

Correlation of The Chronic Kidney Disease Epidemiology Collaboration Equation With Conventional 24-Hour Urinary Creatinine Clearance Test For Estimating Glomerular Filtration Rate In Chronic Kidney Disease Patients

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ABSTRACT

INTRODUCTION

The Glomerular Filtration Rate (GFR) is a direct measure of renal function. Estimation of GFR helps in assessing extent and progression of renal disease, and adjusting dosage of various drugs. In routine clinical practice, the most common method for assessing GFR is performing a 24-hour urine collection for evaluation of creatinine (an endogenous marker) clearance since tests like Inulin clearance are cumbersome and kept for pure research purpose. This test is inconvenient and can be inaccurate as a result of improper collection. Different equations like Cockcroft-Gault and MDRD equation are convenient for estimation of GFR, nevertheless the new Chronic Kidney Disease Epidemiology Collaboration Equation (CKD-EPI equation) was introduced and validated to be accurate in estimating GFR.

This study was conducted to determine a correlation between GFR calculated by the CKD-EPI and the conventional 24-hour urinary creatinine clearance test in chronic kidney disease patients admitted at a tertiary health care setting.

METHODOLOGY

A cross sectional survey of 100 adults with chronic kidney disease admitted via Outdoor Clinic in the Department of Nephrology, Bahria Town Hospital Lahore over a 6-month period were included in the study. After taking informed consent about including them in the study, a blood sample was taken from the patients on the same day of starting 24-hour urine collection by the researcher. Serum creatinine was measured from the blood sample by enzymatic method (creatinine method). GFR was calculated by the CKD-EPI equation separately for males and females using the standardized formula. Patients were explained the 24-hour urine sample collection protocol in the language they understood by the researcher. 24-hour urine was collected in containers without any additive/preservative and the 24 hour creatinine clearance was calculated by the formula. Statistical analysis was conducted using SPSS version 17.

RESULTS

The participants had a mean age of 42.18 ± 12.49 . There were 58 male and 42 female patients. The Karl Pearson correlation coefficient was calculated to see the correlation between GFR calculated by CKD-EPI equation and conventional 24-hour urinary creatinine clearance test and was found to be 0.679 which denotes a positive correlation. P value was found to be 0.01 which is significant ($p < 0.05$).

CONCLUSION

There is a positive correlation between the estimated GFR calculated by the CKD-EPI equation and conventional 24-hour urinary creatinine clearance test. Hence, the straightforward CKD-EPI equation can be used instead of the troublesome 24 urinary creatinine clearance test to calculate the eGFR without running the risk of inaccuracies.

KEYWORDS: *Chronic kidney disease, Chronic kidney disease Epidemiology collaboration equation, Glomerular filtration rate, 24 hour urinary creatinine clearance.*

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INTRODUCTION

Chronic kidney disease (CKD) is an important and growing health problem. The health economic burden of CKD is substantial; consequently, much focus has been placed on identification of patients in earlier phases of CKD, where appropriate intervention may be most effective.¹ Accurate estimation of glomerular filtration rate is crucial for the detection of CKD.²

In routine clinical practice, the most common method for assessing GFR is performing a timed urine collection for evaluation of creatinine (an endogenous marker) clearance.³ This test is inconvenient and can be inaccurate as a result of improper collection.⁴

More recently, the use of GFR estimating equations has been recommended in clinical practice which provide a simple, rapid and reliable modality of assessing kidney function.⁵ Several GFR prediction equations that take into account the serum creatinine and certain patient variables (age, gender, race, height and weight) have been shown to generate sufficiently precise, unbiased and easily calculated eGFR.^{6,7} The CKD-EPI equation was introduced recently and is considered to be the most accurate among the 46 different validated eGFR equations currently available.⁷ The latest CKD Epidemiology Collaboration Equation (CKD-EPI equation) estimate of renal function is calculated as follows:⁸

For women with a plasma creatinine >0.7 mg/dl

$$\text{GFR} = (\text{plasma creatinine}/0.7)^{-1.209} \times (0.993)^{\text{age}} (\times 166 \text{ if black; } \times 144 \text{ if other})$$

