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ORIGINAL ARTICLE

Utility of Estimated Glomerular Filtration Rate Equations in Nigerians with Stable Chronic Kidney Disease

Utilitaire d'équations glomérulaire estimé la vitesse de filtration dans les Nigérians souffrant d'insuffisance rénale chronique stable

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ABSTRACT

BACKGROUND: **Chronic kidney disease (CKD) is a global public health problem. The incidence and prevalence are increasing worldwide, while the outcomes remain poor and treatment cost high. Unfortunately, CKD in Sub-Sahara Africa is usually diagnosed late and supported with limited treatment facility.**

OBJECTIVE: **This study aimed at filling the gap created by late diagnosis by assessing utility of estimated glomerular filtration rate (eGFR) in Nigerians and possibly proposing routine reporting of eGFR for earlier diagnosis of CKD.**

METHODS: **This study was carried out among patients with established and stable chronic kidney disease (CKD) from the renal unit of the University of Ilorin Teaching Hospital. A total of 64 patients with CKD, comprising 48 males and 16 females were selected by simple random sampling technique for the study. Their creatinine clearance using 24-hour urine collection method, the Cockcroft and Gault [CG] formula and Modification of Diet in Renal Disease (MDRD) formula was determined. Creatinine clearance from CG formula and endogenous creatinine clearance were corrected to 1.73m^2 body surface area.**

RESULTS: **The mean creatinine clearance from 24-hour urine collection was 21.75ml/min/1.73m^2. We obtained 32.18 ml/min/ 1.73m^2 from Cockcroft and Gault and 26.56 ml/min/ 1.73m^2 from MDRD formulae respectively. There was no statistically significant difference between the mean creatinine clearance values obtained from the 24-hour urine collection when compared with those obtained from the Cockcroft-Gault formula (p >0.5) and the MDRD formula (p > 0.5). Also, when creatinine clearance from 24-hour urine collection was subjected to correlation analysis; correlation coefficients of 0.905 and 0.904 were obtained for Cockcroft-Gault and MDRD formula respectively.**

CONCLUSION: **Our results thus show that the formula method (eGFR) for calculating clearance is 95% reliable in patients with chronic kidney disease in this environment. To promote early detection of CKD which is usually amenable to treatment we recommend routine reporting of eGFR. WAJM 2011; 30(6): 432–435.**

Keywords: **Cockcroft-Gault; Chronic kidney disease; Glomerular filtration rate; MDRD; Nigerians; Modification of Diet in Renal Disease Fortmula.**

RÉSUMÉ

CONTEXTE: L'insuffisance rénale chronique (IRC) est un problème mondial de santé publique. L'incidence et la prévalence sont en augmentation dans le monde entier, tandis que les résultats restent médiocres et les coûts élevés de traitement. Malheureusement, CKD en Afrique sub-saharienne est habituellement diagnostiquée tardivement et pris en charge avec installation de traitement limitée.

OBJECTIF: Cette étude visait à combler le vide créé par un diagnostic tardif en évaluant l'utilité du taux de filtration glomérulaire estimé (EGFR) dans les Nigérians et les rapports de routine de proposer éventuellement des DFGe pour un diagnostic plus précoce de la néphropathie chronique.

MÉTHODES: Cette étude a été réalisée chez les patients atteints de maladie rénale établie et stable chronique (IRC) de l'unité rénale du Centre Hospitalier Universitaire de Ilorin. Un total de 64 patients atteints de néphropathie chronique, comprenant 48 hommes et 16 femmes ont été sélectionnés par la technique d'échantillonnage aléatoire simple pour l'étude. Leur clairance de la créatinine de 24 heures en utilisant la méthode de collecte d'urine, la formule de Cockcroft et Gault [CG] formule et Modification of Diet in Renal Disease (MDRD) formule a été déterminée. Clairance de la créatinine de formule de CG et de clairance de la créatinine endogène ont été corrigées pour 1.73m2 de surface corporelle.

