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Original research article

Comparison of glomerular filtration rate by various methods among potential kidney donors of patients with end-stage renal disease

[1]Dr. Anuradha Kavadi, [2]Dr. Manisha Sahay, [3]Dr. Kiranmai Ismal, [4]Dr. Sharmas Vali

[1]Assistant Professor, Department of Nephrology, Osmania Medical College, Hyderabad, Telangana, India.

[2,3]Professor, Department of Nephrology, Osmania Medical College, Hyderabad, Telangana, India.

[4]Associate Professor, Department of Nephrology, Osmania Medical College, Hyderabad, Telangana, India.

Corresponding Author: Dr. K. Anuradha

Abstract

Evaluation of GFR is one of the prime components of the donor evaluation. It helps in assessment of risks of kidney disease among the potential donors. Selecting donors with minimal long-term risk of kidney failure is important. Glomerular filtration rate can be affected by various factors like dietary protein intake, exercise, pregnancy, obesity, hyperglycemia, use of antihypertensive drugs, etc. Hence there is a need to assess the health of kidney of donors to ensure successful transplantation among end stage renal disease patients. A cross-sectional study was undertaken to compare various methods to estimate Glomerular filtration rate (GFR) in 60 potential kidney donors who are either first degree relative/spouse of ESRD patients in the Department of Nephrology at Osmania General Hospital from January, 2017 to January 2019. The mean age of the study population was 42 ± 11.5 years and mean serum creatinine was 0.83 ± 0.1 mg/dl. The mean GFR as measured by Diethylene Tri amine Penta Acetic acid (DTPA) was 90.6 ± 11.1 ml/min/1.73 m^2. The estimated glomerular filtration rate (GFR) as per creatinine clearance method and Chronic Kidney Disease Epidemiology (CKD-EPI) Creatinine equation was found to be 97.8 ± 21.4 and 93.6 ± 18.1 ml/min/1.73 m^2 respectively.

Conclusions: Estimation of GFR is better by creatinine clearance method and CKD-EPI Creatinine equation method.

Keywords: Glomerular filtration rate, End-stage renal disease, creatinine clearance method

Introduction

Measurement of Glomerular filtration rate (GFR) is considered as standard for assessing renal function. GFR measurement in living kidney donors ensures that the donor will be left with sufficient nephron mass to avoid end-stage renal failure during their life expectancy and ensure adequate renal function in the recipient. Keeping this in view, the accuracy of the measurement of GFR is of prime importance [1]. Inulin clearance is the gold standard for determination of GFR, as inulin is closest ideal filtration marker. However, Inulin is not freely available and cannot be used frequently. Accurate determination of the GFR is also possible using the clearance of a radiolabeled compound such as radiolabeled Iothalamate, Diethylenetriamine Penta Acetic Acid (DTPA-99mTc), or ethylenediaminetetraacetic acid (51Cr EDTA). These methods are limited in terms of availability [2].

As an alternative, a number of easy-to-use mathematical equations, incorporating different anthropometric variables and biological parameters, have been developed to predict ('estimated GFR'), rather than to directly measure GFR ('measured GFR'). The most common methods utilized to estimate the GFR are the creatinine clearance, and estimation equations based upon the plasma creatinine concentration, namely the Cockcroft-Gault (CG) equation and Modification of Diet in Renal Disease (MDRD) equations [3, 4]. These formulas have some limitations for use in kidney donor workup, as they were developed based on data from patients with reduced renal function and often end up underestimating the renal function [5]. Chronic Kidney Disease Epidemiology collaboration developed a new equation (CKD-EPI) which aims to eliminate the above error, as it has taken normal population also in consideration and has been widely accepted [6].

Serum cystatin C is a cationic non glycosylated cysteine proteinase inhibitor which is freely filtered at the glomerulus. Serum cystatin C can help in early detection of acute kidney injury [7].

Since there are so many methods available for estimation of GFR there is a need to establish which method is best to assess renal function among healthy donors.

Objective: The objective of the study was to compare various methods of GFR estimation like CKD-EPI,

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MDRD, C-G, 24-hour urinary clearance method, CYSTATIN-C GFR with DTPA in potential kidney donors who are either first degree relative/spouse of ESRD to evaluate their clinical utility.

Material and Methods

Study Design: Hospital based cross-sectional study.

Study Area: Department of Nephrology, Osmania General hospital-Tertiary care center, Hyderabad, Telangana.

