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Prevalence of Chronic Kidney Disease Based on MDRD and CKD-EPI Equations among Patients attending Abubakar Imam Urology Centre, Kano

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ABSTRACT

Background: Chronic kidney disease (CKD) is an important and most common noncommunicable disease. Presently, about 700 million people have CKD and the global prevalence of CKD is on the increase since 1990 due to the increase in the prevalence of DM, and hypertension which are the most common cause of CKD. The condition is often asymptomatic in its early stages; therefore, early testing is important. Thus, this study aimed to determine the prevalence of the various CKD stages based on eGFR using MDRD and CKD-EPI equations in patients with urological disorders in Kano, Nigeria. **Method:** One hundred patients comprising of seventy-nine males (79%) and 21 (21%) females were recruited. The mean age of the subjects was 54.22 ± 16.92 years. Biochemical parameters were measured on Architect C4000 Chemistry analyzer, ABBOT, USA. eGFR was calculated using the MDRD and CKD-EPI equations. The Statistical Package for the Social Sciences (SPSS, version 23) was used for statistical analysis.
Result: Gender-related analysis shows differences in the mean of all the biochemical parameters measured ($p < 0.001$). The overall CKD prevalence was 40% with highest CKD stage being CKD stage 2 (28% and 45%) using the MDRD and CKD-EPI equation respectively. Only one-percent of the patients had a prevalence of CKD stage 5 using the MDRD equation. Pearson correlation studies shows no significant relationship between the two eGFR equations ($r = 0.148$; $p = 0.141$).
Conclusion: The high prevalence of CKD in this study warrants for the early screening of patients to prevent their progression to end-stage kidney failure (ESKF).

Keywords: Chronic kidney disease, Diabetes mellitus, End-stage kidney failure, Estimated glomerular filtration rate, Hypertension.

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INTRODUCTION

A conglomeration of different pathological processes that leads to abnormal kidney function and a progressive decline in kidney function defines chronic kidney disease (CKD) (1). This abnormalities in kidney function are identified by the presence of an abnormality of kidney structure or function or both; that is present for at least 3 months (2). CKD is an important and one of the most common noncommunicable diseases globally (2). In 2017, the global prevalence of CKD was put at 9.1% translating to about 700 million people with the condition and the prevalence of CKD was on the increase since 1990 reaching up to 29.3% (3). In addition, the prevalence of CKD stages according to the Kidney Disease Improving Global Outcomes (KDIGO) is also on the increase being estimated at 6–7.5% in Italy (CHARES study) and 13% globally (4). This could be attributed to the increase in the prevalence of DM, and hypertension which are the most common cause of CKD coupled with the fact that, CKD is often asymptomatic in its early stages thus making early testing using eGFR important (2). In terms of mortality, CKD have now become the 12th leading cause of deaths and have resulted in about 4.9% of global deaths in 2017 with most of the CKD burden falling on low-income countries (3). Although diabetes and hypertension are the most common causes of CKD, other causes such as urological diseases have a prevalence that is not exactly known in adults (4). But in most African countries, urological emergencies are dominated by urine retention and urogenital infections (5) which account for a large number of admissions in urology centers (6) with some report showing that, urological disorders accounted for about one-third of all of surgical admissions in hospitals (6). Nevertheless, urological pathologies are generally more common after the age of 50 years and their prevalence increases with increase in age while in the mid-thirties, the pathologies may be more frequently dominated by sexually transmitted diseases (6).

Urological pathologies can be congenital or acquired but the most frequent are vesico-ureteral reflux (VUR), that could culminate in reflux nephropathy and recurrent urinary tract infections (UTIs), leading to the development of pyelonephritis, and urinary tract obstruction. Other include anatomical and functional alterations [ureteropelvic junction syndrome, bladder neck stricture, congenital urethral valves, urethral stenosis, nephrolithiasis, malignancies and benign prostatic hyperplasia (BPH)], and the overactive bladder, especially in the females (4). These pathologies may present with an insidious onset and slow progression, which make them difficult to identify and define despite well-known complications. However, hypertension, proteinuria, urine concentration defects, hyperkalemia, metabolic acidosis, focal and segmental glomerulosclerosis and CKD are the most common complications that have a significant impact on long-term kidney and cardiovascular prognosis (4). In general, CKD is commonly diagnosed using serum creatinine, however, serum creatinine is of limited value in this task, as it is classically known that creatinine will rise over normal values only when 50% of glomerular filtration rates (GFR) have already been lost in addition to its secretion by the tubular cells (7). These limitations have led to the introduction of the creatinine-based equations which were proposed to offer improvement in GFR estimation over serum creatinine. The Modification of Diet in Renal Disease (MDRD) study equation is one of the most commonly used (7). It was recommended that, eGFR based on the MDRD formular shall be automatically calculated for every request for serum

