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Comparison of 24 Hour Urine Creatinine Clearance with Estimated GFR Using 2009 CKD-EPI Formulae

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Original Research Article

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Abstract: The Glomerular filtration rate (GFR) is useful in the detection and estimateon of prognosis of chronic kidney disease (CKD) patients. Several methods are available to measure or estimate the GFR. The 24 hour urine collection for the estimation of GFR has been shown by studies to be more reliable than serum creatinine-based eGFR formulae. The eGFR by creatinine based formulae is known to be rapid and reliable means of approximation of creatinine clearance. The most commonly used equations to estimate GFR are serum creatinine based 2006 MDRD and 2009 CKD-EPI formulae. The objective of this study is to compare 24 hour urine creatinine clearance with estimated GFR using 2009 CKD-EPI and to identify at which stage of CKD the estimated GFR correlates closely with 24 hour urine creatinine clearance. It is a retrospective study. The laboratory requisition for 24 hour creatinine clearance in the period from January 2015 to December 2015 was collected retrospectively. There was a total of 120 laboratory request for 24 hour creatinine clearance in the specified period. Out of the total 120 patients, 46 were female patients with age range (18-75 years) and 74 were male patients with age range (18-75 years). The eGFR by CKD-EPI formulae had a statistically insignificant p-value ($p > 0.05$) in the III nd, IV th and Vth stages of CKD. This showed that 2009 CKD-EPI formulae had good approximation of 24 creatinine clearance in three stages of CKD. The 2009 CKD-EPI creatinine based GFR estimation provides a more accurate assessment of 24 hour creatinine clearance in in the IIInd, IVth and Vth stages of CKD. It is a good measure of kidney function than measuring serum creatinine alone but has certain limitations.
Keywords: Glomerular Filtration rate, Creatinine Clearance, Chronic Kidney disease, CKD-EPI Formulae.

INTRODUCTION

The common method for Glomerular Filtration rate (GFR) assessment is evaluation of 24 hour urine collection for creatinine clearance [1]. Several methods are available to measure or estimate the GFR. Most methods involve the ability of the kidneys to clear an exogenous marker like inulin or endogenous marker like creatinine and cystatin-C [2]. The GFR is useful in the detection and estimateon of prognosis of chronic kidney disease (CKD) patients [3]. GFR is also used as a guide to monitor the dosage of really excreted drugs. The 24 hour urine collection for the estimation of GFR has been shown by studies to be more reliable than serum creatinine-based eGFR formulae [4]. But the 24 hour creatinine clearance for GFR estimation is inconvenient to the patient and also overestimates the GFR because of tubular secretion of creatinine [6,7]. The eGFR by creatinine based formulae is known to be rapid and reliable means of approximation of creatinine clearance [5]. There are approximately 25 different equations for eGFR calculation. The most commonly used equations to estimate GFR are serum creatinine based 2006 MDRD and 2009 CKD-EPI formulae [6].

The Modification of Diet in renal disease 1999 (MDRD) formula was one of the most widely used formulas for estimating GFR [7]. The MDRD 1999 formulae included six variables (Age, Sex, Race, Serum Creatinine, Albumin and Urea nitrogen) for estimating GFR [7]. Then MDRD 2000 formulae was modified to a variable formulae and later in 2006, the formulae was simplified for use with serum creatinine traceable to Isotope Dilution Mass Spectrometry [7]. The 2006 MDRD formulae were found to be more accurate when compared with older formulae like Cockcroft-Gault formulae because of greater precision and lesser bias. But the major limitation of using MDRD formulae was identified to be systematic bias which underestimate GFR at higher levels and imprecision throughout the range. In 2009 CKD-EPI creatinine formulae was introduced to overcome the limitations of earlier creatinine based formulae especially 2006 MDRD formulae [8]. The CKD-EPI (Chronic Kidney Disease

Epidemiology Collaboration equation) has been suggested as a more accurate estimate of eGFR. The CKD-EPI creatinine based formulae has the same variables as the MDRD Formulae but diabetes, weight and organ transplant status were considered for developing the formulae [9].

The objective of this study is to compare 24 hour urine creatinine clearance with estimated GFR using 2009 CKD-EPI and to identify at which stage of CKD the estimated GFR correlates closelly with 24 hour urine creatinine clearance.

