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A Comparison of three Methods to Estimate the Glomerular Filtration Rate in Diabetic Patients at the Ngaoundere Regional Hospital (Cameroon)

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ABSTRACT

Estimation of Glomerular Filtration Rate (GFR) can be done using different methods. The cheaper and most available are those with formulas to determine the estimated GFR. The majority of these formulas have been developed among extra- African populations. In Sub-Saharan Africa, 3 formulas are almost used to estimate GFR which are MDRD, CG and CKD-EPI. This present study was conducted to assess the importance of these formulas as estimators of GFR for diabetic among African Populations. The study was conducted at the Ngaoundere Regional Hospital. Only diabetics from 30 to 78 years attending the regional hospital were enrolled in the study. After enrolment, diabetics with very high values of urea and/or creatinine were excluded. We evaluated CG, MDRD and CKD–EPI as estimators of GFR. Creatinine clearance of 24 hours has been considered as gold standard method. 60 participants were included for sex ratio (M/F) 1.5. The average eGFR of diabetics with high Blood Pressure was lower (91.2 ml / min) than diabetics with lower Blood Pressure (102 ml / min) according to ClCr24. A significant correlation (0.975) between MDRD and CKD-EPI was found when measuring eGFR. It was less significant between CG and MDRD (0.663) and; between CG and CKD-EPI (0.729). A strong similarity was noticed between MDRD and CKD-EPI (92%) while it was smaller between MDRD and CG (55%) and between CKD-EPI and CG (63%) when estimating the stage of kidney diseases. Compared to ClCr24, similarity in half results was found with MDRD (50%) and less than half with CKD-EPI (48%) and CG (38%). The study shown higher value of fasting blood glucose of diabetics attending the Ngaoundere Regional Hospital (212.1 ± 83.0 mg / dl) than the normal recommandation (127-144 mg / dl) for diabetic patients. The average value of the eGFR with MDRD (76.6 ± 20.0 mL / min) was closer to CKD-EPI (78.8 ± 20.4 ml / min) (P<0,001 ; X2=0,976). eGFR was lower in diabetics with high Blood Pressure compared to diabetics with low Blood Pressure. Estimation of CKD stages using MDRD and CKD shown significant similarity. In conclusion, CKD-EPI and MDRD estimated better the GFR. MDRD presented values that were closer to the Creatinine clearance of 24 hours. Further studies are needed with more participants to evaluate the best formula between MDRD and CKD-EPI for the estimation of GFR in Sub-Saharan diabetic population.

Key words: CG, MDRD, CKD-EPI, CrCl24, diabetes, eGFR.

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Introduction

Chronic Kidney Disease (CKD) is characterized by slow, progressive and irreversible damage of kidney cells, followed by the loss of the glomerular function for 3 months at least. It is mainly caused by immune mediated injury, chronic metabolic dysfunctions and mechanical stress [1, 2]. The prevalence of CKD in sub-Saharan population is around 13.9% without disproportion amid rural and urban settings, and it is estimated that, by 2030 more than 70% of CKD patients with End-stage of renal disease (ESRD) will be resident in low-incomes countries, the typical case with most African countries [1]. In Cameroon, the prevalence of CKD has been reported at 7.3% using proteinuria measurement and 4% using the Cockcroft and Gault method [3, 4]. The main risk

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factors for the development of CKD are hypertension, diabetes, drug metabolites, bacterial and viral infections, obesity, cancer, chronic inflammation diseases and alcohol. Diagnosis CKD is based on the estimation Glomerular Filtration Rate (GFR) which is the total volume of blood filtered by the nephrons per unit of time [2]. GFR expressed in ml/min reflects the capacity of functional nephrons [5]. Diabetes is characterized by chronic high blood sugar levels as a result of a gene-mediated lack or insufficiency in insulin or its binding receptors, or secondary to insulin resistance and systemic glucose overload [6]. Uncontrolled diabetes can cause several end-organ pathologies such as renal disease, retinopathy and cardiovascular diseases [7]. Different methods are actually used to estimate the GFR. The ones frequently used are Cockcroft &Gault (CG), the Modification of Diet in Renal Disease (MDRD) and, the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) methods [8]. Although, these formulas are widely applied in Cameroonians hospital[9]. This should serve as a motivation for scientist to carryout in-depth studies in African populations to validate existing formulas to better the estimation of kidney function [10]. As such, we were guided to perform this study among diabetic persons in Ngaoundere to estimate and compare GFR using three different methods clinical employed worldwide.