creatinine in people over 18 years (8). The original recommendations stipulated that GFR be reported in mL/min or mL/min/1.73m^2 (9). Moreover, an eGFR was to be reported for all patients above 18 years of age, and all values greater than 60mL/min/1.73m^2 were to be reported as '>60mL/min/1.73m^2' rather than an exact figure. In 2007 in a revised recommendation, the limit for reporting an exact figure was raised to '>90mL/min/1.73m^2 (8). Given that the MDRD equation was developed in a population with sub-optimal kidney function, its accuracy in predicting GFR is best reflected in those with mild kidney impairment. It is also recognized that MDRD tends to under estimate kidney function in those with a normal eGFR >90mL/min/1.73m^2. In response to these concerns, the Chronic Kidney Disease Epidemiology Collaboration Initiative Group (CKD-EPI) developed and validated a new equation in 2009 designed to match the accuracy of the MDRD equation at GFR <60L/min/1.73m^2 and to offer greater accuracy at higher GFR minimizing the over diagnosis of CKD with the MDRD equation (8). Thus, this study was aimed at determining the prevalence of the various CKD stages based on eGFR calculated using MDRD and CKD-EPI equations in patients with urological disorders in Kano, Nigeria.

Materials and methods

Patient's recruitment: This is a cross-sectional study conducted at Abubakar Imam Urology Centre Kano. In all, a total of 100 patients presenting with various urological disorders were recruited. The patients (mean age 54.22 ± 16.92 years) comprised of 79 (79%) males and 21 (21%) females with mean age of 56.5 ± 16.47 and 45.5 ± 16.12 years respectively. All subjects gave their consent to participate in the study before being recruited.

Inclusion criteria: all patients presenting with urological disorders at the hospital were considered eligible for inclusion in the study.

Exclusion criteria: patients with AKI, cancer, HIV, infectious or inflammatory conditions or taking medications for such conditions were excluded from the study. Pregnant women were also excluded.

Experimental Study protocol: Five milliliters (5mLs) of blood was collected aseptically from each subject. The sample was then transferred into a gel activator tube and allowed to clot and spun at 1500 rpm for 5 minutes. Serum was separated and transferred to a pre-labelled container and stored at -20^{o}C until analysis. Measurement of blood pressure (performed using the dorminant arm while the subject was in a sitting position and after resting for about ten minutes), weight (measured in kilogramme with clinic measuring scale), and height (measured in meters with clinic measuring ruler) were performed on the study day and recorded. Other clinical and anthropometric indicies including age, gender, and any other relevant medical history including medications were also obtained. The study protocol was reviewed and approved by the Ethics Committees of the Kano State Ministry of Health (Ref. SHREC/2021/2315; NHREC Approval number; NHREC/17/03//2018)

Laboratory analysis

Measurement of BUN, serum creatinine, sodium, potassium, chloride and bicarbonate was done on Architect C4000 Chemistry analyzer, ABBOT, USA. Estimated glomerular filtration rate was calculated

using the Modification of Diet in Renal Disease (MDRD) and Chronic Kidney Disease Epidemiology Collaboration Initiative Group (CKD-EPI) equations. The Statistical Package for the Social Sciences (SPSS, version 23) was used for statistical analysis. Body mass index (BMI) was calculated as weight (kg)/height (m^2).

