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USUAL VALUES OF GLOMERULAR FILTRATION RATE BY THE CG, MDRD AND CKD-EPI METHODS IN A SENEGALESE ADULT POPULATION

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ABSTRACT The estimation of the glomerular filtration rate (GFR), whose formulas are usually based on serum creatinine, is a fundamental data in clinical nephrology. The concept of "reference" or usual values adopted by health professionals is essential because of the paucity of research on the usual values of GFR in black Africa. The Modification of Diet in Renal disease (MDRD) and Chronik Kidney disease-Epidemiology collaboration (CKDEpi) equations were determined in non-African populations. Usual values specific to the black African population by the evaluation of the formulas of Cockroft and Gault (CG), MDRD and CKD-Epi must be rigorous and are the subject of this study. The GFR was determined using the CG, MDRD and CKD-Epi formulas in a sample of 233 presumed healthy Senegalese adults (118 men, 115 women). SPSS and Excel 2016 software were used for statistical analysis. A value of $P<0.05$ was considered statistically significant. The determination of the GFR by the Cockcroft method overestimates the CKD values by 10.24 (9.82 - 14.53) with $p=0.001$ and that of the MDRD by 7.47 (5.91 - 9.03) the CKD values with $p=0.001$. For a GFR measurement uncertainty of +/- 10%, the CG and CKD formulas cannot be superimposed with a low correlation coefficient $r = 0.52$ and a coefficient of determination $R^2 = 0.28$; whereas those of MDRD and CKD-Epi are on the other hand superimposable with $r = 0.79$ and $R^2 = 0.63$. Thus, the CKD-Epi formula should be preferred for determining the usual value of GFR in a healthy person.

KEYWORDS : usual value – Senegalese population – CG-MDRD – CKD-Epi

1. INTRODUCTION

Renal function, although the kidneys have other functions, is conventionally evaluated by the glomerular filtration rate (GFR) which corresponds to a volume of plasma completely filtered by the kidneys per unit of time. The GFR is expressed in ml/min indexed and normalized for a body surface of 1.73 m_2, making it possible to compare individuals with each other (1). It makes it possible to define chronic kidney disease (CRD), which corresponds to the presence of structural or renal function abnormalities that have persisted for more than 3 months, as evidenced by proteinuria, hematuria, hydro-electrolyte disorders, abnormalities in renal imaging and/or a GFR < 60 ml/min/1.73m_2.

CKD is classified into five stages according to the level of GFR according to the recommendations of KDIGO "kidney disease - Improving global outcomes 2012" (2).

The determination of the GFR by the dosage of creatinine in the urine requires the collection of 24-hour urine which often poses problems and imposes constraints for a quality collection.

Thus, formulas have been developed to estimate the GFR as recommended by the guidelines of the international expert committees NFKQDOQI (National Kidney Foundation kidney Disease Outcome Quality Initiative) and KDIGO (Kidney Disease Improving global Outcome) (3). These include the formula of Cockcroft and Gault (1976), the simplified MDRD formula (Levey et al., 2009 Modification of Diet in renal disease). and that of CKD-EPI (Chronic Kidney Disease Epidemiology), was recently designed. It is then necessary to evaluate these formulas in our context for a good appreciation of the renal function.

The objective of this work is to determine the usual values of the GFR in order to retain only the most suitable estimation formula for a supposedly healthy Senegalese person.

2. MATERIALS AND METHODS

This is a prospective analytical study, carried out in subjects received for a health checkup during the year 2019.

The samples and the dosage of serum creatinine were carried out in the medical biochemistry laboratory of the Faculty of Medicine of Cheikh Anta Diop University in Dakar.

For each patient we collected: sex, age, weight, height Subjects presumed healthy included in the study benefited from a blood sample after fasting for 8 hours after informed

consent. The dosage of creatinine by the compensated Jaffé method gives with picrate an orange-yellow complex in an alkaline medium. The rate of color formation is proportional to the creatinine concentration in the sample. We used the Biosystems® A15 automated analyzer, the calibration of which is carried out according to the supplier's recommendations.

