Iran J Nucl Med. 2023;31(2):129-136 [Serial No. 61]

Homepage: https://irjnm.tums.ac.ir/

ORIGINAL RESEARCH ARTICLE

How do various methods of GFR estimation correlate? A study in a group of Indian volunteer kidney donors

Siddharth Washimkar[1], Manjit Sarma[1], Shanmugam Manigandan[1], Renjitha Bhaskaran[2], George Kurian[3]

[1]*Department of Nuclear Medicine and Molecular Imaging, Amrita Institute of Medical Sciences, Cochin, Kerala, India*

[2]*Department of Biostatistics, Amrita Institute of Medical Sciences, Cochin, Kerala, India*

[3]*Department of Nephrology, Amrita Institute of Medical Sciences, Cochin, Kerala, India*

ARTICLE INFO

Article History:
Received: 21 August 2022
Revised: 18 December 2022
Accepted: 18 December 2022
Published Online: 20 May 2023

Keyword:
Glomerular filtration rate
Double plasma sampling method
Gates' method
Single plasma sampling method
Cockcroft Gault method

*Corresponding Author:
Dr. Manjit Sarma
Address: Department of Nuclear Medicine and Molecular Imaging, Amrita Institute of Medical Sciences, (Amrita Vishwa Vidyapeetham), Cochin-6802041, Kerala, India
Email: drmanjitsarma@gmail.Com

ABSTRACT

Introduction: Correlation of Glomerular Filtration rate (GFR) obtained by Double Plasma sampling method (DPSM), Single Plasma sampling method (SPSM), Cockcroft Gault method and Gates' method in prospective voluntary kidney donors.

Methods: Fifty-six prospective donors sent for [^{99m}Tc]Tc-DTPA renogram were prospectively included. GFR was obtained by Double Plasma sampling, Single Plasma sampling, Cockcroft Gault and Gates' method using standard protocols. Intra-class correlation coefficient, Pearson correlation coefficient and difference in mean and median GFR between GFR values obtained by DPSM as reference method and other methods were calculated.

Results: GFR obtained by SPSM, Cockcroft Gault method and Gates' method show poor, moderate and good agreement respectively with GFR obtained by DPSM (reference method). There was statistically significant mild positive correlation between GFR obtained by DPSM with GFR obtained by SPSM and statistically significant moderate positive correlation between GFR obtained by DPSM with Cockcroft Gault method and Gates' method. The mean and median score of GFR obtained by SPSM, Gates' method and Cockcroft Gault method were lower, higher and significantly higher respectively than GFR obtained by DPSM.

Conclusion: GFR obtained by Gates' method correlates well with Dual Plasma Sampling Method (DPSM, reference standard) and Cockcroft Gault Method overestimates GFR by a large extent amongst prospective voluntary kidney donors.

Use your device to scan and read the article online

How to cite this article: Washimkar S, Sarma M, Manigandan S, Bhaskaran R, Kurian G. How do various methods of GFR estimation correlate? A study in a group of Indian volunteer kidney donors. Iran J Nucl Med. 2023;31(2):129-136.

https://doi.org/10.22034/IRJNM.2023.40083

INTRODUCTION

Volume of fluid filtered by the renal glomerular capillaries into Bowman's capsule per unit time is called Glomerular filtration rate (GFR) [1]. Continuous infusion of inulin with urine and plasma sampling is considered "gold standard" for GFR estimation. However, this is technically difficult and hence rarely performed in clinical setting. GFR can be fairly accurately calculated from the rate of clearance of an exogenous tracer activity (commonly [^{99m}Tc]Tc-DTPA) from the plasma, which is also considered a precise method simulating inulin clearance. Multisampling technique for clearance of exogenous tracer activity is however cumbersome to be performed in routine clinical practice [2]. Sampling techniques have been simplified by reducing the number of blood samples to two or even one. The two sample or double plasma sampling method (sampling at 1 and 3 hr) could reduce the error to 4 ml/min [3]. Double plasma sampling method using Russell's formula is highly reliable method for the valid estimate of true GFR [4]. Sampling methods are invasive and hence camera-based scintigraphic method to evaluate GFR evolved and were supposedly comparable to sampling methods of GFR determination [5]. Gary Gates et al. in 1984 derived GFR from scintigraphic [^{99m}Tc]Tc-DTPA uptake in the kidneys. Because of its simplicity, it soon became popular. It also can identify the individual renal function, whereas other methods evaluate the global renal function [6]. But scintigraphic techniques are supposed to be less accurate than plasma clearance of labelled chelates [7].