MATERIALS AND METHODS

It is a retrospective study. The laboratory requisition for 24 hour creatinine clearance in the period from January 2015 to December 2015 was collected retrospectively. All the requests for 24 hour creatinine clearance in the specified period irrespective of provisional diagnosis were included in the study. There was a total of 120 laboratory request for 24 hour creatinine clearance in the specified period. Out of the total 120 patients, 46 were female patients with age range (18-75 years) and 74 were male patients with age range (18-75 years).

For estimation of 24 hour creatinine clearance; the data collected were age, sex, height, weight, race, a serum specimen and a 24 hour urine specimen of the patient was collected and then 24 hour creatinine clearance was estimated by the following formulae.

24 hour creatinine clearance= urine creatinine* Urine volume/serum creatinine *1440.

Then e-GFR was calculated by 2009 CKD-EPI formulae.

2009 CKD-EPI formulae = 141 x min (SCr/κ, 1)α xmax (SCr /κ, 1)-1.209 x0.993Age x1.018 (if female) x1.159 (if Black)

{κ = 0.7 (females) or 0.9 (males), α = -0.329 (females) or -0.411 (males), min = indicates the minimum of SCr/κ or 1, max = indicates the maximum of SCr/κ or 1}

Creatinine was estimated by modified Jaffe method using ERBA system pack in automated analyser. The Calibrator used for Creatinine is traceable to a Isotope Dilution Mass Spectrometry (GC/IDMS) method.

STATISTICALANALYSIS

The statistical analysis was performed using Microsoft Excel. The paired-t-test was used for statistical analysis since all participants came from same population and all had paired results.

RESULTS

Table-1: Comparison of all pparticipants included in the study by paired-t-test, between 24 hour creatinine clearances with egfr using 2009 ckd-epi

METHOD	TOTAL PARTICIPANTS	MEAN	SD	P- value
24 hr creatinine clearance	120	52.15	29.46	<0.05
2009- CKD-EPI formulae	120	56.02	27.68	

Table-2: Comparison of egfr in male participants included in the study by paired-t-test, between 24 hour creatinine clearances with egfr using 2009 ckd-epi

METHOD	MALE PARTICIPANTS	MEAN	SD	P- value
24 hr creatinine clearance	74	51.25	33.48	<0.05
2009- CKD-EPI formulae	74	55.32	36.12	

Table-3: Comparison of egfr in female participants included in the study by paired-t-test, between 24 hour creatinine clearances with egfr using 2009 ckd-epi

METHOD	FEMALE PARTICIPANTS	MEAN	SD	P- value
24 hr creatinine clearance	46	53.20	32.58	<0.05
2009- CKD-EPI formulae	46	57.70	33.64	

Table-4: Comparison of egfr in different stages of ckd between between 24 hour creatinine clearances with egfr using 2009 ckd-epi

Ckd stages	No of participants	24 hr creatinine clearance	2009- ckd-epi formulae	P-value
I	27	105.29	112.46	<0.05
II	21	73.83	79.66	<0.05
III	49	46.10	49.78	0.4
IV	18	25.68	27.86	0.3
V	5	9.89	10.33	0.7
ALL	120	52.15	56.02	<0.05

[Table-1] shows the comparison of all participants by paired-t-test between 24 hour creatinine clearances with eGFR using 2009 CKD-EPI. A statistically significant difference ($p<0.05$) was observed between 24 hour creatinine clearance with eGFR using 2009 CKD-EPI when all participants included in the study were compared.

[Table-2,3] shows the sex wise comparison of all participants independent of age. This showed statistically significant difference ($p< 0.05$) between 24 hour creatinine clearances with eGFR using 2009 CKD-EPI in both sexes.

[Table-4] shows the comparison of eGFR in five stages of CKD (Stage I >90 ml/min, Stage II 60-89 ml/min, Stage III 30-59 ml/min, Stage IV 15-29 ml/min and Stage V <15 ml/min) between 24 hour creatinine clearance with eGFR using 2009 CKD-EPI. The eGFR by CKD-EPI formulae had a statistically insignificant p-value ($p > 0.05$) in the IIInd, IVth and Vth stages of CKD. This showed that 2009 CKD-EPI formulae had good approximation of 24 creatinine clearance in three stages of CKD.