Material and Method

This study was performed in diabetic population from March to December 2014, wherein diabetic persons resident in Ngaoundere for at least 3 years, attending the Ngaoundere Regional Hospital for their medical visits, and who duly provided a written consent were enrolled. Pregnancy, severely illness, being on dialysis and refusal to sign the consent form, represented our exclusion criteria. We collected data on socio-demography, anthropometry, and personal history using a questionnaire. 5ml of whole venous blood sample was collected into dry tubes, left to clot (5-10 minutes), centrifuged at 2000rpm for 3 minutes with serum subsequently separated into eppendorf tubes and stored at -20˚C prior to weekly badge measurements of creatinine and urea concentrations. Participants were further provided 5L sterile, leak-proof containers for 24hour urine collection towards urine creatinine/24H measurement, after properly explaining the procedure to them individually. They were properly directed on how to collect the entire 24H urine sample, and sufficiently advised on how to avoid chemical contamination of urine. After collection, urine samples were homogenised and 3mL set apart in eppendorf tube for creatinine analysis. All biochemical measurements were done using aSemi Auto Chemistry Analyser.

We measured blood glucose following the Trinder method based on an enzymatic colorimetric reaction as previously described by Trinder. The normal range for blood glucose was considered as 74-106 mg/dl for adult less than 60 years, and 82-115 mg/dl for those 60 years and above. Serum urea levels were determined based the enzyme colorimetric reaction where urea is hydrolized enzymatically into ammonium ion and carbon dioxide, where after, the ammonium ions react with salicylate and hypochlorite in presence of nitroprusside as catalyst to form a green indophenol, with reference range stated at 13.0-43.0 mg/dl for adults aged less than 60, and 17.0-49.0 mg/dl for those aged 60 years and above. In order to determine serum creatinine levels, according to Fabiny, the Jaffe technique was employed, with normal values considered as 0.6-1.1 mg/dl for women, and 0.9-1.3 mg/dl for men [11, 12, 13, 14].

To estimate the GFR, we used Cockcroft &Gault (CG), the Modification of Diet in Renal Disease (MDRD) and, the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) method.

We made use of the CG formula developed in 1976 [8] thus: **CG cr**= ((40-age)(weight in kg))/(72xScr(mg/100mL))

To estimate the GFR following the MDRD method, we used a simplified version of the formula thus:

MDRD cr =186 x (creatinine (µmol/l) x $0.0113)^{1,154}$ x $age^{0,203}$x 1.21 x 0.742(if woman)

The following equations proposed by Levey et al [15] were used for the determination of GFR in accordance with the CKD-EPI method

Table 1: Formulas to estimate the GFR with CKD-EPI method

	Creatininemiae estimated in µmol/l (mg/dl)	Formula to use
Black women	≤62 (≤0,7)	GFR = 166 x $(créat/0,7)^{-0,329}$ x $(0,993)^{âge}$
	>62 (>0,7)	GFR = 166 x $(créat/0,7)^{-1,209}$ x $(0,993)^{âge}$
Black men	≤80 (≤0,9)	GFR = 163 x $(créat/0,9)^{-0,411}$ x $(0,993)^{âge}$
	>80 (>0,9)	GFR = 163 x $(créat/0,9)^{-1,209}$ x $(0,993)^{âge}$

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Quality Assurance

Ethical Considerations

The study protocol and the consent procedure obtained ethical approval from the Institutional Review Board of the Faculty of Science of the University of Ngaoundere, and the ethical committee of the Regional Hospital of Ngaoundere, Cameroon(No1232/L/RC/RA/DSP/HR/NGD/CLE).

Data Analysis

Data were keyed into a Microsoft Excel spreadsheet (version 2010) and the Statistical Package for Social Sciences (SPSS) version 20.0 software. The Chi-squared test was used to study the differences between proportion. We used the Pearson independent, ANOVA, and the T-test to compare variation between means. Statistical significance was fixed to 5%.

