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Original Article

Gender disparity in prevalence and risk factors of chronic Kidney disease among patients with type 2 diabetes in Northeastern Nigeria.

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ABSTRACT

Introduction: Diabetes mellitus is a metabolic disorder that is responsible for up to 5% of premature deaths worldwide. Diabetic kidney disease is the leading cause of end-stage renal disease. This study aims to evaluate gender disparity in prevalence and risk factors of diabetic kidney disease in northeastern Nigeria. **Methodology:** The study population consisted of adult patients with type 2 diabetesrecruited consecutively at the diabetes clinic of the University of Maiduguri Teaching Hospital, Maiduguri. Socio-demographic and anthropometric variables including age, sex, weight, height, BMI, as well as laboratory parameters, were obtained from each patient. Glomerular filtration rate was derived from the CKD-EPI formula using serum creatinine. **Results:** Two hundred and sixty-one adult patients with type 2 diabetes were recruited consecutively from the Diabetes outpatient clinic of the University of Maiduguri Teaching Hospital, Maiduguri. There were 167(64%) females and 94(36%) males. The mean ages of males and females were 51.10±12.23 years and 48.76±11.00 years, respectively (p= 0.115). The mean duration of diabetes was similar between males and females (7.24±7.18 vs 6.87±6.02 years, p= 0.652). Females had a higher BMI compared with males (28.49±6.27Kg/M^2 vs 26.41±4.86Kg/M^2 p= 0.003). Fasting blood glucose, Low-density lipoprotein cholesterol and PCV were more deranged in females than among males (9.53±4.72 mmol/L vs 11.10±5.97mmol/L p= 0.020; 2.84±1.03mmol/L vs 3.19±1.03mmol/L p=0.009; 34.49±5.33% vs 33.11±4.54% p= 0.026). Out of the study population, 83(74.1%) females had renal dysfunction compared with 29(25.9%) males. The risk factors for progressive kidney disease among female patients were age >45 years (Exp (B) 1.799, 95% CI= 1.165-3.805)and systolic blood pressure >140mmHg (Exp (B)= 1.592, 95% CI= 0.772- 3.284). **Conclusion:** Diabetic kidney disease among our cohorts with type 2 diabetes was more prevalent among females compared with males and the risk factors associated with this disparity were older age, high BMI, poor glycaemic control, low PCV and elevated LDL cholesterol.

Keywords: *Diabetic kidney disease, Gender difference, Prevalence, Risk factors*

Introduction

Diabetes mellitus is a metabolic disorder of public health importance in both developed and developing nations of the world responsible for up to 5% of premature deaths worldwide.[1] Diabetic kidney disease

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(DKD) is the leading cause of ESRD in the world, responsible for additional morbidity and mortality among patients with diabetes.[2] The prevalence of diabetic kidney disease in northeastern Nigeria has been reported to be 42.9% and its contribution to the burden of ESRD is projected to increase.[3] Several risk factors have been found to contribute to the development and progression of DKD.[4] There is growing evidence showing the disparity in the prevalence, risk factors and progression of DKD between males and females.[5] This discovery created the need to develop a targeted intervention for each category of patients. Research into the underlying factors responsible for these disparities between males and females may provide opportunities for novel treatment of DKD through personalized and targeted therapies.

Although the prevalence of DKD in Nigeria is similar to that of the USA and Europe; the burden of DKD-related ESRD is higher in developed countries.[3,6] This disparity is attributable to demographic and lifestyle differences as well as the possible role of genetic factors in the progression of DKD to ESRD.

The role of sex in determining the prevalence of DKD and its risk factors underscores the contribution of social and hormonal factors in the pathogenesis of DKD. Epidemiologic studies have shown that a disparity existed in the prevalence and risk factors of DKD between males and females.[7,8] However, studies have been inconsistent in attributing one sex or the other as a risk factor for progressive DKD.

This study aims at evaluating the gender differences in prevalence and risk factors of diabetic kidney diseases among patients attending the diabetes outpatient clinic of a tertiary health centre in northeastern Nigeria.

Materials and Methods

This was a cross-sectional hospital-based study conducted at the Diabetes clinic of the University of Maiduguri Teaching Hospital, Maiduguri, north-eastern Nigeria. The clinic serves as a regional referral centre in the northeastern region of Nigeria comprising six states and occasionally receives patients from neighbouring countries of Niger, Chad and Cameroon. The region has a projected population of 23.5 (13.5% of Nigeria's population) million. Two hundred and sixty-one consecutive, consenting adult patients with type 2 diabetes, attending the diabetes outpatient clinic were recruited for the study from January 2019 to December 2019. Their socio-demographic characteristics, duration of diabetes and biochemical parameters were obtained and recorded using a well-structured questionnaire. Anthropometric parameters such as weight, height and waist circumference were measured for each patient. Blood pressure was measured on the right arm in the sitting position and the average of two readings was recorded. Blood specimen was collected after 8-hour fasting for assay of electrolytes, urea, creatinine, serum lipids, glucose, glycated haemoglobin and uric acid. The early morning urine specimen was collected and immediately analysed using Medi-Test combi-9® (Macherey-Nagel, Germany) strip for protein, glucose and ketones. Urine samples were analysed within 30 minutes of the collection with the test strips immersed into the urine for 5 seconds and read against the colour codes on the container after 30 to 60 seconds. Serum creatinine was analysed with Roche Cobas C311® clinical chemistry analyzer using a photometric system at a wave length of 505. Estimated Glomerular filtration rates (eGFR) were calculated for each patient using the chronic kidney disease epidemiology collaboration formula with correction for black ethnicity (CKD-EPI equation).