Study Duration: January 2016-January 2019.

Study Population: Potential voluntary kidney donors who were first degree relatives/spouses of ESRD patients who were undergoing donor evaluation during study period.

Sample Size: A total of 60 healthy donors were selected.

Data Collection: After obtaining permission, any donor who is ≥ 18 years of age, first degree relatives and Spouses of ESRD patients and have given informed consent were included. A detailed history including age, relation with the patient, and history of hypertension, diabetes mellitus, and physical examinations including height and weight and blood pressure (BP), Body mass index (BMI) were documented. Serum creatinine was measured by the kinetic Jaffe method in a central laboratory accredited by the National Accreditation Board for Testing and Calibration Laboratories (N.A.B.L). Measured GFR was assessed by 99Tc DTPA by GATES method and 24-hour creatinine clearance method. Estimated GFR was assessed by MDRD, COCKROFT-GAULT method, CKD-EPI-cystatin C, CKD-EPI-creatinine-cystatin c and CKD-EPI-CREATININE method.

Ethical Clearance: Ethical clearance was taken from the Institutional Ethical Committee. Personal identification data was not collected to maintain study subjects' confidentiality.

Data Analysis: Data was analyzed using Microsoft excel and Epi info version 7. The descriptive statistics are expressed in percentages and mean values. Statistical test of significance like unpaired t test were applied where ever necessary. Correlation and regression coefficient was done to establish relation between variables.

Results

Table 1: Distribution of study population as per demographic and biochemical characteristics

Characteristics	Total (n = 60)	Males (n = 8)	Females (n = 52)	P value
Mean age (years)	42 ± 11.5	46.25 ± 7.4	41.3 ± 11.9	0.25
BMI (kg/m^2)	23.96 ± 3.87	23.1 ± 3.4	24.09 ± 3.95	0.5
Sr. Creatinine(mg/dl)	0.83 ± 0.1	0.95 ± 0.1	0.8 ± 0.1	0.001
Sr. Albumin (mg/dl)	4.3 ± 0.2	4.4 ± 0.2	4.2 ± 0.2	0.01
Cystatin C (mg/dl)	0.84 ± 0.1	0.85 ± 0.07	0.8 ± 0.1	0.1
Mean HbA1c (%)	5.41 ± 0.3	5.4 ± 0.3	5.4 ± 0.3	1
Mean BSA (m^2)	1.53 ± 0.1	1.62 ± 0.09	1.5 ± 0.1	0.001

In the present study, it was found that the mean age of study population was 42 ± 11.5 years and mean Body mass index was 23.96 ±3.87 kg/m^2. Majority (86.7%) of the study population were females and 13.3% were males. The mean serum creatinine was 0.83 ± 0.1 mg/dl and mean Serum albumin levels were 4.3 ± 0.2 mg/dl. The mean Cystatin C levels in study subjects was 0.84 ± 0.1 mg/dl and mean HbA1c was 5.41% and the mean body surface area was 1.53 m^2. (Table 1)

Table 2: Estimated and measured glomerular filtration rate in healthy individuals

GFR (ml/min/1.73 m^2)	Mean ± SD	Males	Females
DTPA	90.6 ± 11.1	89.8 ± 6.1	90.7 ± 11.7
CKD-EPI Creatinine equation	93.6 ± 18.1	98.6 ± 17.2	92.8 ± 18.2
CKD-EPI Creatinine Cystatin C equation	95.2 ± 15.4	95.3 ± 11.3	95.2 ± 16.1
MDRD	81.95 ± 19.3	81.3 ± 18.9	82.03 ± 19.5
Cockcroft-Gault method	82.8 ± 24.4	89.75 ± 12.3	81.75 ± 25.7
Creatinine clearance	97.8 ± 21.4	90.8 ± 25.8	98.9 ± 20.8
CKD-EPI Cystatin C equation	95.9 ± 16.06	98.6 ± 10.7	95.5 ± 16.7

The mean glomerular filtration rate (GFR) as measured by Diethylene Tri amine Penta Acetic acid (DTPA)

