	30.6 ±9.1	32.4 ± 8.4	-1.8 (-3.4, -0.2)*
BMI (kg / m^2)	25.0 ±4.7	25.2 ±3.9	25.0 ± 5.1	0.2 (-0.7, 1.1)
Waist Circumference (cm)	86.2 ± 11.1	84.7 ±9.1	86.9± 12.1	-2.2 (-4.3, -0.1)*
Waist: Hip Ratio (WHR)	0.9 ± 0.1	0.9 ±0.1	0.9 ± 0.1	0.0 (0.0, 0.0)

* =Statistically significant, BF = Body Fat Percentage, BMI = Body Mass Index

and diastolic hypertension were more prevalent in females but was not statistically significant (32.1% vs. 31.7% and 26.0% vs. 24.2% for systolic and diastolic hypertension respectively).
Diabetes mellitus was commoner in males but was not statistically significance (2.5% and 1.9%, *P= 0.677*). Initial overall prevalence of proteinuria was 4.4% but reduced to 3.6% after re-assessment at 3-months. Proteinuria was commoner in males compared to females but was just short of statistical significance (6.2% and 2.5%, *p= 0.054*).

Independent Risk Factors Associated with Sex

Table 3 shows the independent risk factors associated with sex and age. The odds of females having central obesity are 16.7 times the odds of males having central obesity; similarly, the odds of females having high BF are 2.7 times the odds of males having high BF. Females had 122-fold the odds of men having high WHR. The odds of drinking alcohol are 92% less compared to males. These observations were

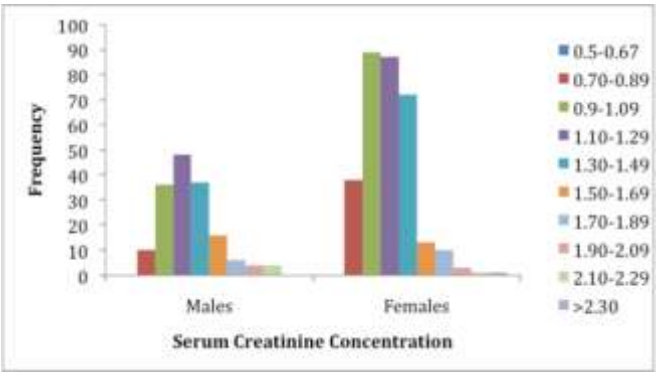
Table 2: Risk Factors Associated with Sex

Factors	Sex						P value
	Total		Male		Female		
	n=476	%	n=161	%	n=315	%	
Family History of HTN	38	7.9	12	7.4	26	8.2	0.859
Family History of DM	39	8.2	13	8.1	27	8.6	0.155
Cigarette smoking	19	3.9	19	11.8	0	0.0	<0.0001*
Alcohol use	111	23.3	90	55.9	21	6.7	<0.0001*
Use of Skin lightening agents	36	7.6	11	6.8	25	7.9	0.405
Use of NSAIDS	132	27.7	40	24.8	92	29.2	0.315
Herbal Medicine Use	111	23.3	34	21.1	77	24.4	0.425
Diabetic	10	2.1	4	2.5	6	1.9	0.739
Systolic Hypertension	152	31.9	51	31.7	101	32.1	1.000
Diastolic Hypertension	121	25.4	39	24.2	82	26.0	0.738
Obesity (BF)	273	57.3	66	40.9	207	65.7	<0.0001*
Obesity (BMI)	67	14.1	17	10.6	50	15.9	0.127
Central obesity	143	30.0	7	4.3	136	43.2	<0.0001*
Proteinuria	18	3.8	10	6.2	8	2.5	0.054
Waist-Hip ratio	432	90.7	118	73.3	314	99.7	<0.0001*