RÉSULTATS: La clairance de la créatinine moyenne de la collection d'urine de 24 heures était 21.75ml/min/1.73m2. Nous avons obtenu 32,18 ml / min / 1.73m2 de Cockcroft et Gault et 26,56 ml / min / 1.73m2 de MDRD formules respectivement. Il n'y avait pas de différence statistiquement significative entre les valeurs moyennes obtenues à partir de clairance de la créatinine de la collecte de l'urine de 24 heures lorsque comparés à ceux obtenus à partir de la formule de Cockcroft-Gault (p> 0,5) et la formule MDRD (p> 0,5). En outre, lorsque clairance de la créatinine de collecte de l'urine de 24 heures a été soumis à une analyse de corrélation; coefficients de corrélation de 0,905 et 0,904 ont été obtenues pour de Cockcroft-Gault et MDRD, respectivement.

CONCLUSION: Nos résultats montrent donc que la méthode de la formule (DFGe) pour le calcul de la clairance est de 95% fiables chez les patients atteints d'insuffisance rénale chronique dans cet environnement. Pour promouvoir le dépistage précoce de la néphropathie chronique, qui est habituellement sensibles au traitement, nous recommandons de rapports de routine de l'EGFR. **WAJM 2011; 30 (6): 432–435.**

Mots-clés: formule de Cockcroft-Gault; maladie rénale chronique; taux de filtration glomérulaire; MDRD; Nigérians; Modification of Diet in Fortmula maladie rénale.

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Abbreviations: CG, Cockcroft and Gault; **CKD,** Chronic Kidney Disease; **eGFR,** Estimated Glomerular Filtration Rate; **IDMS,** Isotope Dilution Mass Spectrophotometry; **MDRD,** Modification of Diet in Renal Disease;

INTRODUCTION

The publication of the Kidney Disease Outcomes and Quality Initiative (KDOQI) clinical practice guidelines for the evaluation, classification and stratification of chronic kidney disease (CKD) in 2002 was a landmark event.[1] This is because CKD is a global public health problem, the incidence and prevalence of which are increasing while the outcome remains poor and treatment cost high. In the above document, CKD was defined as "the presence of markers of kidney damage or of estimated glomerular filtration rate (eGFR) <60 mL · min^{-1} · ($1.73m^{-2}$) [<1 mLs^{-1} · ($1.73\ m^{-2})^{-1}$] for three months or more".[1–3]

Current evidence suggests that some of the adverse outcomes of CKD can be prevented or delayed by early detection and treatment. Unfortunately, CKD in Nigeria is both diagnosed late and supported with limited treatment facility.[4] The nephrology community now stratifies CKD into five stages.[5] However, it is noteworthy that three of the five stages of CKD (stages 3, 4 and 5) were arbitrarily defined and based solely on the absolute threshold of eGFR (standardized to $1.73m^2$ body surface area).

Current guidelines recommend the use of the Cockcroft-Gault (CG) and modification of diet in renal disease (MDRD) equations for estimating the GFR in the management of patients with chronic kidney disease (CKD) [5,6]. The current treatment guidelines that depend heavily on the eGFR values and the age-long well established limitations of endogenous creatinine clearance determination procedure provide us with limited alternative as clinical chemistry Laboratorians. If we want to make our mandatory contribution to the evaluation and management of CKD in this part of the world we have to explore eGFR. Equations for estimating GFR offer a rapid method of assessing renal function in patients with kidney disease.

In the developing countries, endogenous creatinine clearance determination has remained the practical tool for determining the GFR, being only available in tertiary health care facilities. The use of prediction equations for estimating the GFR would, thus, meet the needs of the majority of primary care physicians, leading to the early and rapid detection of patients with CKD. To facilitate early detection of CKD, many national and international organisations now recommend automatic/routine reporting of estimated glomerular filtration rate (eGFR) whenever serum creatinine is measured.[7–9] As a follow up to our earlier work[10] in this centre, evaluation of currently advocated and common equations for the determination of eGFR among our patients with stable CKD has become necessary.