Statistics and calculations

All data collected was analyzed using Statistical Package for Social Sciences (SPSS) version 23.0. (SPSS Inc., 233 South Wacker Drive, Chicago, USA). Comparison between genders was performed using Student t-test while the prevalence of the various CKD stages was determined using the Chi-squared test. Pearson correlation test was used to determine the correlation between MDRD and CKD-EPI equations. A p-value of < 0.05 was considered as statistically significant.

Definitions

Chronic Kidney Disease Categorization

The categorization was based on the Kidney Disease Outcome Quality Initiative (KDOQI) and Kidney Disease Improving Global Outcomes (KDIGO) recommendation (10,11);

Stage GFR Description

1. > 90 mL/min/1.73m^2 normal kidney function but urine findings- or structural abnormalities or genetic trait- point to kidney disease.
2. 60 – 89 mL/min/1.73m^2 mildly reduced kidney function, and other- findings (as for stage 1) point to kidney- disease.

3A 45 – 59 mL/min/1.73m^2 moderately reduced kidney function.

3B 30 – 44 mL/min/1.73m^2 moderately reduced kidney function.

4. 15 – 29 mL/min/1.73m^2 severely reduced kidney function.
5. < 15 mL/min/1.73m^2 or dialysis very severe, or end-stage kidney failure.

Modification of Diet in Renal Disease (MDRD) Equation (12);

eGFR (mL/min/1.73 m^2) = 175 x (creatinine, mg/dL)$^{-1.154}$ x (age, years.)$^{-0.203}$ x 0.742 (if female)

Chronic Kidney Disease Epidemiology Collaboration Initiative Group equation (CKD-EPI) (13);

$eGFR = 141 \times \min(S_{cr}/\kappa, 1)^{\alpha} \times \max(S_{cr}/\kappa, 1)^{-1.209} \times 0.993^{Age} \times 1.018$ [if female] $\times$ 1.159 [if black]

where, Scr is serum creatinine in mg/dL, k is 0.7 for females and 0.9 for males, α is -0.329 for females and -0.411 for males, min indicates the minimum of Scr/k or 1, and max indicates the maximum of Scr/k or 1.

RESULTS

The results are expressed as mean ± SD as appropriate. In this study, gender-related analysis shows significant differences in the mean age, height, weight, BMI and serum creatinine ($p < 0.001$; table 1). Table 2 shows the prevalence of various CKD stages calculated based on estimated glomerular filtration rate using the MDRD and CKD-EPI equations. The overall prevalence of CKD was 40% (table 2). In addition, the CKD stage with the highest prevalence based on the two equation was CKD stage 2 with a prevalence of 28% and 45% respectively while the least prevalent stage was CKD stage 5 with only one-percent (based on MDRD equation). However, none of the patient had CKD stage 5 when the CKD-EPI equations were used. In addition, table 3

shows the Pearson correlation analysis between the two estimated glomerular filtration rate equations of MDRD and CKD-EPI. No correlation between the two equations was observed (r = 0.148; p = 0.141).

Table 1. Age, anthropometric indices and serum creatinine of patients studied

Parameters, Mean ± SD	Categories of subjects			
	Male (n = 79)	Females (n = 21)	All (n = 100)	p – value
Age (years)	56.5 ± 16.47**	45.5 ± 16.12	54.22 ± 16.92	0.007
Height (m)	1.65 ± 0.08**	1.56 ± 0.07	1.64 ± 0.09	0.001
Weight (kg)	62.4 ± 9.57*	68.1 ± 3.33	63.59 ± 1.11	0.036
BMI (kg/m^2)	37.73 ± 6.32**	43.38 ±10.3	39.08 ± 7.61	0.002
Creatinine (µmol/L)	85.89 ± 45.47**	100.17 ± 33.2	89.23 ± 43.4	0.001

