PERFORMANCE OF RENAL FUNCTION PREDICTION EQUATIONS IN A GROUP OF HOSPITALIZED CHRONIC KIDNEY DISEASE PATIENTS

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Summary

Chronic kidney disease (CKD) has evolved as a silent killer if not managed in its early stage. Measurement of perfect creatinine clearance is mandatory to prepare a clinical action plan for the patients of CKD of different stages. With a view to select a better formula which is cheap and easy-to-perform we designed the present cross-sectional study. The study was conducted in the Departments of Biochemistry and Nephrology, Chittagong Medical College & Hospital, Chittagong. We enrolled 60 adult patients of both sexes suffering from chronic kidney disease without any cardiovascular instability and renal replacement therapy. The study compared the most widely used equations to measure creatinine clearance - the Cock Croft-Gault (CG) and the simplified Modification of Diet in Renal Disease (MDRD) with conventional creatinine clearance. The mean ($\pm SD$) age of the patients was 52.22 (± 13.39). Among the 60 participants 45(75%) were male and 15 (25%) were female. Most of the patients were from rural area (60%), average socioeconomic condition and were illiterate (48.3%). 50% ware Hypertensive and only 20 % ware diabetic. The mean ($\pm SD$) creatinine clearance (CrCl) measured by conventional method, Cockcroft and Gault equation and MDRD equation were 11.4 (± 13), 12.9 (± 15.7) and 12.3 (± 13.8) ml/min respectively. The difference of the mean between CrCl (CG) and CrCl (MDRD) was not significant ($p>0.05$).Though these formulae overestimate the creatinine clearance rate to some extent, linear regression analysis showed that both the equation significantly (<0.01) predict the conventionally measured creatinine clearance from our study. So, it can be concluded that CrCl (CG) and CrCl (MDRD) equations can predict the conventionally measured creatinine clearance but both of them overestimate the conventionally measured creatinine clearance.

Key words: chronic kidney disease (CKD); creatinine clearence (CrCl); cock croft-gault (CG) formula; modification of diet in renal disease (MDRD) equation

Introduction

Chronic kidney disease (CKD) is a recently recognized public health burden[1]. It poses a large and growing morbidity, mortality and financial burden. The prevalence and incidence rate of chronic (CKD) patients are continuously increasing all over the world including Bangladesh. Untreated CKD may progress to End stage renal disease (ESRD) and is associated with increased cardiovascular morbidity and mortality and all-cause mortality. Evidence suggests that some of these adverse outcomes can be prevented or delayed by early detection and management of CKD[2]. To level off these incidence rates, various initiatives, such as The National Kidney Disease Outcomes Quality Initiatives (K/DOQI) and European Best Practice Guidelines, recommended the use of creatinine based prediction equation to estimate the GFR from serum creatinine[3]. In adults the most widely used formulae are Modification of Diet in Renal Disease (MDRD) study population equation and Cockcroft and Gault formula (CGF)[4,5].

The glomerular filtration rate (GFR) is traditionally considered the best overall index of renal function in health and disease. Because true GFR (by radio-Iohexol) and 24hr creatinine clearence(CrCl) are difficult to measure in clinical practice most clini-cians depend on creatinine based above formulae dependant on some demographic and anthropometric values (age, sex, and body size)[6]. The current Kidney Disease Outcomes Quality Initiatives (K/DOQI) have provided clinicians to stratify CKD into different stages by estimating GFR with these formulas which are inexpensive, reliable, and widely available[7]. However, theses prediction equations have not been validated in subjects with

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normal or supra-normal GFR [8]. McLigeyo tried to evaluate these formulas among the subjects with a wide range of GFR (3.5-145 ml/min). He considered the formula of Cockcroft and Gault (CG) was the best and MDRD equation is comparable [9].

Considering all these references this study was aimed and designed to measure performance of estimated GFR (eGFR) formula (CG and MDRD) in comparison to conventional creatinine clearance in hospitalized CKD patients in Chittagong Medical college Hospital. This will verify at least partially the value of these cheap cost-effective methods in screening CKD patients in country like Bangladesh with limited resources.