Although various methods are available, reliability of estimate of GFR is an issue given the varied clinical settings like early detection of renal impairment, for renal function monitoring, for dosing of nephrotoxic drugs and evaluation of potential kidney donors. Hence, we tried to evaluate various methods available with us in a group of potential voluntary kidney donors, as correct GFR estimation is critical.

METHODS

Ethical clearance and informed consent

The study was cleared by ethical committee of our university and informed consent was obtained from the patients regarding inclusion into study.

Patients

From August 2018 to August 2020, fifty-six prospective kidney donors sent for [^{99m}Tc]Tc-DTPA renogram were prospectively included. Patients with extravasation of [^{99m}Tc]Tc-DTPA during injection were excluded.

[^{99m}Tc]Tc-DTPA renogram

Patients were hydrated with 1000 – 1500 ml oral fluids 30-60 minutes prior to start of study. Height in centimeters (cm) and weight in kilograms (kg) was documented. Labelled [^{99m}Tc]Tc-DTPA radioactivity of about 185-222 MBq with radiochemical purity of more than 95% was withdrawn in the two syringes containing equal activity and volume. Out of two, one syringe (standard syringe) was allowed to stand 24 hours in radioactive waste storage/decay room and second syringe was taken for injection to the patient in a lead shielded canister. Standard protocol for gamma camera acquisition and processing was used.

Sampling method

Venous blood samples (4 ml) were collected in vacuum test tubes at 60th and 180th minute following [^{99m}Tc]Tc-DTPA injection from contralateral arm through direct IV (cubital) access. Vacuum test tubes containing venous blood were allowed to stand in radioactive waste storage/decay room in a test tube holder for 24 hours. Next day 1 ml of plasma from each of vacuum test tubes was pipetted by thermoscientific pipette meticulously by taking care not to disturb the interface between the plasma and the red cells and was emptied into two test tubes. Standard syringe containing radioactivity was emptied into jar containing one liter water. Water from the jar was drawn in and pushed back from the syringe to make sure that no radioactivity remained in the standard syringe. 1 ml of water containing radioactivity in jar was withdrawn from another fresh 3 ml syringe and was emptied in a test tube. Following this, tap water was poured in a 100 ml flask. The injected syringe from the last day of injection was taken out. Using the same syringe, water from the flask was withdrawn and all the residual contents in the syringe (mainly containing residual radioactivity and blood) was rinsed and mixed with water and was emptied in the same flask. Needle along with the cap were removed and were put in a test tube. One ml of this mixture containing the residual radioactivity and blood particles was withdrawn in a fresh 3 ml syringe, which was then emptied in a test tube. All five test tubes kept in the test tube stand were taken for counting in our Captus 3000 Well counter using Captivia Software. Background counts were obtained for 1 minute.

Next, all the five test tubes were counted in the well counter one by one. Their counts (kilo counts per minute) in window centered 15 % - 20% over 140 keV were recorded. Five counts obtained were a) 60-minute plasma sample count b) 180-minute plasma sample count c) Standard Count d) Wash Count and e) Needle Count. [^{99m}Tc]Tc-DTPA plasma clearance by SPSM and DPSM was calculated using Russell's method.

Cockcroft Gault Method

For men, the formula (140-age)×(ideal body weight in kg) / 72×serum creatinine was used. For women, this result is multiplied by the factor 0.85.