The objective of this study was to determine the creatinine clearance using the Cockcroft and Gault[11] [CG] formula and the MDRD[12] equations, testing for their suitability when compared with the traditional 24 hour urine collection method in Nigerians with CKD and stable serum creatinine value. This was with the aim to evaluating the reliability of eGFR result using CG and the MDRD equations in this environment.

SUBJECTS, MATERIALS, AND METHODS

A total of 64 patients with CKD, comprising of 48 males and 16 females were recruited by simple randomly sampling technique for the study after obtaining the approval of the institution's Ethical Committee. Creatinine clearance was determined using 24-hour urine collection method, the Cockcroft and Gault[11] formula and MDRD[12] formula. The precautions taken during 24-hour urine collection included: (i) adequate education of all the subjects to empty their urinary bladder and throw away the urine at time zero, (ii) to empty their bladder at time 24 hours and include the urine in the one for submission, (iii) the urine samples were collected in duplicates and the mean taken, (iv) the use of funnel by women subjects for urine collection, and (v) all the subjects were requested to report any error during the urine collection.

The raw values obtained from CG equation were adjusted for body-surface area; a comparison with normal values for creatinine clearance requires measurement of height, computation of body-surface area, and adjustment to $1.73m^2$.[13] Our creatinine assays were reported in SI Units. We used the four-variable original MDRD equation since our creatinine assay was not traceable to Isotope Dilution Mass Spectrophotometry [IDMS]. The CG equation utilises serum creatinine as well as age, gender and body weight, while the original four-variable MDRD equations take into consideration age, gender and race in addition to the patients' serum creatinine.

The patients were not on drugs such as cimetidine, cotrimoxazole or Probenecid. Also, patients with diabetic ketoacidosis, obese patients, severely malnourished, amputees, paraplegics and those with other muscle wasting disease were excluded from the study. Fluid was allowed freely. The weight, age, gender and race of the patients were recorded.

The height of all the patients was equally recorded; and used in calculating the body surface area. The endogenous creatinine clearance was calculated using the formula

$$\text{Corrected } C_{cr} = \frac{\text{Ucr x V x } 1.73}{S_{cr}\ x\ h\ x\ 60\ x\ BSA}$$

Where C_{cr} = creatinine clearance; U_{cr} = concentration of creatinine in urine V = volume of urine; Scr = concentration of creatinine in serum; H = period of collection of urine in hours; Where BSA = body surface area. Calculation of the body surface area was from the formula of DuBois and DuBois.[14]

BSA = ($W^{0.425}$ x $H^{0.725}$) x 0.007184; Where W = weight in kilograms; H = height in centimeters. The Cockcroft–Gault formula used was:

$$\text{Ccr (ml/min)} = \frac{[(140 - \text{Age in years}) \text{ x (weight in Kg) x(F)}]}{\text{Scr}(\mu\text{mol/L}) \text{ x } 0.8136 \text{ x BSA}} - \frac{\text{x } 1.73}{}$$

Where F = 1 if male, and 0.85 if femalel BSA = body surface area. Calculation of the body surface area was from the formula of DuBois and DuBois:[14] BSA = ($W^{0.425}$ x $H^{0.725}$) x 0.007184; where W = weight in kilograms; H = height in centimeters.

The Original four-variable MDRD Study Equation we used was:

eGFR (mL/min/$1.73\ m^2$) = 186 x $(S_{cr}/88.4)^{-1.154}$ x $(Age)^{-0.203}$ x (0.742 if female) x (1.210 if African).

The results are presented as mean ± SD; paired student t-test was used to determine the level of significance between the mean values of creatinine clearance of the 24-hour urine collection and the clearances obtained through the Cockcroft-Gault and MDRD formulae. Endogenous creatinine clearance from 24 hours urine collection was subjected to correlation analysis against the values obtained from Cockcroft-Gault and MDRD formulae respectively.

