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Research Article

eGFR-THE BETTER PREDICTOR IN CKD IN INDIAN POPULATION

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ABSTRACT

To compare S. Creatinine & estimated GFR the glomerular filtration rate (GFR) by using Cockcroft-Gault (CG) and Modification of Diet in Renal Diseases (MDRD) formula in diabetics and hypertensive is the best overall index of renal function in health and disease. Insulin clearance is the gold standard but since it is time consuming and is invasive technique it is poorly specified.

The study was conducted retrospectively reviewed individuals in a hospital on A total number of 320 cases from dec 2013 to dec 2014 in them 120 cases of type II DM, 120 cases of hypertensives and 100 cases of both type II DM and hypertensive patients of age group between 20-70Years who had a Macrovascular complication chronic kidney disease, according to their stages of CKD, as stages I,II,III,IV,V. THE Serum Creatinine was calculated and compared with Cockcrost-Gault and MDRD approaching Annai Medical college & hospital, Pennalur, Sriperumbadur, Chennai.

GFR Estimation (e GFR): MDRD study Equation (GFR ml/min/1.073m2 r GFR = 186 × (S Cr) -1.154 × (age)-0.203 × (0.742 if female) × (1.210 if African American) Cockcrost-Gault (CG ml/min0 = (140-age) × weight /0.85 (if females)/ (SCr Mean ±SD of S. Creatinine, MDRD and cock craft & Gault S.Creatinine increased and eGFR is decreased in stages III, IV,V of CKD when Compared to stages I , II. CKD is taking under stages comparing with eGFR ,MDRD equation and Cockcroft-Gault formula .see the statistical data eGFR is high the serum creatinine is decreased ,s.creatinene increased eGFR is decreased but statically significance in s.creatinine is the p 0.01 ,MDRD p value <0.001 and Cockcroft-Gault p ≤0.05. This shows us that MDRD p <0.001 is highly significant than S.Creatinine and Cock craft & Gault.

MDRD study is most significant than Cock graft & gaults S- Creatinine in predicting the risk and for instituting appropriate therapy to reduce the incidence of the chronic kidney disease e GFR is better predictor

Keywords: S. Creatinine, glomerular filtration rate, Modification of Diet in Renal Diseases (MDRD), Cockcroft-Gault.

INTRODUCTION

Chronic kidney disease is defined as kidney damage or a glomerular filtration rate (GFR) Less than 60 ml/ 1.73 m2 for 3 months[1] the glomerular filtration rate (GFR) is the best overall index of renal function in health and disease. Insulin clearance is the gold standard but since it is time consuming and is invasive technique it is poorly specified. [2] The normal mean value for GFR in healthy young men and women is approximately 130 ml/min per 1.73 m2 and 120ml/min per 1.73 m^2 and declines by approximately 1ml/min per 1.73m^2 per year after 40 years of age. Serum creatinine concentration is affected by alteration is renal handling, metabolism of creatinine and methodological interferences in its measurements may have profound impact. His e GFR can be estimated from serum creatinine concentration, age, sex, ethnicity, and body size. [3] .To facilitate detection of chronic kidney disease The 4-variable modification of diet in Renal Disease (4-v MDRD) and Cockcroft-Gault equations are commonly used for estimating glomerular filtration rate (GFR).[4] This 4-variable (MDRD) equation is currently the most widely used and best studied. GFR cannot be measured directly. The urinary or plasma clearance of an ideal filtration marker, such as inulin iothalamate or iohexol, is the gold standard for the measurement of GFR.[5] However; this is cumbersome and not used in clinical practice. Instead, serum levels of endogenous filtration markers, such as

creatinine, have traditionally been used to estimate GFR, along with urinary measurements in some cases. However, serum creatinine alone is not an adequate marker of kidney function. The National Kidney Disease Education Program (NKDEP) of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), National Kidney Foundation (NKF), and American Society of Nephrology (ASN) recommend estimating GFR from serum creatinine. Two commonly used equations are the Modification of Diet in Renal Disease (MDRD) Study equation and Cockcroft- Gault equation.[6, 7] Both equations use serum creatinine in combination with age, sex, weight, or race to estimate GFR and therefore improve upon several of the limitations with the use of serum creatinine alone. The Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation is a new equation based on serum creatinine. [8] The Cockcroft-Gault formula was developed in 1973 using data from 249 men with creatinine clearance (CCr) from approximately 30 to 130 mL/m2. It is not adjusted for body surface area.CCr={((140-age) x weight)/(72 SCr)} x 0.85 if female where CCr is expressed in milliliters per minute, age in years, weight in kilograms, and serum creatinine (SCr) in milligrams per deciliter.