Clinical factors and statistical analysis

Sex, height, weight and serum creatinine were recorded as clinical factors. Statistical analysis was performed using IBM SPSS version 20.0 software. Intra-class correlation coefficient was computed for finding the agreement between the values. To find the linear relationship between values, Pearson correlation coefficient was computed and its statistical significance was tested using linear regression t test. To test the statistical significant difference in the mean and median scores between different measures Wilcoxon Signed rank test was used.

RESULTS

Patients

The mean age of the donors was 47.04±9.045 years.15 (26.8%) were females and 41(73.2%) were males. The mean height of the patients was 158.5±9.3 cm and mean weight of the patients was 67.2±12.8 kg. Distribution of various variables is as shown in Table 1 and Figure 1.

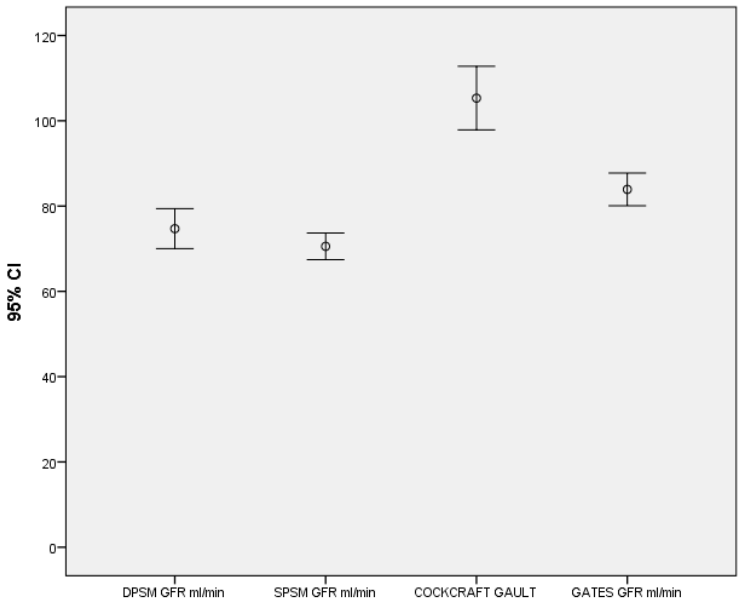

Fig 1. Error-Bar Charts of GFR graphically displaying tables of means and its 95% confidence interval

Table 1. Distribution of variables

Variables	Number of patients	Minimum	Maximum	Mean±SD
Age (years)	56	29	65	47.04±9.00
DPSM GFR (ml/min)	56	36	118	75.21±17.40
SPSM GFR (ml/min)	56	55	116	70.48±11.20
Cockcraft Gault GFR (ml/min)	54	59	175	105.31±27.30
Gates GFR (ml/min)	56	54	120	84.54±14.50

Among the total sample, 15(26.8%) were males and 41(73.2%) were females.

Agreement (intra-class correlation) of GFR obtained by DPSM with other methods

GFR obtained by SPSM shows a poor agreement (intra-class correlation =0.411) (Figure 2), GFR estimated by Cockcroft Gault method shows a moderate agreement (intra-class correlation=0.563) (Figure 3) and GFR obtained by Gates' method shows a good agreement

(intra-class correlation =0.795) (Figure 4) with GFR obtained by DPSM (reference method).

Correlation of GFR obtained by DPSM with other methods

Correlation analysis showed statistically significant mild positive correlation between DPSM GFR with SPSM GFR (r=0.284, p value=0.034) (Table 2 and Figure 5). There was statistically significant moderate positive correlation between DPSM GFR with Cockcroft Gault GFR (r=0.435, p value<0.001) (Table 3 and Figure 6) and with Gates' method GFR (r=0.671, p value<0.001) (Table 4 and Figure 7).