Definition and KDIGO classification of CKD

Patients who had eGFR $\leq$ 60ml/minute/1.73M^2 were considered to have chronic kidney disease (CKD). Patients were also grouped based on the KDIGO GFR staging. G1: GFR >90 ml/min/1.73 m2; G2: GFR 60–89 ml/min/1.73 m2; G3a: GFR 45–59 ml/min/1.73 m2; G3b: GFR30-44, G4: GFR 15–29 ml/min/1.73 m2 , G5: GFR <15 ml/ min/1.73 m2 . Albuminuria level A1: <30mg/g, A2: 30-300mg/g, A3: >300mg/g. Patients who have GFR <60ml/min/1.73m2 and/or albuminuria >30mg/g are considered to have chronic kidney disease. Hyperfiltration is defined as GFR >120ml/min/1.73m2 and albuminuria <30mg/g in females and >130ml/min/1.73m2 and albuminuria <30mg/g in males.

Statistical Analysis

Data collected were entered into a computer and

analyzed using the Statistical Package for Social Sciences (SPSS Inc Chicago IL USA) version 21. Continuous variables were expressed as mean (±SD) and an association between them was determined using student t-test. Discrete variables were expressed as percentages and proportions and their association was determined using Chi-squared test. Probability (P)values<0.05 were considered significant. Results are presented as Tables and Figures where appropriate. Analysis for risk factors was done using binary logistic regression.

Ethical approval

Ethical approval was sought and obtained from the University of Maiduguri Teaching Hospital's research and ethics committee. Consent from the patients was also sought before the recruiting subjects for the study.

Results

Two hundred and sixty-one adult patients with diabetes were consecutively recruited in the study. Their ages ranged from 18 to 78 years with a mean age of 49.60±11.49 years. There were 167(64%) females. Table 1 shows the distribution of socio-demographic and clinical variables of female and male patients with diabetes.

Table 1: Distribution of socio-demographic and clinical variables among male and female patients with diabetes

Variable	Male(n=94)	Female(n=167)	P
Age(year)	51.10±12.23	48.76±11.00	0.115
Duration of Diabete (years)	7.24±7.18	6.87±6.02	0.652
BMI(Kg/M^2)	26.41±4.86	28.49±6.27	0.003*
Weight(Kg)	78.47±15.77	76.12±16.64	0.265
SBP(mmHg)	131.20±9.28	130.98±18.84	0.927
DBP(mmHg)	81.23±13.60	80.35±10.40	0.558
Waist circumference(cm)	93.21±16.76	91.99±16.54	0.568
Glycated Hb(%)	10.09±9.61	9.44±2.76	0.412
FBG(mmol/l)	9.53±4.72	11.10±5.97	0.026*
Total cholesterol(mmol/l)	4.80±1.17	5.09±2.85	0.246
HDL(mmol/l)	1.14±0.55	1.17±0.37	0.609
LDL(mmol/l)	2.84±1.03	3.19±1.03	0.009*
TG(mmol/l)	1.92±1.06	1.78±0.97	0.271
Sodium(mmol/l)	138.28±5.10	137.76±6.09	0.487
Potassium(mmol/l)	4.28±0.66	4.21±0.91	0.532
Bicarbonate(mmol/l)	20.01±1.48	20.22±1.69	0.320
Urea(mmol/l)	8.25±10.24	7.75±5.56	0.603
Creatinin(µmol/l)	150.42±124.82	135.92±87.22	0.273
eGFR(ml/min/1.73M^2)	75.77±36.11	66.67±38.08	0.057
Uric acid(mmol/l)	414.70±66.24	396.93±147.94	0.374
PCV(%)	34.49±5.33	33.11±4.54	0.026*
Proteinuria			
Negative	51	93	X^2=1.263
Positive	43	74	P=0.738

Table 2 shows that females constituted 74.1% of diabetic kidney disease patients in our cohort.

Table 2: Proportion of patients with diabetic kidney disease among males and females.

	Normal Renal Function	Renal dysfunction	Total
Male	65(43.6%)	29(25.9%)	94
Female	84(56.4%)	83(74.1%)	167
	149	112	

χ^2 =8.723, p=0.003

Females outnumbered males in all stages of GFR with a marked difference in patients who have GFR <60ml/minute/1.73M^2(χ^2= 11.168, p= 0.048). Figure 1 shows the distribution of GFR stages according to gender.