t-test, *p < 0.05, **p < 0.001

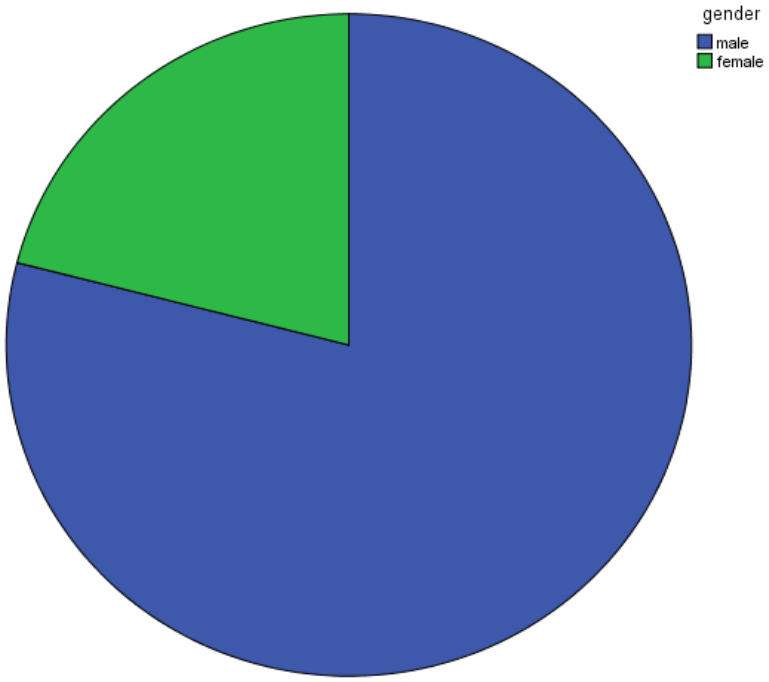

Figure 1. Shows the gender-related distribution of the patients

Table 2. Prevalence of CKD stages based on estimated glomerular filtration rate as calculated using the MDRD and CKD- EPI equations.

Stages (mLs/min/1.73m^2)	**MDRD (n = 100)**	**CKD-EPI (n = 100)**
Stage 1: (n, %) e-GFR ≥ 90 – normal kidney function	59 (59)	68 (68)
Stage 2: (n, %) e-GFR 60 - 89 – mildly reduced kidney function	28 (28)	15 (45)
Stage 3 (n, %) e-GFR 30 – 59 – moderately reduced kidney function	11 (11)	16 (16)
Stage 4 (n, %) e-GFR 15 - 29 – severely reduced kidney function	0 (0)	1 (1)
Stage 5 (n, %) e-GFR < 15 – very severe or end-stage kidney function	1 (1)	0 (0)
Overall CKD prevalence rate, n, (%)	40 (40)	32 (32)

Table 3. Pearson Correlation analysis between MDRD and CKD-EPI Equations

Parameters	Pearson Correlation	
	Coefficient (r)	p- value
MDRD vs. CKD-EPI	0.148	0.141

DISCUSSION

The final common pathological manifestation of many chronic kidney diseases is renal fibrosis which represents the unsuccessful wound-healing of kidney tissue after chronic, sustained injury and is characterized by glomerulosclerosis, tubular atrophy, and interstitial fibrosis. However, tubular atrophy, interstitial fibrosis, and scarring are closely associated with GFR and proteinuria (14). This is because, tubular epithelial cells are stimulated to synthesize inflammatory products including reactive oxygen species and chemokines by various abnormally-filtered urinary proteins, including complement, cytokines, and albumin (14). Therefore, these agents attract inflammatory cells into the renal interstitium and initiate interactions with interstitial myofibroblasts. As fibrosis evolves, injured tubular epithelia lose their regenerative capacity and undergo apoptosis leading to tubular atrophy and creating non-functional glomeruli (14). In addition, early in CKD injury, interstitial capillaries become increasingly permeable allowing many plasma proteins that normally never reach the renal interstitium to be able to do so and trigger an inflammatory response. A progressive decline in the surface area of interstitial capillaries leads to hypoxia within the kidney and affects the function of cells usually involved in the degradation of collagen which is synthesized in healthy kidneys. Collagens, basement membrane proteins, proteoglycans, and glycoproteins become deposited in the chronically-damaged kidney; the area of fibrotic interstitium affected is closely associated with both renal function and long-term renal prognosis (14).