Results

Sixty diabetic patients aged between 30 to 78 years old were enrolled into this study, with a mean age of 53±12.5 years. Women represented 60% of the study population, 87% of them resided in an urban area, while 65% were without any formal education. The durations of diabetic status of our participants ranged from 1 to 25 years. 28% of study participants had a family history of diabetes and hypertension while 40% were without (P=0.07). Furthermore, 47% of participants presented with either a systolic (≥140mmHg) or diastolic (≥90mmHg) hypertension or both. Obesity was recorded at 33%, with its prevalence being higher in females (39%) than males (25%).

The mean fasting blood glucose was 212.1±83.0 mg/dl, and men presented significant higher values than women (237.0±90.5 mg/dl versus 195.5±74.9 mg/dl, P=0.017). Also, the mean serum creatinine level in men (1.2±0.2 mg/dl) was higher compared to that in women (1.0±0.2 mg/dl). The mean volume of 24 hour urine collected was 1906±710 ml.

Table 2: Mean distribution of biochemical parameters

Biochemical markers	Women	Men	General
Fasting Blood Glucose (mg/dl)	195.5±74.9	237.0±90.5	212.1±83.0
Blood Urea (mg/dl)	33.4±27.5	26.5±12.9	30.6±22.9
Blood Creatinine (mg/dl)	1.0±0.2	1.2±0.2	1.1±0.2
Urine Creatinine 24h (mg/dl)	90.3±24.0	96.6±35.2	92.8±28.8
Urine volume of 24h (ml/24h)	1727±537	2175±854	1906±710

Following estimation of GFR using three methods and subsequent comparison with gold standard (creatinine clearance), the findings in the table proceeding table were obtained:

Table 3: Comparison of mean GFR obtained from various estimation methods

Method	Women (ml/min)	Men (ml/min)	General (ml/min)
CG	75.0±24.4	64.7±11.4	70.8±24.4
MDRD	74.4±20.3	79.5±19.8	76.6±20.0
CKD-EPI	78.0±22.3	79.9±17.5	78.8±20.4
ClCr24 (Refer.)	101.4±40.8	104.0±39.3	102.0±39.6

With the CG method, eGFR of women (75.0±24.4 ml/min) were higher than men (64.7±11.4) (P<0.001) and, it presented the lower mean value for the general population (70.8±24.4 ml/min). We got important correlation and statistically significant between ClCr24 (our reference method) and MDRD (P<0.001; X2=0.523) and, between ClCr24 and CKD-EPI (P<0.001; X2=0.511). We got also significant correlation between ClCr24 and CG (P=0.014; X2=0.334). We found high and important correlation between MDRD and CKD-EPI (P<0.001; X2=0.976). During the estimation of the stages of CKD, we found 92% of similarity between MDRD and CKD-EPI while, 63% between CKD-EPI and CG and, 55% between MDRD and CG. Regarding the reference method, 50% of similarities were found between ClCr24 and MDRD, 48% between ClCr24 and CG and, 38% between ClCr24 and CG. Whatever the method used, diabetics with high arterial blood pressure (systolic and/or diastolic) presented significantly lower eGFR than those with normal arterial pressures, CG (P=0.002), CKD-EPI (P=0.016) and MDRD (P=0.020). In the comparison of eGFR between obese and non-obese persons, we observed nonsignificant differences with CKD-EPI (P=0.383), MDRD (P=0.567) and ClCr24 (P=0.624), while, using CG (P<0.001) recorded statistically significant differences.