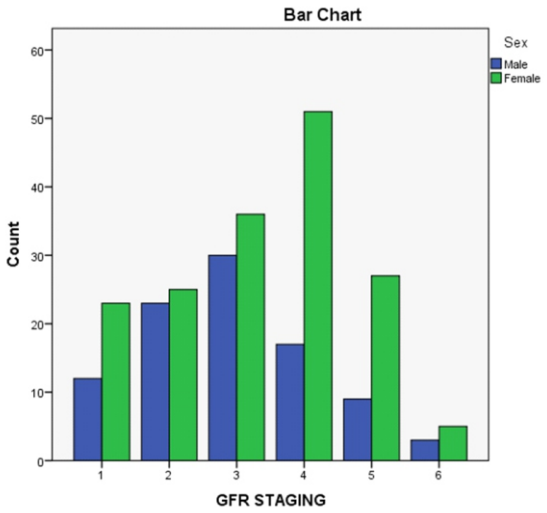

Figure 1: Distribution of various stages of GFR between males and females.
1=Hyperfiltration, 2=stage 1, 3= stage 2, 4= stage 3, 5= stage 4, 6= stage 5

Using multilinear regression analysis to determine factors associated with increased risk of diabetic kidney disease among female patients; GFR<60ml/minute was found to be associated with female gender(EXP(B)=2.105, p=0.014, 95% CI for EXP(B):1.165-3.805).

Table 3: Multiple logistic regression analyses showing factors associated with increased risk of diabetic kidney disease among female patients.

Variable	Exp(B)	P	95% CI for EXP(B Lower	Upper
GFR<60ml/min/1	2.105	0.014*	1.165	3.805
Age >45 years	1.799	0.266	0.639	5.065
BMI>30Kg/M	.574	0.118	0.287	1.151
Systolic blood pressure>140mmH	1.063	0.871	0.509	2.222
Diastolic blood pressure >90mmH	1.592	0.208	0.772	3.284
Fasting blood glucose >8mmol/l	1.563	0.201	0.788	3.102
Glycated Hb >7.5	1.223	0.561	0.620	2.411
Total cholesterol >6mmol/l	1.542	0.140	0.868	2.741

Discussion

This study evaluated the gender differences in prevalence and risk factors for diabetic kidney disease among patients with type 2 diabetes in Maiduguri, northeastern Nigeria. This study found that females have a higher prevalence of diabetic kidney disease (74.1% vs 25.9%). The prevalence of diabetic kidney disease among women in this study is higher than reported by Chiroma *et* al,[3] but similar to that reported by Brar *et al*[9] who found that women had a higher prevalence of chronic kidney disease than men. However, their finding reveals that men tended to progress to ESRD than females. In this study, there was no preponderance of chronic kidney disease risk factors (hypertension, high glycated haemoglobin, albuminuria and hyperuricaemia) among females suggesting that other yet unidentified factors may have been responsible for the higher burden of DKD in them. Biologic differences exist between sexes which may confer initiating factors such as hypertension and diabetes mellitus as well as progression factors such as inflammation and fibrosis.[10] The role of hypovitaminosis D in the promotion of these factors is being appreciated.[11] Women in our environment often secluded at homes, are deprived of adequate sunlight exposure and essential nutrition.

Our study also found a sex-related disparity in the prevalence of risk factors of chronic kidney disease. Women had a higher prevalence of dyslipidaemia and obesity than men. A similar study by Yu MK *et al*[12] has found that women had a higher prevalence of hypertension, dyslipidaemia and obesity among their cohort with diabetes.

There is a significantly higher proportion of females with stages 3 to 5 CKD in our study and women with eGFR <60ml/minute/1.73M^2 out-number males with a ratio of 1:2.7. This finding suggests that females tend to have more progressive diabetic kidney disease as compared to males. Poor glycaemic control among females may have contributed to the development of long term diabetic complications. Women have poorer adherence to anti-diabetic medications.[13] Other factors such as cultural and economic factors have put medical care beyond the reach of many women in our setting. High out-of-pocket expenses coupled with the lack of universal health insurance coverage for disadvantaged populations have made it difficult for many women to regularly take their anti-diabetic drugs.

Similar to the finding by Brar *et al*[9] Female sex was associated with the development of progressive kidney disease in this study. Other factors analyzed such as hypercholesterolaemia, age >45 years, obesity, and fasting hyperglycaemia were not significant in females. These findings may suggest that other yet to be identified factors such as genetic differences may play important roles in the differences in the prevalence of diabetic kidney disease among males and females. Studies by Okoye *et al*[14] in southern Nigeria, showed that disparities existed in the prevalence of chronic kidney disease between males and females.[14] In a study evaluating the global disparities of chronic kidney disease among males and females by Bibkov *et al*, the burden of advanced chronic kidney disease was similar between males and females. However, the prevalence of advanced chronic kidney disease was higher among females and there were a disproportionately higher number of males who had access to renal replacement therapies.[15]

This study is limited by the cross-sectional study design; follow up of patients for a longer duration was needed to establish renal disease progression. It is also a hospital-based study, making it subject to selection bias; others who may have the disease would have been missed due to their inability to afford hospital care.

Conclusion: This study revealed that the prevalence of chronic kidney disease among women with diabetes is higher than in males in northeastern Nigeria. The common risk factors associated with this difference were obesity, hypercholesterolaemia, fasting hyperglycaemia and low packed cell volume.

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