The National Kidney Disease Education Program led the process of standardization of the creatinine assays in clinical laboratories. This was completed in 2010. After standardization, most clinical laboratories' serum creatinine results declined by 0.1-0.3 mg/dL. The CKD-EPI equation was developed for use only with standardized values. The MDRD Study equation has been re-expressed for standardized serum creatinine. Use of the re-expressed MDRD Study equation with standardized serum creatinine improves the accuracy of GFR estimates using that equation. The Cockcroft-Gault equation has not been re-expressed for use with standardized serum creatinine.GFR estimates using the Cockcroft-Gault equation with standardized serum creatinine will generally be higher and less accurate than with non-standardized creatinine.[9] Kidney disease can be a particularly devastating complication, as it is associated with significant reductions in both length and quality of life [10, 11] A variety of forms of kidney disease can be seen in people with diabetes, including diabetic nephropathy, ischemic damage related to vascular disease and hypertension, as well as other renal diseases that are unrelated to diabetes [12, 13]. In this chapter, we will discuss how to screen for and diagnose chronic kidney disease (CKD) in people with diabetes, how to treat them with an aim to slow progression of CKD and discuss the impact of CKD on other aspects of diabetes management. The earliest stage of diabetic nephropathy is hyper filtration, where the glomerular filtration rate (GFR) is significantly higher than normal. Identification of hyper filtration is not clinically useful, as it is difficult to determine from routine testing.

During the early stages of diabetic nephropathy, the rate of loss of renal function is relatively slow (1 to 2 mL/min/1.73 m^2 per year) and not impressively higher than what is seen in the general population (0.5 to 1 mL/min/1.73 m^2 per year). However, late in the overt nephropathy phase, the rate of decline of renal function can accelerate (5 to 10 mL/min/1.73 m^2 per year). Thus, significant renal dysfunction is not usually seen until late in the course of diabetic nephropathy[14].

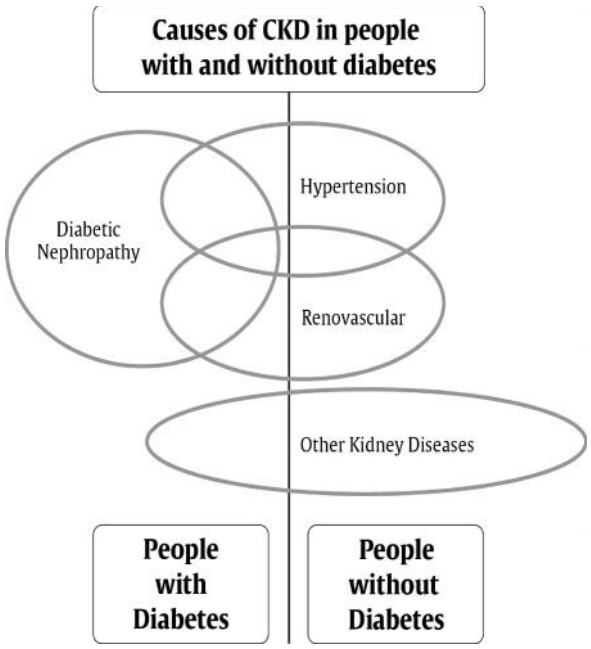

Figure 1: Causes of chronic kidney disease (CKD) in people with and without diabetes.

The inclusion of age and gender, in this equation was to simply the endogenous creatinine production, which does vary with age and by gender.