Materials and methods

This is a Cross sectional comparative observational study between February 2007 and April 2008. All patients (sixty)suffering from chronic kidney disease admitted in the Department of Nephrology, Chittagong Medical College Hospital, Chittagong during this period were enrolled. Inclusion criteria were i) age >18 years <65 years and ii) Participants who were willing to give written informed understood consent. Patients unwilling to give written informed understood consent and Patients having renal transplantation or dialysis were excluded. The study was approved by the ethical committee of Chittagong Medical College Hospital (CMCH), Chittagong. Written informed consent was taken from all patients. A structured case record form including Sociodemographic variables (Age, Sex, Occupation, Socioeconomic condition, inhabitant, and educational status) and anthropometric variables (weight, height) was prepared. CKD was diagnosed by history, history of Hypertension [HTN], Diabetes mellitus [DM], past history of Glomerulonephritis(GN)and obstructive uropathy(OUP), Ultrasonographic features (small kidneys, increased echoigenicity and/or cortical thinness) and high Serum creatinine(S.Cr) persisting for ≥3 months. Fasting blood sugar (FBS) and 24 hr creatinine clearence (CrCl) were measured. Body weight was measured in kilograms by standard floor-mounted weighing machine. Blood pressure >140/90mm Hg was taken as HTN. Blood sample was collected after taking proper aseptic precaution. A fasting plasma glucose level of >7.0 mmol/L and 2 hours post prandial plasma glucose level of >11.1 mmol/L were taken as diabetes[10]. 24 hours' urine was collected by

the patients with the help of trained nurses. Volume of the 24 hours' urine was measured and recorded. Urine sample was analyzed for creatinine level. All the biochemical tests were done in the Department of Biochemistry, Chittagong Medical College, Chittagong. Patients were properly prepared for ultrasonogram of renal system. Patients were sent for ultrasonogram with full urinary bladder. Ultrasonogram was done in the Department of Nuclear Medicine, Chittagong Medical College, Chittagong. All data were compiled and analyzed by using the "Statistical Package for Social Sciences (SPSS)," Version-12 for Windows.

Formula used in data analysis:

1. CrCl (ml/min)

$$= \frac{\text{Urinary creatinine level (mg/dl) x 24 hours Urine volume (ml)}}{\text{Plasma creatinine level (mg/dl) x 1440 (min)}}$$

2. CrCl by Cockcroft and Gault formula (ml/min)

$$= \frac{[140\text{-age (year)] x weight (kg) x (0.85 if female)}}{[72 \text{ x Plasma creatinine level (mg/dl)]}}$$

3. CrCl by MDRD study equation (four variable)[6]

$= 186.3$ x Plasma creatinine level $(\text{mg/dl})^{-1.154}$ x age $(\text{year})^{-0.203}$ x (0.742 if female) ml/min

Results

The present cross-sectional study was carried out in the department of Biochemistry and Nephrology, Chittagong medical college, Chittagong during the period of February 2007 to April 2008. 60 patients suffering from CKD without cardiac instability and predialysis were enrolled. We hypothesized that CG and MDRD study formula may predict the creatinine clearance in patients with chronic kidney disease and we analyzed the data by computer based software 'SPSS' for windows verson 12. Data were expressed as mean ± SD. Confidence level was fixed at 95% level and 'p' value of 0.05 or less was considered significant. Student't' test for quantitative (continuous) variables, chi-square test for categorical variable and correlation and regression analysis were done where applicable. Scattered plot chart with best fitting line was drawn to show association.

Table I shows that two-third of patients are below 60 years, mostly male (75%), one-tenth from affluent family, 60% from rural area, and half are illiterate.

Table II shows that almost half of patients had HTN, oedema and anaemia but incidence of DM and ESRD each is equal to or less than one-quarter.

Table III shows that 54 out of 60 patients had features of CKD by USG.

Table IV shows that Creatinine clearence by CG formula and MDRD equation predict the conventionally estimated creatinine clearance but both of them overestimate it to some extent. But the difference of the means between CrCl (CG) and CrCl (MDRD) is not significant (p=0.234 ;> 0.05).

Fig 1 and 2 shows relation shows correlation between conventional with CG and Conventional with MDRD equation respectively. They are strongly correlated. As shown by adjusted R^2 value (>0.9)

Table I : Demographic variables (n=60)

Characteristics	frequency	Percentage
Age (Years)		
<60	41	68.33
>60	19	31.67
Sex		
Male	45	75
Female	15	25
Socio-economic status [α, γ]		
Poor	18	30
Average	35	58.33
Affluent	7	11.67
Inhabitant		
Rural	36	60
Urban	24	40
Educational status [β]		
Illiterate	29	48.33
Literate	31	51.67

α Poor = Family income < BDT 5000/month
Average = Family income BDT 5000-15000/month
Affluent = Family income > BDT 15000/month.
β Illiterate= who cannot read or write
γ Referance-11

Table II : Clinical characteristics of Patients (n=60)

Characteristics	frequency	Percentage
Anaemia	25	41.7
Oedema	36	60
HTN	30	50
DM	12	20
ESRD	15	25

Table III : Distribution of patients by Ultrasonographic findings (n=60)