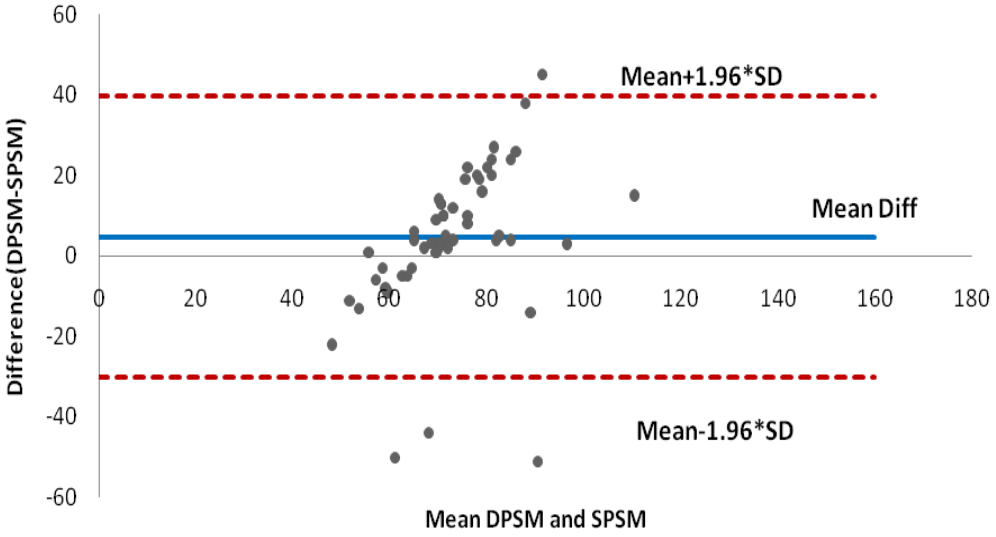

Fig 2. Intra-class correlation coefficient between DPSM and SPSM GFR is 0.411 (poor agreement). The bias was 4.7±17.8 with lower limit of agreement (-30.25) and upper limit of agreement (+ 39.72)

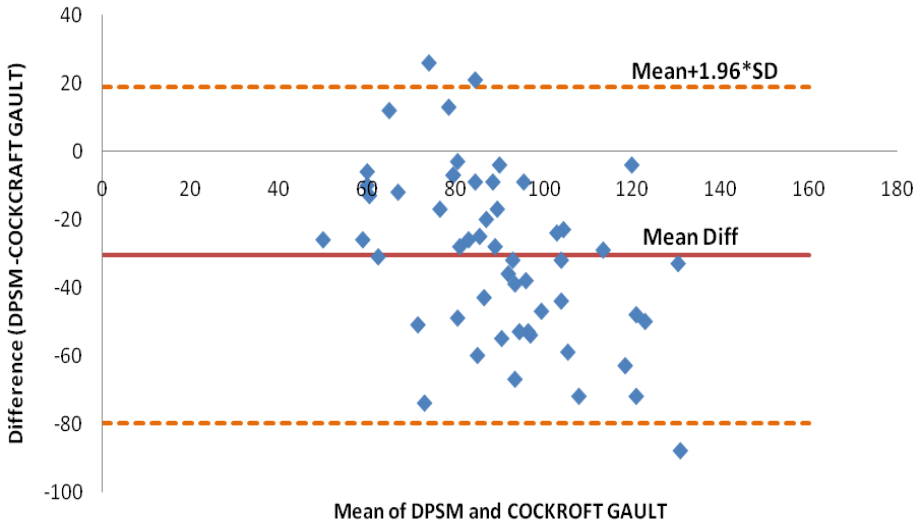

Fig 3. Intra-class correlation coefficient between DPSM and Cockcroft Gault GFR is 0.563 (moderate agreement). The bias was -30.6 ± 25.19 with lower limit of agreement (-79.99) and upper limit of agreement (18.78)