Use of e GFR estimates:

1) Detection of chronic kidney disease

2) Monitoring progression of chronic kidney disease
3) Evaluation and management of complications
4) Medications
5) Screening test

Diabetic nephropathy occurs due to glomerular hypertension, hyper filtration.

Micro albuminuria is the first manifestation of injury due to the glomerular filtration barrier Hypertensive nephropathy occurs due to hemodynamic stress causing massive fibrinoid necrosis of afferent arteriolar glomeruli, thrombotic angiopathy, acute renal failure & nephritic urinary sediments

MATERIAL & METHODS:

The study was conducted on 100cases of type II DM, 100 cases of hypertensives and 120 cases of both type II DM and hypertensive patients of age group between 20-70 Years, approaching Annai Medical college & hospital, Pennalur, Sriperumbadur, Chennai. GFR Estimation (e GFR): MDRD study Equation (GFR ml/min/1.073m2 r GFR = 186 × (S Cr) -1.154 × (age)-0.203 × (0.742 if female) × (1.210 if African American) Cockcrost-Gault (CG ml/min0 = (140-age) × weight /0.85 (if females)/ (SCr)) Diabetes was defined by FBS, PLBS and HbA1c levels. Hypertensives were classified if they had a mean blood pressure ≥ 140mm Hg Systolic or 90mm Hg diastolic or with history of under treatment. Plasma glucose was measured by Glucose-oxidize method .Serum creatinine were measured by using a kinetic alkaline picrate assay. A blood sample is taken by syringe from a vein of hand. Depending on the formula used, a person's age, sex, race, height, and weight may also be needed. GFR is expressed in /min/1.73 m^2, SCr is serum creatinine expressed in mg/dL, and age is expressed in years. The data was analyzed by graph phad prism.

RESULT:

Hypertension was considered with systolic 140 mm Hg or 90mm Hg diastolic. Plasma glucose was measured by Glucose-oxidize method .Serum creatinine were measured by using a kinetic alkaline picrate assay .S.Creatinine increased and eGFR is decreased in stages III, IV,V of CKD when Compared to stages I , II.

CKD is taking under stages comparing with eGFR ,MDRD eqation and Cockcroft-Gault formula .see the statistical data eGFR is high the serum creatinine is decreased S. creatinene increased eGFR is decreased but statically significance in s.creatinine is the p 0.01 ,MDRD p value <0.001 and Cockcroft-Gault p ≤0.05

DISCUSSION:

This pragmatic study comparing the Cockcroft-Gault, MDRD, and CKD in a clinical setting showed that overall mean bias was smallest for MDRD. The highest accuracy, however, was reached with CKD and MDRD. As expected, CKD estimated GFR closest to the directly measured GFR in patients with a GFR of ≥90 ml/min per 1.73 m^2, whereas MDRD remained best when GFR ranged from 15 to 29 ml/min per 1.73 m2. Differences in accuracy between MDRD and Cockcroft-Gault, however, were small and highly statistically significant. Our finding that the MDRD formula gave the best overall accuracy and agreement after classification in subgroups of GFR is in line with the original publication on this formula [15]. The present data add that the performance of the MDRD formula is dependent on age and GFR. That the relation between mean biases of the formulas over subgroups of GFR was not linear. Mean bias was largest in those with a GFR in stage 2 CKD. Most studies showed a larger bias in stage 2 than in stage 3 CKD for Cockcroft-Gault or MDRD [16, 15] which is in contrast to our findings. The relatively small number of patients in the subgroups in our study as well as in some of the afore mentioned studies [16,14] could be an explanation for this difference; however, studying the accuracies over the subgroups, all formulas showed a pattern in which the accuracies became smaller per GFR subgroup, which is in line with others [16,17] Furthermore, the regression analysis that was based on the absolute bias per patient did show a linear relation between the GFR and the absolute bias.

In this study, we found no significant differences in accuracies between MDRD and Cockcroft-Gault formulas within subgroups. It could be that the number of patients within subgroups was too small to detect these differences; however, most subgroups were large enough to measure a difference of the MDRD and Cockcroft-Gaul formulas. This makes it more likely that the accuracy of MDRD and Cockcroft-Gault are indeed highly in line with each other; however, in the elderly and in those with a low body weight or BMI, Cockcroft-Gault remains a good alternative. Our finding that the MDRD or the seems to be the best option for young patients is in agreement with the results of Donadio et

Table 1: Comparison of baseline characteristics and other biochemical parameters between study groups.