In this study, there is the predominance of males over females' patients which is consistent with a previous finding elsewhere (15,16). Male predominance in this situation could be related to the nature of urological pathologies especially prostatic tumors which have increase prevalence in males than females. In addition, obstetrics and gynecology (O&G) sometimes share conditions which may be more common in females than males such as urinary incontinence and urinary tract infections. In addition, a gender-related differences in age, serum creatinine and BMI between the genders was observed in this study. Differences in serum creatinine between male and females have been reported by several workers (17,18) and could mainly be attributed to the differences in muscle mass. Previous studies have shown that, high BMI (overweight or obese) was an important risk factor for a variety of chronic diseases (19,20,21,22). The gender-related difference in mean BMI between male and females in this study is in agreement with the finding of Forrester et al, (23), a finding which could be attributed to the differences in dietary habit, sedentary lifestyle nature of the women in the environment as well as the perception of obesity as a sign of "well-being" in the society especially with regards to women. The mean age of the patients in this study agrees with reports elsewhere in which the mean age of the subjects under study was reported to range from 39.0 ± 11.0 to 54.8 ± 12.8 years (24). It should be noted that, most of the subjects visiting the urological clinics are those mostly in their mid-fifties due to the high prevalence of prostatic cancer and problems related to urine incontinent.

Moreover, reports have indicated that, all stages of CKD are associated with increased risks of cardiovascular morbidity, premature mortality, and/or decreased quality of life. In the present study, there is a high prevalence of overall CKD stages of 40% among our patients. This finding of high prevalence of overall CKD stages among the urological patients in this study is a testimony of the

strength of this study. Similar to our findings, Shafi et al, (25) reported that, the prevalence of CKD stages 1,2 and 3 in Caucasians were 58.3, 35.0 and 6.3% respectively using the MDRD study equation; the prevalence of these stages was 69.0, 24.6 and 6.0% respectively using the CKD-EPI study equation. It should be noted that, a documented report has shown that, the prevalence of CKD is on the increase since 1990 (3), with various prevalence reported from the general populations in Taiwan, Japan, China, Canada and the US (26,27,28,29,30,31,32). In Nigeria, report by Oluyombo et al, (33) shows the prevalence of CKD to be 18% in a rural community in South-Western Nigeria. Similar study in the South-East Nigeria however, reported a prevalence of 11.4% in rural setting, and 11.7% in semi-urban dwellers (34). Furthermore, a study from North-West Nigeria documented CKD prevalence of 26% (35), thus suggesting overall high prevalence of CKD in all the population. As stated elsewhere, pathologies related to urology are more common after the age of 50 with their prevalence increasing with advancing age. Indeed, most of the patients in this study fall within the age range of 40-71 years (table 1), which may indeed account for the high prevalence of CKD observed in the patients. Although, most of the studies quoted were population-based studies compared to our study that was hospital-based, nevertheless, the findings in all the studies emphasizes the need for urgent measures to arrest the trend in the increase in the prevalence of CKD in our population especially those related to urological pathologies bearing in mind the inadequacy of facilities to cater for the patients in form of hemodialysis and the prohibitive cost associated with the modalities.

There was no correlation between MDRD and CKD-EPI equations (table 3) in this study ($r = 0.148$; $P = 0.141$). However, a previous study has reported that, the highest agreement between GFR estimates in their study was that between MDRD and CKD-EPI equations (36), a finding that contrasted the present finding. However, Evans et al, (37) compared the performance of 5 different estimated GFR equations, CG, MDRD, CKD-EPI, Mayo Clinic and Lund-Malimo equations with measured GFR (ioxehol clearance) in 2098 CKD patients with advanced renal failure. The findings of this study shows that, all the equations displayed reasonable performance at population level with the best overall performance achieved by Lund-Malimo and CKD-EPI equations followed by MDRD (37). Indeed, previous studies have reported that, the CKD-EPI equation have less bias than the MDRD study equation and provided more precise GFR estimation at GFR $\geq$60mL/min/1.73m^2 (25). In addition, even at GFR <60mL/min/1.73m^2, the bias of the CKD-EPI equation was less than that of the MDRD study equation. The limitation of the study is that, it did not measure urinary albumin, an important parameter used for the correct definition of CKD.

CONCLUSION

There is high prevalence of overall CKD in our patients which call for drastic measures aim at preventing the progression of patients to ESKF through early routine screening of patients for CKD at the clinic level.

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