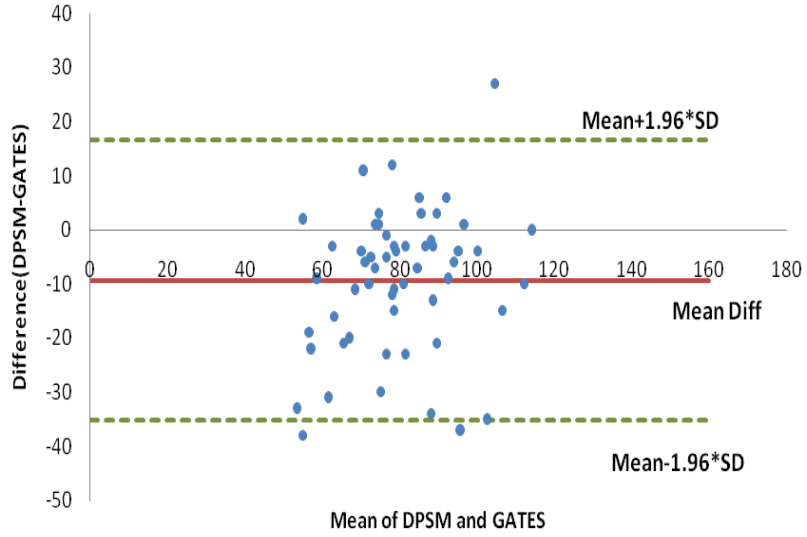

Fig 4. Intra-class correlation coefficient between DPSM and Gates method is 0.795 (good agreement). The bias was -9.3 ± 13.22 with lower limit of agreement –35.24 and upper limit of agreement 16.6

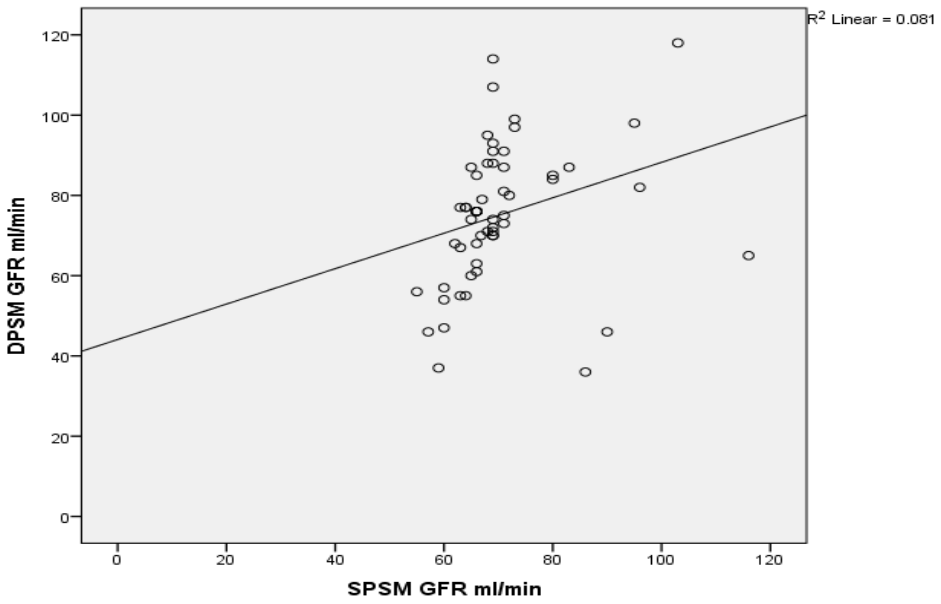

Fig 5. Correlation between GFR (ml/min) obtained by DPSM and SPSM

Table 2. Correlation between GFR (ml/min) obtained by DPSM with SPSM

GFR	DPSM GFR ml/min		
	n	p value	r
SPSM GFR ml/min	56	0.034	0.284

There was statistically significant mild positive correlation between DPSM GFR ml/min with SPSM GFR (r=0.284, p value=0.034) (Figure 5).