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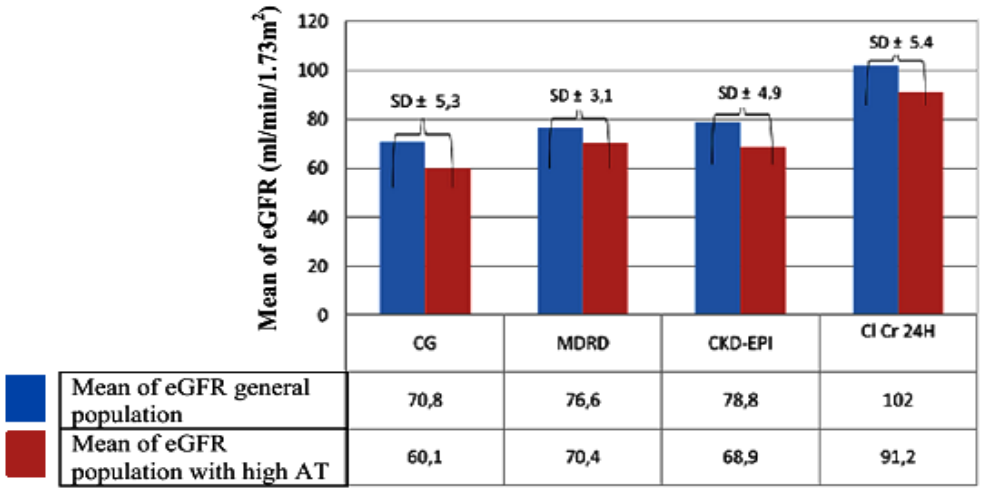

Figure 1: Comparison of GFR estimates between study participants with and without arterial hypertension

Discussion

We found the mean age of diabetics (53±12.5 years) closed to the mean age of population living in low-incomes countries (54 years) where the prevalence of diabetics will double (+107) in 2030 [16]. The prevalence of diabetic people living in rural zone was twice (13%) greater than Sobngwi's study did in 2000 which was around 6% [17]. Diabetic patient still consume alcohol (15%) despite its hyperglycemia effect while tobacco was no noticed [18]. The family history (parent or sibling) of diabetes was no significant (PV=0.07) among the entire participants. Fasting blood sugar (212.1±83.0 mg/dL) was greater than normal range recommended for diabetic under treatment (127 – 144 mg/dL) compared to Feteh et al study [19, 20]. Men presented high fasting blood sugar (237.0±90.5 mg/dL) than women (237.0±90.5 mg/dL). The increasing of fasting blood sugar in men could result from their indoor live style as described by Zeba but, it's no corroborate with Pancha's study did among general population where inactivity was fund high in women compared to men [20, 21]. Serum creatinine in men (1.2±0.2 mg/dl) and women (1.0±0.2 mg/dl) were in normal range recommended for diabetic population [15]. The mean of 24 hours urine volume (1906±710 mL) was in normal range (1000 – 2000 mL) for daily micturition volume for healthy human [22]. No difference in eGFR between women (101.4±40.8 ml/min/1.73m2) and men (104.0±39.3 ml/min/1.73m2) was found using ClCr24 (PV>0.05). All the three methods used to evaluate the kidney function under estimation GFR comparing to ClCr24. CG shown the lowest one estimation (70.8±24.4 ml/min/1.73m^2) while CKD-EPI shown the higher one estimation (78.8±20.4 ml/min/1.73m2). MDRD (70.8±24.4 ml/min/1.73m2) was more closed to the ClCr24 with high correlation and significance results (PV<0.001; X2=0.523); followed by CKD-EPI (PV<0.001; X2=0.511) as demonstrated by Agoons et al [23]. Higher correlation with important significance were found during estimation of eGFR between MDRD (76.6±20.0 ml/min/1.73m2) and CKD-EPI (78.8±20.4 ml/min/1.73m2) (PV<0.001; X2=0.976) and, 92% of similarity were found during the estimation of different stages of CKD, which one prove the closed proximity between those two methods [24, 25]. MDRD method was the important one who presented least similarity with the reference method during estimation of CKD's stages. Arterial tension status influence the estimation of GFR whatever the method used and, diabetic patients with DAT ≥ 90 mmHg and/or SAT ≥ 140 mmHg presented their eGFR greater than whom with low DAT and SAT. As found by Fontelaet at, we noticed that the BMI influence the estimation of GFR in diabetic population using CG (PV<0.001) while nothing with CKD-EPI (PV=0.383) and MDRD (PV=0.567) [25].

Conclusion

This study did in diabetic population has shown the under-estimation of kidney filtration MDRD, CG and CKD-EPPI GFR compared to ClCr24. MDRD and CKD-EPI estimated better the GFR and, MDRD results were more closed to the reference method. Further studies are needed with more participants to evaluate better these 3 methods in Sub-Saharan diabetic population.

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