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was 90.6 ± 11.1 ml/min/1.73 m^2. The estimated glomerular filtration rate (GFR) as per CKD-EPI Creatinine equation was found to be 93.6 ± 18.1 ml/min/1.73 m^2 and as per CKD-EPI Creatinine Cystatin C equation was 95.2 ± 15.4 ml/min/1.73 m^2. As per Modified Diet in Renal Disease (MDRD) equation the estimated GFR was found to be 81.95 ± 19.3 ml/min/1.73 m^2 and according to Cockcroft-Gault method was 82.8 ± 24.4 ml/min/1.73 m^2. The mean glomerular filtration rate as per creatinine clearance was 97. 8 ± 21.4 ml/min/1.73 m^2. (Table 2)

Table 3: Correlation values between measured GFR and estimated GFR

	Correlation value	Interpretation
Correlation between DTPA & CKD-EPI Creatinine equation	0.364	Moderate Positive Correlation
Correlation between DTPA & CKD-EPI Creatinine Cystatin C equation	0.377	Moderate Positive Correlation
Correlation between DTPA & MDRD	0.349	Moderate Positive Correlation
Correlation between DTPA & Cockcroft-Gault method	0.342	Moderate Positive Correlation
Correlation between DTPA & Creatinine clearance	0.473	Moderate Positive Correlation
Correlation between DTPA & CKD-EPI Cystatin C equation	0.2	Weak Positive Correlation

Correlation was done between measured GFR and estimated GFR among healthy voluntary donors. There was moderate positive correlation between measured and estimated GFR calculated by using CKD-EPI creatinine equation; CKD-EPI Creatinine Cystatin equation; MDRD equation; Cockcroft-Gault method and Creatinine clearance. There was weak positive correlation between measured and estimated GFR calculated using CKD-EPI Cystatin C equation. (Table 3)

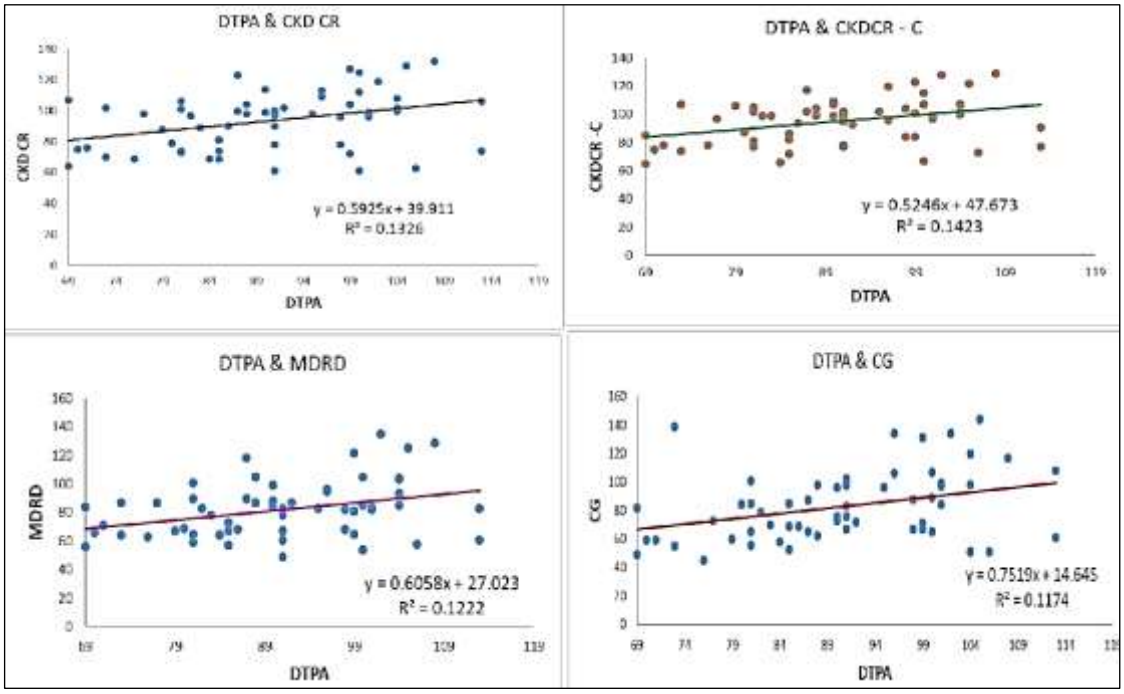

Fig 1: Regression analysis between measured GFR and estimated GFR

Simple linear Regression analysis between measured GFR and estimated GFR by CKD-EPI Creatinine equation method shows that the coefficient is 0.59 of GFR by DTPA method. The coefficient indicates that for every additional ml/min/1.73 m^2 increase in GFR by DTPA method there will be an average increase in estimated GFR by 0.59 times assessed through CKD-EPI creatinine equation method. The difference in the means of measured and estimated GFR by CKD-EPI Creatinine equation was found to be statistically highly significant ($p<0.001$) using independent t test. (Figure 1)