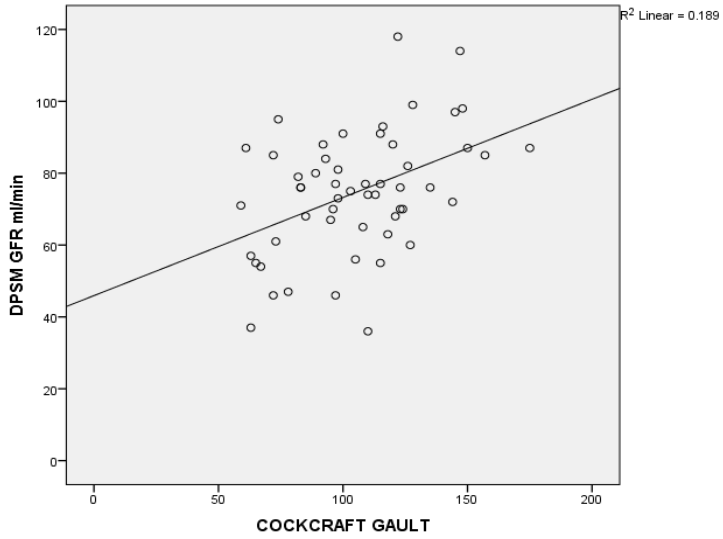

Fig 6. Correlation between GFR (ml/min) obtained by Cockroft Gault method and DPSM

Table 3. Correlation between GFR (ml/min) obtained by DPSM with Cockcroft Gault method

GFR	DPSM GFR ml/min		
	n	p value	r
Cockcroft Gault ml/min	54	0.001	0.435

There was statistically significant moderate positive correlation between DPSM GFR (ml/min) with GFR obtained by Cockcroft Gault method (r=0.435, p value<0.001) (Figure 6).

Table 4. Correlation between GFR (ml/min) obtained by DPSM with Gates' method

GFR	DPSM GFR ml/min		
	n	p value	r
GATES GFR ml/min	54	<0.001	0.671

The results of correlation analysis showed there was statistically significant moderate positive correlation between DPSM GFR ml/min with Gates GFR ml/min (r=0.671, p value<0.001) (Figure 4).

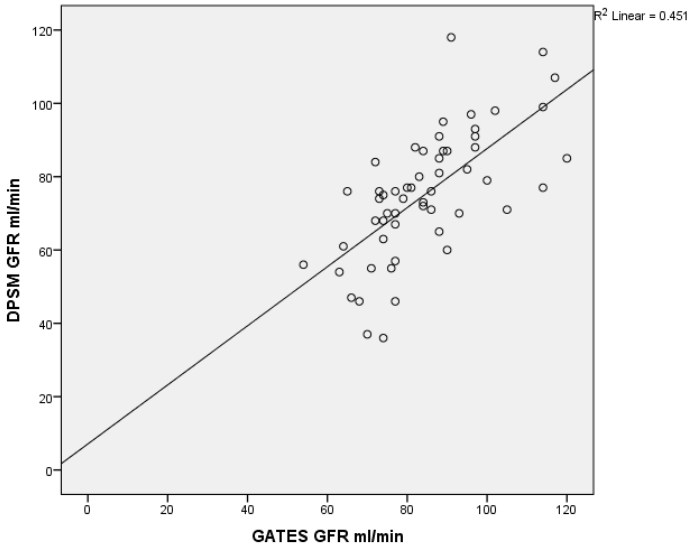

Fig 7. Correlation between GFR (ml/min) obtained by Gates' method and DPSM

Table 5. Comparison between GFR (ml/min) obtained by DPSM and SPSM

Variable	DPSM n=56			SPSM n=56			p value
	Mean	SD	Median (IQR)	Mean	SD	Median (IQR)	
GFR (ml/min)	75.21	17.43	76 (65.5-87)	70.48	11.21	68(65-71)	0.003

The mean and median values of GFR obtained by SPSM are lower than those obtained by DPSM and statistically borderline significant with p value = 0.003.

Table 6. Comparison between GFR (ml/min) obtained by DPSM and Cockcroft Gault Method

Variable	DPSM n=54			Cockcroft Gault method n=54			p value
	Mean	SD	Median (IQR)	Mean	SD	Median (IQR)	
GFR (ml/min)	74.70	17.20	76 (65.5-87)	105.31	27.35	106.5(83-123)	<0.001

The mean and median values of GFR obtained by Cockcroft Gault method are much higher than those obtained by DPSM and statistically significant with p value < 0.001.