Number of subjects	320
Sex (M/F) %	194/126
Age (In Years)	53±11.7
HbA1c (%)	8.04 ± 0.643
FBS (mg/dl)	190.59 ±37.48
PP2BS (mg/dl)	293.04 ±30.1
Total Cholesterol (mg/dl)	198.08 ± 40.69
Triglycerides total (mg/dl)	139.22 ±44.43
Blood Pressure (mmHg)	156 ± 10/85 ± 15

Table 2: Mean ±SD of S. Creatinine, MDRD and cock craft & Gault.

CKD Stages	e GFR	S.creatinine		MDRD		Cock craft &Gault	
		Mean	SD	Mean	SD	Mean	SD
I	≥90	0.8	0.14	92.1	4.6	95.2	4.2
II	60-89	1.2	0.11	62.3	6	77	11.6
III	30-59	1.74	0.31	43	7.1	52.1	8.6
IV	15-29	2.8	0.8	27.2	5.7	27.5	6.2
V	<15	6.23	2.25	9.5	3	12.4	4.8

S. Creatinine increased and eGFR is decreased in stages III, IV,V of CKD when Compared to stages I , II.

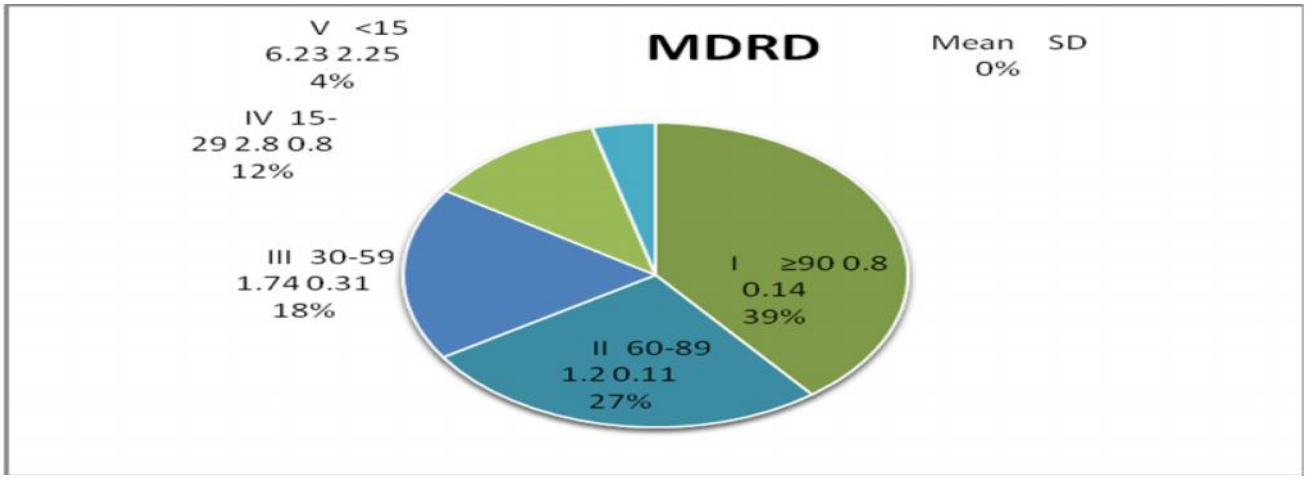

Table: 3 't' test & P value of S.Creatinine , MDRD and Cock craft & Gault

S. Creatinine		MDRD		Cock craft & Gault	
t-test	P value	t-test	P value	t-test	P value
10.0472	0.01	17.62727	0.001	8.047494	≤0.05
12.3588	0.01	25.95559	0.001	21.54112	≤0.05
11.013	0.14	39.62551	0.001	40.42962	≤0.05
10.7719	0.01	67.26349	0.001	58.05704	≤0.05

This t test shows us that MDRD is highly significant than S. Creatinine and Cock craft & Gault.

al. [18]. Using these formulas in the elderly is also supported by others [23, 19], although not by all [17, 20]. This difference might be caused by small differences in bias and precision between the formulas in the elderly, because all formulas had smaller absolute biases in these subjects. For Cockcroft-Gault, a relation between its bias and age has been shown before [19, 21, and 22].