After calculating the serum creatinine, we estimated the glomerular filtration rate by three different methods which are: the method of Cockroft and Gault, that of Modification of Diet in Renal Disease (MDRD) and that of Chronic Kidney Disease – Epidemiology (CKD). -Epi) taking into account several parameters, namely weight, age, sex.

The CG formula: GFR (ml/min) = [kx (140 – age) x weight] / PCr µmol/L

With: K = 1.23 for men K = 1.04 for women Cockcroft clearance should be normalized on the body surface The simplified MDRD formula called "abbreviated" and comprising four variables: serum creatinine, age, sex and ethnic origin.

GFR (mL/min/1.73 m²) = 175× [PCr (µmol/L) /88.4] –1.154 × age –0.203 × 0.742

Race: 1.21 for Black Americans; 0.763 for the Japanese; 1,233 for Chinese

Table 1: CKD-Epi Formulas in the Black Race

	Serum creatinine value µmol/l (mg/dl)	Formula to use
Women black	≤62 (≤0.7)	GFR = 166 x (creat/0.7)-0.329x (0.993)age
	>62 (>0.7)	GFR = 166 x (creat/0.7)-1.209x (0.993)age
Men black	≤80 (≤0.9)	GFR = 163 x (creat/0.9)-0.411x (0.993)age
	>80 (>0.9)	GFR = 163 x (creat/0.9)-1.209x (0.993)age

The CKD-EPI formula gives, like that of MDRD, an estimate of the GFR; it is normalized on the body surface. The formula is different depending on race, sex and serum creatinine level.

For all the formulas: the age is expressed in years, the weight in Kg, and the Pcr: Serum creatinine. The concordance between the different methods are compared thanks to the regression lines and the method of Bland and Altman. CKD – EPI was taken as the reference method.

3. RESULTS

3.1. Population characteristics

The study population was composed of 233 patients, the average age of our study population was 36 ± 9.41 years with extremes of 21 years and 60 years. A sex ratio of 1.29 shows a male predominance. The 30-40 year age group was the predominant age group (Table I).

Table I: characteristics of the study population

Features	Workforce	Percentage
	233	
Sex		
Man	118	50.60
Women	115	49.40
Age class (years)		
< 30	89	38.20
[30 – 40[	97	41.60
>50	14	6.00

3.2. Mean serum creatinine of the study population

The average and standard deviation of serum creatinine in our study population are 80.24µmol/l ±14.55. This average was significantly higher in men (89.02 ± 13.32) than in women and women (71.23 ± 9.32) with a statistically significant difference Table II).

Table II: Mean serum creatinine in the study population

	Mean +/- SD	Median Mi	n–Max P-value
Creatinemia µmol/l	80.24 +/- 14.55	79.56	53.92 – 110.12
Men	89.02 +/- 13.32	91.49	54.80 – 110.12 0.001*
Women 71.23+/- 9.32	73.37	53.92 – 85.75	

3.3. The average values of the methods for estimating the GFR of the study population

Table III represents the distribution of the mean values of the glomerular filtration rate in (mL/ min/1.73m$_2$) according to the different methods studied.

Table I: statistical description of the usual mean values of the GFR according to the different methods

	Cockcroft	MDRD	CKD
Average (ml/1.73m$_2$) +/-AND	121.83	121.56	111.59
Median	115.91	117.70	108.00

3.3.1 The usual mean values of the GFR according to Cockcroft and Gault in according to age and gender

The GFR according to CG is higher in women and gradually decreases with age and sex. However, this decrease is observed up to the age of 50 in men (figure 1).