Simple linear Regression analysis between measured GFR and estimated GFR by Creatinine Cystatin C equation method shows that the coefficient is 0.52 of GFR by DTPA method. The coefficient indicates that for every additional ml/min/1.73 m^2 increase in GFR by DTPA method there will be an average increase in estimated GFR by 0.52 times assessed through CKD-EPI creatinine Cystatin C equation method. The difference in the means of measured and estimated GFR by CKD-EPI Creatinine Cystatin C equation was found to be statistically significant ($p<0.05$) using independent t test. (Figure 1)

Simple linear Regression analysis between measured GFR and estimated GFR by Modified Diet in Renal Disease (MDRD) method shows that the coefficient is 0.6 of GFR by DTPA method. The coefficient

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indicates that for every additional ml/min/1.73 m^2 increase in GFR by DTPA method there will be an average increase in estimated GFR by 0.6 times assessed through MDRD method. The difference in the means of measured and estimated GFR by Modified Diet in Renal Disease (MDRD) equation was found to be statistically highly significant ($p<0.001$) using independent t test. (Figure 1)

Simple linear Regression analysis between measured GFR and estimated GFR by Cockcroft-Gault (CG) method shows that the coefficient is 0.75 of GFR by DTPA method. The coefficient indicates that for every additional ml/min/1.73 m^2 increase in measured GFR by DTPA method there will be an average increase in estimated GFR by 0.75 times assessed through CG method. The difference in the means of measured and estimated GFR by Cockcroft-Gault (CG) method equation was found to be statistically highly significant ($p<0.001$) using independent t test. (Figure 1)

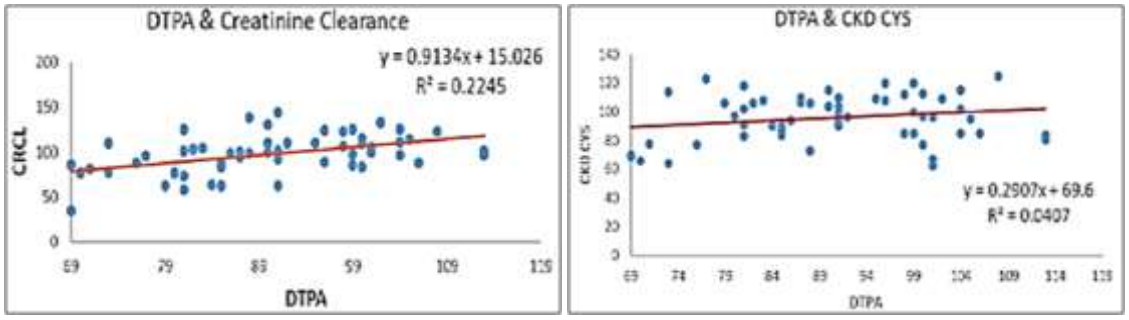

Fig 2: Regression analysis between measured GFR and estimated GFR

Simple linear Regression analysis between measured GFR and estimated GFR by Creatinine clearance method shows that the coefficient is 0.91 of GFR by DTPA method. The coefficient indicates that for every additional ml/min/1.73 m^2 increase in measured GFR by DTPA method there will be an average increase in estimated GFR by 0.91 times assessed through Creatinine clearance method. The difference in the means of measured and estimated GFR by Creatinine clearance method equation was found to be statistically highly significant ($p<0.001$) using independent t test. (Figure 2)

Simple linear Regression analysis between measured GFR and estimated GFR by CKD-EPI Cystatin C equation method shows that the coefficient is 0.29 of GFR by DTPA method. The coefficient indicates that for every additional ml/min/1.73 m^2 increase in measured GFR by DTPA method there will be an average increase in estimated GFR by 0.29 times assessed through CKD-EPI Cystatin C equation method. The difference in the means of measured and estimated GFR by CKD-EPI Cystatin C equation method was found to be statistically highly significant ($p<0.001$) using independent t test. (Figure 2)

Discussion

In our study the mean age of the study population was 42 ± 11.5 years. Majority (86.7%) were females and 13.3% were males. This study findings concurred with a study conducted by S Kakde *et al*. wherein the mean age of population was 41.6 ± 11.3 years and 36% were males [8]. The findings were different to a study conducted by Jahan F *et al*. and Salma Ayub *et al*. where the mean age of study population was 34.31±9.46 years and 32.19 ±8.27 years and 65% were males respectively [9, 10].