Table 3: Independent Risk Factors Associated with Sex and Age

	Univariate analysis		Multivariate analysis	
	Unadjusted OR (95% CI)	P value	Adjusted OR (95 CI %)	P value
Alcohol use				
Male	1		1	
Female	0.08(0.05-0.13)	<0.0001	0.08(0.05-0.13)	<0.0001*
Age	0.99(0.98-1.01)	0.921	1(0.98-1.01)	0.975
Use of Skin lightening agents				
Male	1		1	
Female	0.08(0.049-0.131)		1.431(0.659-3.108)	0.365
Age	0.927(0.9-0.954)	<0.0001	0.925(0.898-0.953)	<0.0001*
Herbal use				
Male	1		1	
Female	1.21(0.77-1.92)	0.407	1.23(0.77-1.95)	0.392
Age	1.02(1.01-1.04)	<0.0001	1.02(1.01-1.04)	<0.0001*
NSAID use				
Male	1		1	
Female	1.25(0.81-1.92)	0.315	1.26(0.81-1.96)	0.306
Age	1.02(1.01-1.04)	<0.0001	1.02(1.01-1.04)	<0.0001*
Systolic Hypertension				
Male	1		1	
Female	1.08(0.70-1.69)	0.707	1.08(0.67-1.73)	0.743
Age	1.04(1.03-1.06)	<0.0001	1.044(1.03-1.06)	<0.0001*
Diastolic Hypertension				
Male	1		1	
Female	1.02(0.68-1.53)	0.932	1.02(0.66-1.59)	0.912
Age	1.05(1.03-1.062)	<0.0001	1.05(1.03-1.06)	<0.0001*
Obesity (BF)				
Male	1		1	
Female	2.759(1.866-4.078)	<0.0001	4.162(2.514-6.891)	<0.0001*
Age	1.084(1.068-1.101)	<0.0001	1.09(1.072-1.107)	<0.0001*
Central Obesity				
Male	1		1	
Female	16.715(7.589-36.814)	<0.0001	18.174(8.163-40.459)	<0.0001*
Age	1.02(1.008-1.031)	0.001	1.025(1.012-1.038)	<0.0001*
Proteinuria				
Male	1		1	
Female	0.393(0.152-1.017)	0.054	0.398(0.153-1.034)	0.059
Age	1.028(1-1.056)	0.047	1.027(1-1.054)	0.05
Waist-Hip ratio				
Male	1		1	
Female	114.424(15.581-840.33)	<0.0001	122.926(16.623-909.024)	<0.0001*
Age	1.045(1.023-1.066)	<0.0001	1.046(1.023-1.069)	<0.0001*

NA=Not applicable



statistically significant in both univariate and multivariate analysis.

The odds for using skin lightening agent was 7% less with every one-year increase in age; while the odds for use of herbal medication and NSAIDs was 2% greater with every one-year increase in age 1.025. Every one-year increase in age is associated with a 4% and 5% greater risk for systolic and diastolic hypertension respectively. Every one-year increase in age is associated with 9%, 5%, and 2% greater odds for having high body fat, high WHR and central obesity respectively. These observations were statistically significant in both univariate and multivariate analysis.

DISCUSSION

This study showed no significant gender differences in the prevalence of CKD although more females had CKD, supporting previous reports from Nigeria and other parts of the world. [5-8] There was a preponderance of females compared to males in this study reflecting the gender distribution in the community studied.[28] Other possible reasons for the female preponderance observed include unavailability of some men who leave home early to their farms and businesses; some refused to have their blood samples collected due to the anxiety of diagnosing an illness. This gender distribution is however similar to results from a systematic a review of CKD prevalence in Nigeria;[29] the researchers observed consistently more females than males in the six studies reviewed. Similarly, the systematic review of the burden of CKD in Sub-Saharan by Stanifer et al[2], observed more female than male participants (68% vs. 42%). These figures generally suggest that females are more disposed, and available for voluntary health screening.

Regarding anthropometric measurements differences were observed across the gender. Although Obesity classes I and II were more prevalent in females, mean weight was higher in males than females, and more males were classified as overweight using the BMI. This trend was also reported from the NHANES study and other researchers [30,31] and may reflect the bias of using BMI as a measure of excess fat accumulation in men who have large muscle mass and skeletal frame.[32] Morbid obesity was only found in females, and this corroborates with data from the NHANES study [30], in which 9.9% of women compared to 5.5% of males were morbidly obese. This probably reflects a combination of hormonal factors, sedentary lifestyle and unhealthy eating habits in females compared to males.[33] Men in the population studied are mostly active small-scale farmers and commercial motorbike riders, while the females are traders and home-keepers suggesting that the females were more sedentary.

As was expected females had greater odds for high BF compared to males;[34] mean BF was higher in females, and obesity defined by BF was significantly higher in females compared to males. Conversely, Amin et al [35], studied a high-risk Asian population and observed that obesity defined using BF (measured by bioimpedance analysis) was 82.3% and 79.5% in males and females respectively, this difference was however not statistically significant. In the current study BF was estimated with the Deurenberg equation that has an estimation error of 4% in elderly men and women [26] and is not validated in Africans; however, our observations corroborate the general knowledge that females have more body fat compared to males. More accurate methods of measuring body fat include bio-impedance analysis, dual energy x-ray absorptiometry (DEXA) and underwater weighing, but would have been cumbersome for population screening.