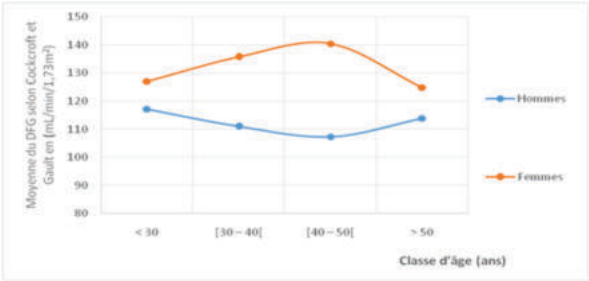

Figure 1: Usual mean values of GFR according to CG according to age and sex

3.3.2 Usual average GFR values according to MDRD according to age and sex

The mean and standard deviation of the GFR according to the MDRD formula of our study population were 121.56/min/1.73m² +/- 27.06.

This average was higher in women than in men with a statistically significant difference. The usual values according to MDRD were higher at the extreme ages in both sexes.

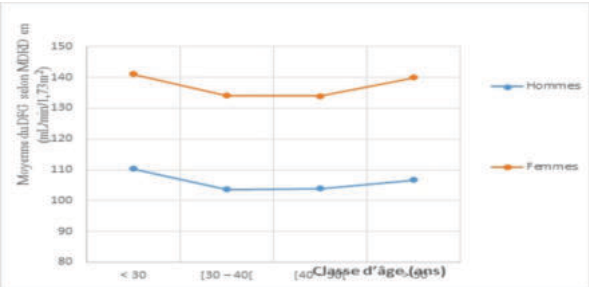

Figure 2: Usual average GFR values according to MDRD

3.3.3 Usual mean values of the GFR by the CKD methodin terms of age and sex

The mean and standard deviation of the GFR according to the CKD method of our study population was 111.59 ml/min/1.73m². +/- 16.33ml/min/1.73m². This average usual value was higher in women than in men and, like the MDRD formula, higher at extreme ages in both sexes (Figure 3).

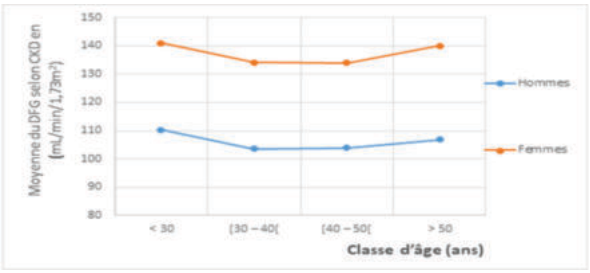

Figure 3: Usual mean values of the GFR by the CKD method as a function of age and gender

3.4 Evaluation of the concordance of the different GFR calculation methods

The agreement between the two methods**ckd-ckd and ckd-Cockcroft**concerns only 28% of patients (figure 4).

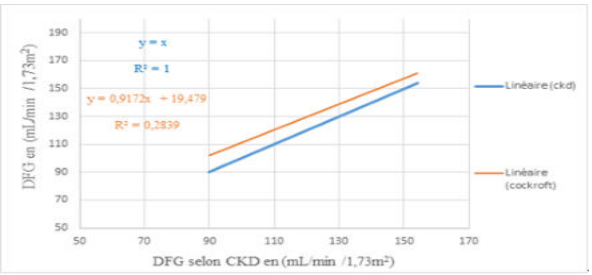

Figure 4: Regression lines of the ckd-ckd and ckd- equations Cockcroft

Also, the determination of the GFR by the Cockcroft method overestimates by 10.24 (9.82 - 14.53) the CKD values significantly (p=0.001) with a bias (95% CI) of 10.18 (Figure 5).

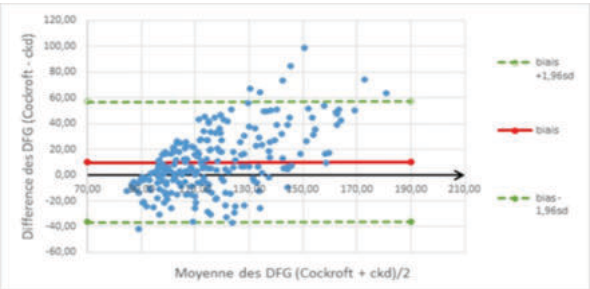

Figure 5: Bland and Altman plot for Cockcroft and ckd

A 63% concordance between the formulas**CKD-CKD and CKD-MDRD**is found between the two methods (Figure 6).