The influence of body composition on the performance of the formulas can be assessed by studying the influence of body mass or BMI. Our results showed that the absolute bias of Cockcroft-Gault was dependent on both of these parameters. For the MDRD formulas, this relation was statistically significant; however, the regression analysis did show point estimates suggesting a smaller absolute bias in patients with a higher body weight or BMI. The relation of the absolute bias with body weight and BMI is surprising given their normalization for BSA. In line with our results, others also found the estimation of Cockcroft-Gault to be more dependent on body weight or BMI than MDRD [16, 22, and 15]. The influence of BMI on the bias of Cockcroft-Gault has been described before [15, 14], although not all studies found this relationship [17, 23].

This study has its limitations. Ideally, we would have measured the plasma creatinine on the same day the GFR measurement was performed in all patients. A plasma creatinine measurement on the same day as the GFR measurement was available for 35 (18%) patients, because of the retrospective data collection; however, a sensitivity analysis of patients with an available plasma creatinine value within 14 days of the GFR measurement (n = 100 [75%]) did not change our conclusions (data not shown). Furthermore, the stable state of the patients was judged by the clinician who requested the GFR measurement. For 35 (53%) subjects, a previous plasma creatinine value was available within 3 months of the GFR measurement (mean 1.24 mg/dl; SD 0.65 mg/dl). The difference between this plasma creatinine and the one used in our study was 0.002 mg/dl (SD 0.14 mg/dl). Given the small differences between the previous plasma creatinine and the used one, we conclude that indeed only stable patients were selected. Another limitation of this study is the relatively limited numbers of patients in the subgroups. This was mainly due to the absence of data on height. We needed this parameter for the normalization of Cockcroft-Gault and measured GFR for BSA to make a valid comparison, because MDRD are expressed that way; however, we were able to include a relevant number of patients, sufficient to allow stratification. Some of the studied parameters were correlated, such as age and GFR. We chose not to correct our findings for these influences because this describes clinical practice in which age and GFR are also correlated.

A strong feature of this study is that we were able to compare both the two most frequently used and the newest equations to estimate kidney function in one heterogeneous cohort against an excellent gold standard method to measure GFR (24). We were able to study the influence of measured GFR, gender, age, body weight, and BMI on the performance of the formulas by stratification on these parameters.

In conclusion, the absolute bias of all formulas is influenced by age. The MDRD formulas are also influenced by GFR, and the Cockcroft-Gault equation is additionally influenced by body weight and BMI. In general, MDRD gives the best estimation of GFR, although the performance is close to that of MDRD.

MDRD study is most significant than Cock graft & gaults S-Creatinine in predicting the risk and for instituting appropriate therapy to reduce the incidence of the chronic kidney disease e GFR is better predictor than serum creatinine in CKD. It is due to that in patients with CKD, extra renal clearance in response of creatinine will increase plasma creatinine in response to falling GFR. So plasma creatinine will not detect patients with stage 2CKD and will also fail to identify stage 3CKD. In clinical practice physicians should be aware of these differences and take them into consideration when they estimate renal functions.

MDRD adavantage over Cockcroft-Gault equation was that it was developed and validated in large population, included both European-American and Afico-Americans and does not require patient weight and it was validated against an iothalamate clearance (silver standard)and reported GFR is corrected for BSA.

Disadvantages: It is not useful in people below 18yrs and older than 70 years, pregnant, very obese, very muscular, have any other serious illness, acute renal failure. eGFR is cost effective and inexpensive, and non invasive technique

than the plasma creatinine. Other parameters used for CKD, along with plasma creatinine are 24 hr protein, S. total protein, 24 urinary creatinine, Protein-creatinine ratio can be measured to asses CKD.

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