Table 7. Comparison between GFR (ml/min) obtained by DPSM and Gates' method

Variable	DPSM n=56			Gates method n=56			p value
	Mean	SD	Median (IQR)	Mean	SD	Median (IQR)	
GFR (ml/min)	75.21	17.43	76 (65.5-87)	84.54	14.53	83.5(74-92.5)	<0.001

The mean and median values of GFR obtained by Gates method are higher than those obtained by DPSM and statistically significant with p value <0.001.

Comparison between mean GFR obtained by DPSM and mean GFR obtained by other methods

The mean and median (IQR) of GFR obtained by DPSM was 75.21±17.43 ml/min and 76(65.5-87) ml/min respectively while mean and median (IQR) of GFR obtained by SPSM was 70.48±11.22 ml/min and 68(65-71) ml/min respectively. The mean and median score of GFR obtained by SPSM were lower compared to those obtained by DPSM. The comparison was statistically borderline significant with p value 0.003 (Table 5). The mean and median (IQR) of GFR obtained by Cockcroft Gault method was 105.3 ± 27.34 ml/min and106.5 (83-123) ml/min respectively. The mean and median score of GFR obtained by Cockcroft Gault Method was much higher compared to those obtained by DPSM. The comparison was statistically significant with p value < 0.001(Table 6). The mean and median (IQR) of GFR obtained by Gates' method was 84.54± 14.53 ml/min and 83.5 (74-92.5) ml/min respectively. The mean and median score of GFR obtained by Gates' method were higher compared to those obtained by DPSM. The comparison was statistically significant with p value < 0.001(Table 7). Two patients did not have serum creatinine value at the time of scan, so we compared the GFR obtained by DPSM and GFR obtained by Cockcroft Gault method between the remaining 54 patients.

DISCUSSION

The primary objective of this study was to assess correlation between GFR obtained by Single Plasma sampling method, Gates' method and Cockcroft Gault method with Double Plasma sampling method (taken as reference method) in voluntary kidney donors. Double plasma sampling method (DPSM) using Russell's formula is known to be a reliable method for GFR estimation. Our study shows that there is a mild positive correlation but poor agreement between GFR obtained by SPSM with that of DPSM, which is similar to other reports [4, 8]. In addition, mean and median values of GFR obtained by SPSM are lower compared to those obtained by DPSM suggesting a possibility of underestimation of GFR obtained by SPSM in normal subjects like donor patients where accurate GFR estimation is required and expected to be done only once as a part of pre-transplant donor work up. However, where serial GFR measurements are expected to be done over time and where very sensitive GFR measurement is not deemed necessary, SPSM may still be practical and obviously less cumbersome. GFR obtained by Gates' method showed good agreement and moderate positive correlation with GFR by DPSM method. Mean and median values of GFR obtained by Gates' method were higher compared to those obtained by DPSM similar to other reports [9,

10]. It is known that insufficient background activity correction in kidneys gives higher values of GFR by Gates' method. Since estimation of correct GFR is critical in prospective kidney donor evaluation, given our experience of significant difference in values of GFR, possibly DPSM should be done if infrastructure exists for calculating total GFR. In addition, the technique of two samples is known to have a significantly lower standard error [3]. DPSM can be done along with estimation of differential GFR from Gates' method keeping in mind that there would be some overestimation of GFR calculated by Gates' method. Other sources of errors include decay statistics, attenuation correction, system dead time and radiopharmaceutical quality [11]. GFR estimated by Cockcroft Gault method showed moderate agreement and moderate positive correlation with GFR obtained by DPSM. The accuracy of GFR obtained by Cockcroft Gault method has always been questioned [12]. In our study too, there was significant difference between mean and median values of GFR obtained by DPSM and that estimated by Cockcroft Gault method. Overestimation has been a problem in people with normal renal function [13]. Our findings also suggest that GFR values using Cockcroft Gault method could significantly overestimate GFR compared to GFR obtained by DPSM in normal individuals. Small changes in serum creatinine may result in large changes in GFR. Hence, GFR estimated by Cockcroft Gault method may is not optimal in estimating GFR in normal individuals though widely used. One limitation of our study was that the repeatability of measurement system, which is an important part of any method comparison study, was not possible in this study as the samples could be taken only at a particular time point due to nature of the study.