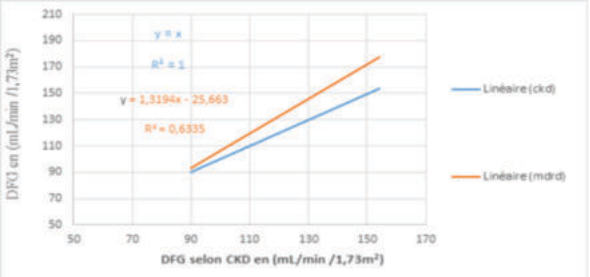

Figure 6: Regression lines of the CKD-CKD and CKD-equations MDRD

Determining the GFR by the MDRD method overestimates the CKD values by 7.47 (5.91 – 9.03) with a p=0.001 and a bias (95% CI) of 7.47 (Figure 7).

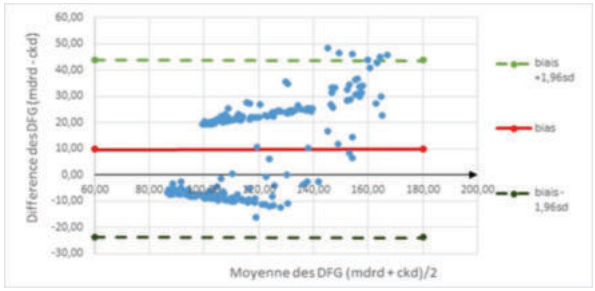

Figure 7: Bland and Altman plot for CKD-MDRD

Clinically, with a bias of 12.18, we have no clinical agreement with a p<0.05 between the two methods of CG and CKD measurement for a measurement uncertainty of +/-10%. So in practice, CG and CKD cannot be superimposed in the same person.

On the other hand, with a bias of 7.47 we have clinical concordance with a p>0.05 between MDRD and CKD-Epi for a measurement uncertainty of +/-10%. Therefore, they can be used for the same person.

4. DISCUSSION

The management of any pathology requires knowledge of the variations of biological markers which allow good clinical management.

Creatinine measurement based on 24-hour urine collection is often subject to multiple errors; formulas have been successively developed based on serum creatinine clearance. This is the formula of Cockroft and Gault, MDRD and CKD-Epi. The objective of this work is to determine the usual values of the GFR using the formulas of Cockcroft and Gault, of the MDRD and of the CKD-EPI in a black Senegalese population and to make a comparison between the three methods.

Our population consists of 233 subjects. The average age is 36 years with a male predominance (50.60%) The age group [31-40] was the most represented, followed respectively by that of [21-30].

The average age of our population is relatively younger 50.6 ± 10 compared to that of John B. Eastwood (12) which is 54.7 ± 11.2. Most studies of GFR have been done in middle-aged adults.

On the other hand, the study of E. YAYO made in Côte d'Ivoire had a younger population 30 ± 4 (5) In addition, the average serum creatinine for our study population is 80.24+/-14.55. This average is clearly higher in men (89.02 µmol/l) than in women (71.23 +/- 9.32 µmol/l) with a statistically significant difference.

However, a slight and progressive increase in serum creatinine is observed according to age groups. It should be noted that the concentration of creatinine is above all dependent on muscle mass; 1-2% of muscle creatine is converted to creatinine (6). The differences observed in creatinine concentrations between men and women, between old and young people, between subjects of different ethnic groups could be explained, in the absence of kidney disease, by the differences in muscle mass between these groups.

Evidenced by the fluctuations observed in various publications such as those of P. JOUBAUD in 2004 (7) with an average serum creatinine higher than ours (137 µmol/l in men against 104 µmol/l in women), John B Eastwood (12) in 2010 in Ghana with values lower than ours (79 µmol/l ±17.4). The average creatinine in humans was 89.7 µmol ± 18.3 against

72.5 µmol/l ± 13.3) and also the case-control study by E .H .M Ndour et al. of 2015 (9) with serum creatinine values of 95.34 µmol/l ± 18.94 slightly higher than ours.