For men with a plasma creatinine >0.9 mg/dl

$$\text{GFR} = (\text{plasma creatinine}/0.9)^{-1.209} \times (0.993)^{\text{age}} (\times 166 \text{ if black; } \times 144 \text{ if other})$$

While the formula to calculate 24-hour urinary creatinine clearance is:

24-Hour Urinary Creatinine Clearance (24-hr CrCl)

$$\text{24-Hour CrCl} = \frac{\text{Urinary creatinine} \times \text{24-hour urine volume}}{\text{Plasma creatinine} \times 1440}$$

This study was conducted to determine a correlation between glomerular filtration rate calculated by the CKD-EPI and the conventional 24-hour urinary creatinine clearance test in chronic kidney disease patients admitted at a tertiary health care setting.

A major limitation of this study is that it does not attempt to correlate the CKD- EPI equation with gold standard measure of GFR estimation i.e. inulin clearance due to its unavailability in the local setting. Hence an attempt was made to correlate the CKD-EPI equation with the most commonly used GFR estimation clinical tool i.e. 24-hour creatinine clearance through this study. We believe this is the first attempt in the Pakistani population.

Materials and Methods

Study Design: Cross sectional survey was carried out in the Department of Nephrology Bahria Town Hospital Lahore over a period of 6 months.

Inclusion Criteria: All adults 18-80 years of age, both genders admitted in hospital with chronic kidney disease having plasma creatinine values greater than 1.3 mg/dL which remained static for more than two weeks were included in the study.

Exclusion Criteria: Patients having end stage renal disease i.e those patients requiring dialysis. Patients confirmed to be taking any drug (Fluoroquinolones, H2 blockers, Cephalosporins, Trimethoprim) which interferes with creatinine clearance as per available record.

Data Collection:

100 adults with chronic kidney disease admitted via outdoor (OPD) in the Department of Nephrology, Bahria Town Hospital Lahore fulfilling the inclusion criteria were included in the study. After taking informed consent, a blood sample was taken from the patients on the same day of starting 24-hour urine collection by the researcher. Serum creatinine was measured from the blood sample by enzymatic method (creatinine method) on 'Dimension' clinical chemistry system which employs a modification of the kinetic Jaffe reaction reported by Larsen. The age of each patient was confirmed from the national identity card by the researcher. GFR was calculated by the CKD-EPI equation separately for males and females by the formula mentioned earlier.

Patients were explained the 24-hour urine sample collection protocol in the language they understood best. The urine was collected in containers without any additive/preservative. Volume of urine passed in 24-hours was measured in milliliters in volumetric flasks. After thorough mixing of urine sample, 1:10 dilutions was prepared manually with deionized water. The 24-hour creatinine clearance was calculated by the formula stated above. All information obtained from the patient was recorded on a predesigned proforma.

Data Analysis The data was analyzed using the SPSS (version 17) analysis computer software. Qualitative variables such as sex were recorded as frequencies/percentages. Quantitative variables such as age were recorded as mean \pm standard deviation. Karl Pearson correlation coefficient was calculated to see the correlation between GFR calculated by CKD-EPI equation and conventional 24-hour urinary creatinine clearance test. P value less or equal to 0.05 was considered to be significant.

Results

We studied 100 patients admitted in the general nephrology ward via outpatient department over a period of six months. There were 58 male (58%) and 42 female (42%) patients (see table 1).

The patients had a mean age of 42.18 ± 12.49 . The age range varied from 20 years to 69 years. The maximum numbers of cases were in the range of 40-49 years of age i.e. 39 cases (see table 2).

Estimated GFR by both the CKD-EPI Equation and 24-hour urinary creatinine clearance method was calculated by following standard protocol and then compared. The Karl Pearson correlation coefficient was calculated by using the Statistical Package for Social Sciences Version 17.0 to see the correlation between GFR calculated by CKD-EPI equation and conventional 24-hour urinary creatinine clearance test and was found to be 0.679.