	Frequency	Percent
Echogenic Kidneys	39	65
Bilateral small kidney	11	18.3
Bilateral hydroureter with thin cortex	4	6.7
Enlarged prostate but no increased Echogenicity or CM [β] undifferentiating	6	10.0

CM [β] = Cortico Medullary

Table IV : Showing creatinine clearance of the patients measured by different method [λ]

	CrCl (con) ml/min (±SD)	CrCl (CG) ml/min (±SD)	CrCl(MDRD) ml/min (±SD)	P value
Mean(±SD) (ml/min)	11.4(±13)	12.9(±15.7)	12.3(±13.8)	0.234
Minimum	2.67	3.06	3.15	
Maximum	73.73	91.48	72.93	

[λ] CrCl (con) = Creatinine clearence by conventional method
CrCl (CG) = Creatinine clearence by Cock-croft Gold equation
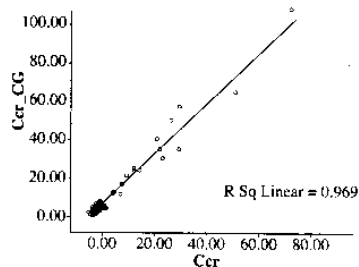CrCl (MDRD)= Creatinine clearence by MDRD equation

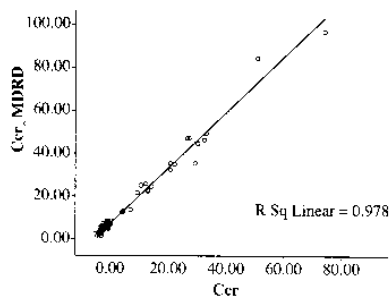**Fig 1:** Scattered plot showing CrCl (con) and CrCl (CG) with best fitting line

Fig 2: Scattered plot showing CrCl (con) and CrCl (MDRD) with best fitting line

Discussion

The present study enrolled 60 patients suffering from chronic kidney disease. We recruited the patients suffering from chronic kidney disease without any cardiovascular instability and renal replacement therapy. Patients aged below 60 years suffer most (68%). This is consistent with the work of Poggio et al. and Jafar et al.[2, 7].

Among the 60 participants 45(75%) were male and 15 (25%) were female. Poggio et al.[7] found 41.9% female gender and Jafar et al.[2] found 54.2% male gender. Both of these findings are inconsistent with our finding. This inconsistency may be due to demographic variation, smaller sample size of our study or the fact that female get less access to treatment in our country. Our study showed only 11% come from affluent family. Jafar et al.[2] also showed 54.2% of sufferers were from low socioeconomic condition. This discrepancy may be due to the difference in operational definition of socioeconomic status in different countries. Most of the patients of CKD are inhabitants of rural area (60%) and are illiterate (48.3%) this finding is similar with Jafar et al.[2] who showed most of the sufferers (76%) are illiterate.

Though, hypertension and diabetes mellitus, the two important risk of CKD are prevalent in urban population, they are suffering less from CKD as evident by the present study. The explanation may be that 80% people of the country are residing in the rural area. So the proportion of patients with CKD coming from rural area will be higher than urban area. Anaemia and oedema were presenting complains in 41.7% and 60% of patients respectively. It is well established that anaemia and oedema may be presenting symptoms of CKD. Levey et al[12] demonstrated that almost half of their patients had mean arterial pressure more than 107 mmHg which was similar to our observation. Similarly Levey et al and Jafar et al found 7% and 10% of their patient diabetic. In our study only 25% patients had the end-stage renal failure (creatinine clearance <5 ml/min), other 75% had the creatinine clearance >5 ml/min. Kuan et al.[4] showed about 50% had been suffering from ESRD. The cause of these dissimilarities may be that Kuan et al studied the patients with end stage renal failure. Most of the patients (54 out 60) had renal parenchymal disease by ultrasonography. Levey et al[12]. also demonstrated that most of their patients had unknown cause followed by the glomerular

disease. Kuan et al[4] described that the mean creatinine clearance of patients with end-stage renal failure predicted from CG formula and MDRD equation overestimates the creatinine clearance of conventional method which is also true for our studies. The difference of the means between CrCl (CG) and CrCl (MDRD) is not significant (p>0.05). This indicates both the formulae similarly overestimate the conventionally estimated creatinine clearance but both the formulas are strongly correlated with conventional method. Before concluding it is to be mentioned that cross sectional study like ours may not reflect the final result.

Conclusion

Richard J. Glassock and Christopher G. Winearls concluded that Cockcroft and Gault equation or MDRD equations are better predictors of the reduced GFR than serum creatinine alone [13]. So, in a country with less logistic support where standardization of serum creatinine assay is not possible, eGFR could be used in monitoring progression of already established CKD Hospitalized patients.

Disclosure

All the authors declared no competing interestes.

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