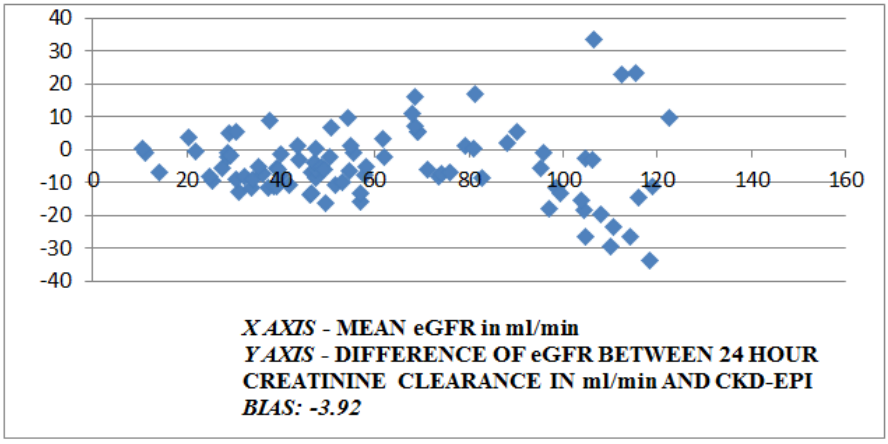

Fig-1: Bland-altman plot between 24 hr creatinine clearance in ml/min and egfr as calculated by 2009 ckd-epi formulae

Fig-1 show the graphical comparison by Bland-altman plot between clearances in ml/min calculated from 24 hour creatinine clearance and eGFR as calculated by 2009 CKD-EPI.

DISCUSSION

The most ideal method for estimation of GFR is clearance of exogenous marker like inulin. This method is expensive, time consuming and technically complicated. Though some studies have found that Cystatin C to be more accurate marker of GFR, other studies have suggested that it does not outmatch creatinine based formulaelike MDRD and CKD-EPI [10,11]. The GFR estimations are done to make a decision of when the patient must begin dialysis. For cases other than emergency factors indicating immediate initiation of dialysis, the time for initiation of dialysis is when GFR drops below 15 ml/min. we undertook a study to compare estimated GFR using 2009 CKD-EPI with 24 hour creatinine clearance. The objective of the study is to compare 24 hour urine creatinine clearance with estimated GFR using 2009 CKD-EPI and to identify at which stage of CKD the estimated GFR correlates closely with 24 hour urine creatinine clearance. Sex wise comparison of all participants included in our study independent of age and stage of CKD showed statistically significant difference ($p<0.05$) between estimated GFR using 2009 CKD-EPI with 24 hour creatinine clearance.

To be a ideal method of GFR estimation, it has to fulfil certain conditions. First and foremost is that it has to be accurate enough to place the patient in its correct stage of CKD. The second condition is that it has to be easy to calculate and the final condition is that it has to demand minimum data as possible. The 2009 CKD-EPI formulae is easy to calculate and requires only age and creatinine data for estimating GFR therby fulfilling second and third condition to be a ideal method of GFR estimation. But the 2009 CKD-EPI formulae showed good approximation ($p >0.05$) of 24 hour creatinine clearance in the IIInd, IVth and Vth stages of CKD.

The GFR evaluation in the validation population demonstrated lesser bias for 2009 CKD-EPI than 2006 MDRD formulae, but there was only moderate improvement in overall accuracy [12]. Another study also demonstrated that 2009 CKD-EPI equation to have a lesser bias, especially at estimated GFR greater than 60 ml/min/1.73 m and hence they recommend 2009 CKD-EPI equation for reporting eGFR replacing 2006 MDRD Study equation. But in our study 2009 CKD-EPI formulae showed good approximation ($p >0.05$) of 24

hour creatinine clearance at values lesser than 60 ml/min/1.73 m. But this study has certain limitation. Alhough there were relatively limited numbers of patients in the subgroups to make a valid comparison, we were able to include a relevant number of patients, sufficient to allow stratification.

CONCLUSION

The 2009 CKD-EPI creatinine based GFR estimation provides a more accurate assessment of 24 hour creatinine clearance in in the IIInd, IVth and Vth stages of CKD. It is a good measure of kidney function than measuring serum creatinine alone but has certain limitations.

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