However, it should be emphasized that the study population of B. Eastwood's work was composed of both healthy adults and adults with pathologies such as diabetes and arterial hypertension.

However, the JAFFE method used for the creatinine assay cannot be excluded from these fluctuations due to lack of specificity with the interference of pseudochromogens. which led to the "compensated Jaffé" method tending to minimize these (6) used by most authors.

Similarly, Jaffe-type colorimetric methods tend to very slightly underestimate serum creatinine at high concentrations with a bias of less than 1% on average, in addition to the uncertainty of the reference method (itself from the order of 1%) (8).

The results of the GFR estimation according to Cockcroft and Gault (CG) showed that the usual mean value of the GFR according to CG of our study population was 121.83 ml/min/1.73m^2 (+/- 28.10).

According to the work of Ndour et al. (9) the value of the GFR by the formula of Cockroft and Gault (9) was 84.88 ml/min/1.73m^2 ±20.09 lower than the average of our population.

The same is true for the study by DENALAYE et al. (10) which demonstrates an average GFR of 73 ± 37 ml/min/1.73m^2 (10) A slight but progressive decrease in GFR according to age groups was observed.

This decline in GFR observed as a function of age corroborates the results of the study by P. JOUBAUD (7) .

In addition, GFR measurement by MDRD found a usual mean value of 121.56 ml/ min/1.73m^2 (+/- 27.06). This average was higher in women (131.54 +/- 27.99ml/min/ 1.73m^2) than in men (105.95+/-21.77ml/min/1.73m^2) with a statistically significant difference.

Some studies, on the other hand, have found values lower than ours, such as that of John B. Eastwood et al. (12), 102.3 ml/min/1.73m^2 ±22.8 or Ndour et al.(9) was 89.67 ml/min/1.

According to several authors such as P.Delanaye, the MDRD formula tends to underestimate the GFR in high values (60 ml/min/1.73m^2) (13).

The usual average GFR value according to CKD-Epi of our study population was 111.59 ml/min/1.73m^2. This average was higher in women (112.15 ml/min/1.73m^2) than in men (111.05+/-16.15 ml/min/1.73m^2) with a statistically significant difference.

According to the study by John B. Eastwood et al. the average GFR estimated by the CKD-EPI equation was 103.1 ml/min/1.73m^2 ±18.7 with a predominance in men (103.6 ml/min/1.73m^2 ±18.2 versus 102.8ml/min/1.73m^2 ±19 (12). In the study by Ndour et al.(51) the mean was 91.18+/-18.81, slightly lower than ours.

Table II: usual mean values of the GFR in ml/min/1.73m^2

Authors	Country	Cockroft	MDRD	CKD
Our study Workforce 233	Senegal (2022)	121.83	121.56	111.59
E. YAYO Workforce 254	Ivory Coast (2017)	106	111	118
Ndour	Senegal (2015)	84.88	89.67	91.18
Workforce 58				
Eastwood	Ghana (2010)	84.1	102.3	103.1
Workforce 944				

The large difference observed in the averages of the GFR according to the studies across different countries can also be explained in addition to the method of analysis by the characteristics of the study population.

The comparative analysis of the three methods confirms the recommendation of the HAS because CKD – Epi seems to be the most reliable method for calculating the GFR even if MDRD and Cockroft can be used.

According to clinical judgment, the CKD-Epi formula is probably one of the best serum creatinine-based equations that everyone agrees on.(14)

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CONCLUSION

After the estimation by the formulas of CG, MDRD and CKD-Epi, usual values of GFR higher than 100ml/mn/m were objectified.

The CKD–Epi formula appears to be the most reliable method for calculating GFR even though MDRD and Cockroft can be used.

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