A positive correlation was noted. The P value was found to be 0.01 which is significant ($p < 0.05$)

Table 1: Distribution of cases by Gender, n=100

	Frequency	Percentage
Male	58	58%
Female	42	42%
Total	100	100%

Table 2: Distribution of cases by age, n =100

Age (Year)	Number	Percentage
20-29	13	13%
30-39	20	20%
40-49	39	39%
50-59	22	22%
60-69	6	6%
Total	100	100%
Mean±SD	42.18±12.49	

Discussion:The two main developments in estimating glomerular filtration rates in the past five years have been reduced inter-laboratory variability with standardised creatinine measurements⁹ and the appearance of the less biased CKD-EPI equation to replace the MDRD and CG equation¹⁰. The most commonly used modality of estimating GFR in clinical practice remains 24-hour urinary creatinine clearance⁴. Even if we overlook the potential inaccuracies of this test this test remains cumbersome for both the clinician and the patient to carry out⁴. In contrast, the CKD-EPI equation has been validated to be more accurate and user friendly¹¹.

The aim of our study was to determine if a strong correlation existed between the estimated glomerular filtration rates calculated by the 24-hour urinary creatinine clearance and the CKD-EPI equation. A strong correlation between the tests would provide us with scientific evidence that CKD-EPI is equally as accurate as 24-hour urinary creatinine clearance whilst being more practical and user friendly. In our study, we found a strong positive correlation between the two tests as determined by the Karl-Pearson's correlation coefficient i.e. 0.679 with a p value of 0.01 which is significant (p<0.05).

These results, produced using standardized creatinine levels, are different from those previously published with CKD-EPI, MDRD and CG equations.¹² With non-standardized creatinine levels, the CG equation was more accurate than MDRD for measuring glomerular filtration rate, whether comparing urine creatinine clearance³ or ^{99m}Tc-DTPA scan as reference methods.¹³ Although, it was still less accurate than the CKD-EPI. Due to the non-

standardized creatinine assay data used these studies were deemed questionable and data with standardized assays remain scarce.

Additionally, the variability inherent in the CG equation depends on the sex, age, body mass index, and glomerular filtration rate of the patient. The accuracy of this value is lower in women, and decreases with lower age and glomerular filtration values, and as BMI increases. On the other hand, the accuracy of the MDRD and CKD-EPI equations is not influenced by these variables. Some authors suggest that the CG equation no longer has clinical relevance, and will not have it until it has been adapted for standardized creatinine and its results have been validated for different populations of patients.¹⁴

With the use of a standardized measure of creatinine, CKD-EPI & MDRD equations have gained a higher level of concordance with glomerular filtration rate. In some studies, a relationship was observed between the bias in MDRD and nutritional state: this equation had a tendency to underestimate glomerular filtration rate in patients with a better nutritional state or higher BMI and the accuracy of the equation also depended on the renal failure stage, with greater variability at higher levels of glomerular filtration rate. No such finding has been reported with the CKD-EPI equation to date. In our study, we did not observe any significant influence of BMI or stage of renal failure on the parameters for concordance between urinary creatinine clearance and the CKD-EPI equation.

Levey et al. proposed that MDRD should be replaced by CKD-EPI in all clinical situations, which raised a considerable amount of controversy¹⁵. It is true that the bias, variation, precision, accuracy, and class correlation coefficient for CKD-EPI are very similar to those of MDRD. However, CKD-EPI still does not provide any observable advantage in stage 4 and 5 chronic renal disease patients, and many clinical and epidemiological studies carried out up to the present day have used MDRD. In our study, we studied the correlation between 24 hour urinary creatinine clearance and the CKD-EPI equation only. The superiority of the CKD-EPI equation over the MDRD equation was not addressed in our study. Further studies with a head to head analysis of the 2 two equations is required to settle this issue.

Keeping in mind the limitations of the sample size, we can conclude that in our population, the CKD-EPI equation provides a glomerular filtration rate that is equivalent to that derived from 24 hour urinary creatinine clearance.

Conclusion

In conclusion, there is a positive correlation between the estimated GFR calculated by the CKD-EPI equation and conventional 24-hour urinary creatinine clearance test. Hence, the straightforward CKD-EPI equation can be used instead of the cumbersome 24-hour urinary creatinine clearance test to calculate the eGFR without running the risk of inaccuracies.

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