In present study, mean Body mass index was 23.96 ±3.87 kg/m^2 which were comparable to a study conducted by S Kakde *et al*. in which the mean Body mass Index (BMI) was 24 ± 3.8 kg/m^2 [8].

In the present study the mean serum creatinine was 0.83 ± 0.1 mg/dl. The present study findings were different when compared to a study conducted by S Kakde *et al*., Jahan F *et al*. in which the mean serum creatinine level was 0.9 ± 0.1 mg/dl [8, 9].

In this study the mean Cystatin C levels in study subjects was 0.84 ± 0.1 mg/dl which concurred with S Kakde *et al*. and Jeffrey W M *et al*. findings of 0.8 ± 0.1 mg/dl [8, 11].

In the present study the mean glomerular filtration rate (GFR) as measured by DTPA was 90.6 ± 11.1 ml/min/1.73 m^2. The measured Glomerular filtration rate (GFR) was 98.4 ± 21.2 ml/min/1.73 m^2 and 101 ml/min/1.73 m^2 among healthy donors in a study conducted by S Kakde *et al*. and Jeffrey M W *et al*. [8, 11].

In the present study the estimated glomerular filtration rate (GFR) as per CKD-EPI Creatinine equation was found to be 93.6 ± 18.1 ml/min/1.73 m^2. The present study findings were comparable to a study by S Kakde *et al*., where the estimated GFR as per CKD-EPI Creatinine equation method was 88.1 ± 15.9 ml/min/1.73 m^2 [8]. The estimated mean GFR by CKD-EPI creatinine equation method in a study by Chung *et al*. was 108.7 ± 18 ml/min/1.73 m^2 which was comparatively higher when compared to present study [12].

In our study, the estimated GFR as per CKD-EPI Creatinine Cystatin C equation was 95.2 ± 15.4 ml/min/1.73 m^2. Similar findings were reported by Jeffrey W M *et al*. (96 ml/min/1.73 m^2) [11].

In this study, as per Modified Diet in Renal Disease (MDRD) equation the estimated GFR was found to be 81.95 ± 19.3 ml/min/1.73 m^2. S Kakde *et al*. reported estimated GFR as per MDRD equation method

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was 78 ± 14.7 ml/min/1.73 m^2 [8].

In the present study, the mean estimated GFR according to Cockcroft-Gault method was 82.8 ± 24.4 ml/min/1.73 m^2. The estimated GFR by CG method was slightly higher in a study conducted by Chung BH *et al*. -109.6 ± 27.9 ml/min/1.73 m^2 [12].

In the present study, the mean glomerular filtration rate as per creatinine clearance was 97. 8 ± 21.4 ml/min/1.73 m^2 which were similar to Salma Ayub *et al*., (99.08 ± 22.25 ml/min/1.73 m^2) [10].

In the current study, the estimated GFR as per CKD-EPI Cystatin C equation was 95.9 ± 16.06 ml/min/1.73 m^2 which concurred with a study by S Kakde *et al*. (97.8 ± 19.9 ml/min/1.73 m^2) [8].

There was moderate positive correlation between measured and estimated GFR calculated by using CKD-EPI creatinine equation; CKD-EPI Creatinine Cystatin equation; MDRD equation; Cockcroft-Gault method and Creatinine clearance. Similar findings were reported by Jeffrey W M *et al*. and Aydin *et al*. [11, 13].

In the present study, the estimated GFR by CKD-EPI creatinine equation method, creatinine clearance and CKD-EPI Cystatin C equation method were almost accurate in predicting GFR closer to measured GFR. The present study findings were similar to a study by S Kakde *et al*., where least bias was found with CKD-EPI Creatinine equation method [8].

Conclusions & Recommendations

Estimation of GFR is better by creatinine clearance method and CKD-EPI Creatinine equation method among healthy donors. CKD-EPI creatinine Cystatin C equation method can also predict the estimated GFR accurately among potential donors. There is need for larger sample study to verify the validity of the predicting equations before applying the results to general population.

Limitations

Total study population was relatively small and there is over representation of females when compared to males.

Conflict of Interest: None.

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