The odds for central obesity, and high WHR were greater in females compared to males. This may be due to hormonal factors, previous pregnancies, and lifestyle. Other researchers have similarly reported higher proportion of central obesity in females compared to males in general population.[36-38] Beigh

et al studied hospitalised patients with diagnosis of myocardial infarction, renal and liver disease, as well as control without these diagnoses, and found central obesity in 63.5% of females compared to 45% in males. [36]

Use of nephrotoxins like NSAIDS, herbal remedies and skin bleaching were generally common in both genders, although the use of skin lighteners was slighter commoner in females. The practice of skin bleaching is common among blacks throughout the world, although most reports are from African countries. [39,40] The reason behind this is linked to deep historical, economic, socio-cultural and psychosocial factors. [41,42] Although this habit is condemned in many African countries, it remains common, due to ineffective regulation of the availability and accessibility of these harmful cosmetic creams; additionally, majority of users are ignorant of the harmful effects, while others overlook them. The regular use and/or abuse of NSAIDs is common among older women who tend to suffer pain from musculoskeletal and arthritic diseases probably due to excess weight gain, and wear and tear. Men in the rural community who were studied, habitually ingest a mixture of NSAIDs as remedy for body pains due to their labour intensive jobs (farmers, labourers, bike-riding). The use of local herbal remedies is also commonplace in Nigeria and many African countries [43] where they are believed to cure a range of illnesses; unfortunately, these remedies are mostly unstandardised and potentially harmful to the kidneys and other organs. [44]

Smoking and alcohol use were commoner in males as was expected, and is corroborated by other studies. Socio-cultural and religious perceptions often deter females from engaging in these habits. Smoking is a risk factor for progression of CKD and for cardiovascular disease.[13,45] Some authors have suggested that smoking as well as other factors may explain the higher rate of CKD progression in males compared to pre-menopausal females. [46,47] Alcohol has also been associated with CKD and progression of the disease; although this study showed that significantly more men drank alcohol, up to 9.2% of females drank alcohol regularly. One study reported an increased risk for hypertension in both males and females who drank alcohol, this risk was observed at 4 drinks per day for women and 1 drink per day in men. [48] The implication is that alcohol use also increases the risk for CKD through hypertension, which is a leading aetiology of CKD and even minimal use (>1 drink per day) in men, should be discouraged.

Dipstick proteinuria was commoner in males, although did not reach statistical significance. Experimental studies suggest that proteinuria and glomerular disease develop more in naturally ageing males than females, mainly due to the protective effect of female sex hormones, higher levels of nitric oxide in females, and glomerulomegaly in males compared to females.[49-52] Gender differences regarding proteinuria is not consistent in the literature, while some studies reported a male preponderance, others have either reported female preponderance or no difference. The technique of detecting or measuring proteinuria varies across studies, and this may significantly explain these inconsistencies. Majority of earlier studies relied on one-time dipstick test or 24hr urine collections while newer studies utilize albumin: creatinine ratio. Although dipstick tests are sufficiently sensitive and specific for screening non-diabetic population for proteinuria; [53] the timing, frequency, and manner of urine collection may be significant sources of error.

Finally, this study observed that increasing age was associated with greater odds for hypertension, high body fat, high WHR and central obesity. These observations confirm the general knowledge that aging is associated with higher risk of cardiovascular disease.

This study is based on one of the few large sample community-based study on epidemiology of CKD in Nigeria. Limitations include the one-time estimation of GFR, however, all patients with urinary abnormalities were re-assessed after three months to establish the persistence of urinary abnormalities. Only individuals with GFR<60ml/min or eGFR >60ml/min with persistent urinary abnormalities were regarded as having CKD. Some risk factors for CKD were not evaluated in this study.

CONCLUSION

This study shows gender differences regarding some risk factors of CKD. The odds for central obesity, high WHR, high body fat percentages are significantly greater in females; while smoking, alcohol use, and overweightness, are commoner in males. Increasing age was associated with greater odds for systolic hypertension, diastolic hypertension, high body fat, high WHR and central obesity; while the odds of using skin lightening agent is less with increasing age. These findings should inform future public health education efforts, and subsequent health interventions.

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Cite this article as: *Okoye OC*, Gender Disparity In Risk Factors For Chronic Kidney Disease In A Rural Community In Southern Nigeria KJMS 2020; 14(1): 62 - 71.