CONCLUSION

Glomerular filtration rate obtained by Gates' method has the best agreement with Dual Plasma Sampling method (DPSM, reference standard). Cockcroft Gault method is seen to overestimate GFR by a large extent amongst our group of voluntary kidney donors. It can be inferred that in absence of facility for conducting sampling methods, Gates' method may well be the method of choice to estimate GFR in voluntary kidney donors. Additionally, if infrastructure exists, both Dual Plasma Sampling method and Gates' method could ideally be combined. Total GFR should be obtained by DPSM and differential GFR can be calculated by Gates' method keeping in mind that there would be some overestimation of GFR calculated by Gates' method.

REFERENCES

1. Earley A, Miskulin D, Lamb EJ, Levey AS, Uhlig K. Estimating equations for glomerular filtration rate in the era of creatinine standardization: a systematic review. Ann Intern Med. 2012 Jun 5;156(11):785-95.
2. Hephzibah J, Shanthly N, Oommen R. Comparison of glomerular filtration rate measured by plasma sample technique, Cockroft Gault method and Gates' method in voluntary kidney donors and renal transplant recipients. Indian J Nucl Med. 2013 Jul;28(3):144-51.
3. Russell CD, Bischoff PG, Kontzen FN, Rowell KL, Yester MV, Lloyd LK, Tauxe WN, Dubovsky EV. Measurement of glomerular filtration rate: single injection plasma clearance method without urine collection. J Nucl Med. 1985 Nov;26(11):1243-7.
4. Mulligan JS, Blue PW, Hasbargen JA. Methods for measuring GFR with technetium-99m-DTPA: an analysis of several common methods. J Nucl Med. 1990 Jul 1;31(7):1211-9.
5. Krawiec DR, Badertscher 2nd RR, Twardock AR, Rubin SI, Gelberg HB. Evaluation of 99mTc-diethylenetriaminepentaacetic acid nuclear imaging for quantitative determination of the glomerular filtration rate of dogs. Am J Vet Res. 1986 Oct 1;47(10):2175-9.
6. Gates GF. Computation of glomerular filtration rate with Tc-99m DTPA: an in-house computer program. J Nucl Med. 1984 May 1;25(5):613-8.
7. Fleming JS, Ramsay B, Waller DG, Ackery D. Measurement of glomerular filtration rate with a portable cadmium telluride detector. Nucl Med Commun. 1987 Sep;8(9):751-7.
8. Hussein M, Younis J, Moustafa H, Elantably I. Comparison of glomerular filtration rate measurement methods between radionuclide in vivo scintigraphic Gates' and plasma sampling. Open Access Maced J Med Sci. 2019 Aug 30;7(17):2734-2738.
9. Jackson JH, Blue PW, Ghaed N. Glomerular filtration rate determined in conjunction with routine renal scanning. Radiology. 1985 Jan;154(1):203-5.
10. Aydin F, Güngör F, Cengiz AK, Tuncer M, Mahsereci E, Ozdem S, Cenkçi M, Karayalçin B. Comparison of glomerular filtration rate measurements with the two plasma sample and single plasma sample, gamma camera Gates, creatinine clearance, and prediction equation methods in potential kidney donors with normal renal function. Nucl Med Commun. 2008 Feb;29(2):157-65.
11. Haycock GB, Schwartz GJ, Wisotsky DH. Geometric method for measuring body surface area: a height-weight formula validated in infants, children, and adults. J Pediatr. 1978 Jul 1;93(1):62-6.
12. Itoh K. Comparison of methods for determination of glomerular filtration rate: Tc-99m-DTPA renography, predicted creatinine clearance method and plasma sample method. Ann Nucl Med. 2003 Oct;17(7):561-5.
13. Lin J, Knight EL, Hogan ML, Singh AK. A comparison of prediction equations for estimating glomerular filtration rate in adults without kidney disease. J Am Soc Nephrol. 2003 Oct;14(10):2573-80.