RESULTS

None of the patients reported any loss or error during urine collection. The descriptive statistics of the patients are displayed in Table 1.

Table 1: Age and Anthropometric Indices of Patients Studied

Variable	Mean(SD)
Age (yrs)	46.87(15.38)
Weight(Kg)	71.22(10.52)
Height(cm)	168.25(10.67)
Body surface area(m^2)	1.81 (0.16)

Table 2: Distribution of Patients with Chronic Kidney Disease by Aetiology

Primary Disease	Number (%)
Hypertensive kidney disease	24(37.5)
Chronic glomerulonephritis	12(18.75)
Diabetic nephropathy	8(12.5)
Polycystic kidney disease	12(18.75)
Acute renal failure	4(6.25)
Benign Prostatic nephropathy	4(6.25)

Presented in Table 2 are the primary diseases leading to CKD in the patients used for the study as obtained from their medical records. From this Table, hypertensive kidney disease accounted for 37.5%, chronic glomerulonephritis and polycystic kidney disease carried equal weights of 18.75% while benign prostatic hypertrophy was the least with 6.25%.

Table 3 shows the mean clearances for endogenous creatinine clearance value from 24 hour urine collection, Cockcroft-Gault and MDRD formulae. It also shows the result of ANOVA when the clearance values from the three approaches were compared. When the mean values were subjected to statistical analysis using Student t-test there were no significant difference at 95% confidence limits. Results of analysis carried out to compare the values are also shown in Table 3.

DISCUSSION

Our study revealed that more males [75%] were afflicted with CKD than females [25%]; this is consistent with the finding of Agaba[15] *et al* in Jos. This may be as a result of the fact that preference is given to the male child in the area of education in this environment; thus, they seek medical attention more than the females whenever they are ill. It may also be because of the challenges associated with their being the bread winners for their families exposing them to diseases' like hypertension which is an established risk factor for CKD. Our study also revealed that the commonest primary disease leading to CKD in patients enrolled for this study was hypertensive kidney disease [37.5%] while benign prostatic hypertrophy (BPH) [6.5%] was the least. This also agrees with the picture in the first world where hypertensive kidney disease is the leading cause of CKD. Our patients' mean age of 46.9 years possibly reflected the low occurrence of BPH among our patients.

Analysis of variance (ANOVA) revealed that there was no significant difference in the creatinine clearance values when endogenous creatinine clearance from 24-hour urine collection and those from CG as well as MDRD were compared. Further analysis using student t-test between mean endogenous creatinine clearance and mean clearance values obtained from the Cockcroft-Gault formula ($p>0.5$) and the MDRD formula ($p>0.5$) also revealed no statistically significant difference. These results thus showed that the formula method for calculating clearance is 95% reliable in patients with chronic kidney disease in this environment. This finding is in agreement with our earlier work in healthy Nigerians.[10]

To further affirm this, a correlation analysis was also performed on the clearances, comparing the values from endogenous creatinine clearance with the results obtained from the formulae. The correlation coefficient of almost unity supports the harmony of the results obtained from these three different methods.

This study had some limitations, the study had a relatively small sample size of only 64 patients and the characteristics of the study population [Nigerians resident in Nigeria] differed from that of the CG [Canadians] and MDRD [Americans] study populations.

It can be suggested, therefore, that in an effort to reduce morbidity and mortality due to late diagnosis of CKD in this environment, routine reporting of eGFR using CG or MDRD equations can be embarked on for estimating GFR.

Table 3: Creatinine Clearance Values by Different Methods

Method	Result
Creatinine Clearance Method, ml/min/1.73^2 [Mean(SD)]	
24-hour Urine Method	21.76(12.79)
Cockcroft-Gault (CG) formula	32.19(24.40)
Modification of Diet in Renal Disease (MDRD) formula	26.56(21.51)
Correlationship – Correlation Coefficient (r)	
Endogenous Crcl vs CG formula	0.905
Endogenous Crcl vs MDRD	0.904

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