# Comparison of CKD-EPI estimated glomerular filtration rate and measured creatinine clearance in critically ill patients with normal plasma creatinine

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## Abstract

**Introduction:** Accurate assessment of renal function is a priority in the management of critically ill patients. Assessment of renal function helps in guiding drug dosing, optimize fluid, acid–base, and electrolyte management. Evidence based medicine in the form of research studies have shown that there exists a poor correlation between CKD-EPI eGFR and creatinine clearance in patients with normal plasma creatinine. Currently there is a paucity of data in India as to whether examining whether eGFR could be used in place of conventional measures for such a purpose, particularly in the critical care environment. The study was done to compare CKD-EPI eGFR with measured urinary CLCR, in recently admitted critically ill patients with normal plasma creatinine concentrations.

**Material and Methods:** The study was a prospective observational study which consisted of recently admitted critically ill patients with normal plasma creatinine concentrations admitted to the ICU of A. J. Institute Of Medical Sciences Hospital, Mangalore on f 100 patients who met a pre-defined criteria done over a period of 2 years from October 2014 to November 2016 after obtaining ethical clearance committee of the institution and informed consent of the patient and/or their legal heir. This was a prospective observational study that was conducted in the intensive care unit Patients who were recently were admitted to the intensive ICU admission, plasma creatinine concentration </= 1.2mg/dL and no history of prior CKD. CKD-EPI eGFR was compared against 8-hour measured urinary CLCR. Data was collected within 48 hours of admission. The collected data was transferred to a master- chart and analyzed for

**Results:** The mean age in our study was 55.43 years, the mean height was 164.55cms, the mean weight was 69.19 kg and the mean BSA was1.7759 males predominated the study cases 62%. males predominated the study cases 62%.16 % cases in our study needed mechanical ventilation On comparison of the mean values of 24 HR Cr CL and CKD-EPI the mean values of CKD-EPI is higher with a difference of 0.9727 is statistically not significant with a p value of 0.726. At a GFR of 90-119.99 ml/min On comparison of the mean values of 24 HR Cr CL and CKD-EPI the mean values of 24 HR Cr CL is higher with a difference of 22.229 is statistically significant with a p value of <0.001. On comparison of the mean values of 24 HR Cr CL and MDRD the mean values of 24 HR Cr CL is higher with a difference of 21.7355 is statistically significant with a p value of <0.001. On comparison of the mean values of 24 HR Cr CL and CG-Cr CL the mean values of 24 HR Cr CL is higher with a difference of 19.29194 is statistically significant with a p value of <0.001.

**Conclusion:** In conclusion, this study has examined CKD-EPI eGFR in comparison to 8-hr measured CLCR in a cohort of recently admitted critically ill patients with normal plasma CR concentrations. Our results suggest poor agreement between these techniques in this population. Whether this represents a true limitation of CKD-EPI eGFR, or an intuitive discrepancy based on the problems with endogenous CLCR, remains uncertain. Notwithstanding this, until additional data are available on the utility of CKD-EPI eGFR for drug dose adjustment, particularly in identifying ARC, we would recommend clinicians consider using CLCR for this purpose.

**Keywords:** Glomerular filtration rate, Renal Disease, CKD-EPI.

## Introduction

Accurate assessment of renal function is a priority in the management of critically ill patients. Assessment of renal function helps in guiding drug dosing, optimize fluid, acid–base, and electrolyte management. Though plasma creatinine concentrations are within the reported reference range the normal values in the critically ill have been associated with both augmented creatinine clearance (CLCR),[1] and occult acute kidney injury (AKI).[2]

The most commonly applied formula developed to estimate the glomerular filtration rate (eGFR) is the Modification of Diet in Renal Disease (MDRD),[3] newer CKD Epidemiology Collaboration (CKD-EPI)[4] equations and Cockcroft Gault Creatinine Clearance.

Though MDRD and CKD-EPI equations improved the quality of care for patients with CKD, there is a concern about the ubiquitous application of eGFR, particularly in dose modification.[9]

Evidence based medicine in the form of research studies have shown that there exists a poor correlation between CKD-EPI eGFR and creatinine clearance in patients with normal plasma creatinine.[10]

Currently there is a paucity of data in India as to whether examining whether eGFR could be used in place of conventional measures for such a purpose, particularly in the critical care environment. The aims and objectives of the study was to compare CKD-EPI eGFR with measured urinary CLCR, in recently admitted critically ill patients with normal plasma creatinine concentrations.

## Materials and Methods

The study was a prospective observational study which consisted of recently admitted critically ill patients with normal plasma creatinine concentrations admitted to the ICU of A. J. Institute Of Medical Sciences Hospital, Mangalore on f 100 patients who met a pre-defined criteria done over a period of 2 years from October 2014 to

November 2016 after obtaining ethical clearance committee of the institution and informed consent of the patient and/or their legal heir.

**Method of collection of data**

It was a hospital based prospective observational study done on recently admitted critically ill patients with normal plasma creatinine concentrations admitted in the ICU of AJ Institute of Medical Science.

A study of 100 patients was done over a period of 2 years from October 2014 to November 2016

These were the pre-defined criteria:

**Inclusion Criteria**

1. Recent ICU admission
2. Plasma creatinine </= 1.2mg/dL
3. No history of prior CKD

**Exclusion Criteria**

1. < 18 years
2. Pregnancy
3. Rhabdomyolysis
4. Admission plasma creatinine kinase > 5000IU/L (RIFLE criteria)

**Methodology**

1. This was a prospective observational study that was conducted in the intensive care unit
2. Patients who were recently were admitted to the intensive ICU admission, plasma creatinine concentration </= 1.2mg/dL, and no history of prior CKD.
3. CKD-EPI eGFR was compared against 8-hour measured urinary CLCR.
4. Data was collected within 48 hours of admission.
5. The collected data was transferred to a master- chart and analyzed.

**Statistical Analysis**

Statistical analysis was done using SPSS software version 23.0. A 'p' value less than 0.05($p<0.05$) is considered significant.

The collected information was summarized as percentage and proportions.

To study the prevalence of work related musculoskeletal disorders frequency and percentage was used.

The rest collected data was analyzed using mean, mode for demographic data and frequency percentage for the analysis of the clinical data.

## Results and Observations

**Table 1: Demographic data**

| | Mean | Standard Deviation |
|---|---|---|
| Age | 55.43 | 16.00332 |
| Height | 164.55 | 8.079623 |
| Weight | 69.19 | 10.24911 |
| BSA | 1.7759 | 0.158516 |

**Table 2: Gender**

| | | Count | % |
|---|---|---|---|
| Gender | F | 38 | 38 |
| | M | 62 | 62 |

**Table 3: Admission type**

| Admission type | | Frequency | Percentage |
|---|---|---|---|
| Admission type | Elective | 10 | 10 |
| | Emergency | 69 | 69 |
| | Surgical emergency | 10 | 10 |
| | Trauma | 11 | 11 |

**Table 4: Variation of creatinine in the various admissions**

| | | | Mean | N | Std. Deviation | BIAS | | t Value for paired T -Test | P value | R | P value of correlation |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | Mean Difference | Std. Deviation | | | | |
| Overall | | 24 HR Cr CL | 102.131 | 100 | 29.2996 | | | | | | |
| | Pair 1 | CKD-EPI | 80.035 | 100 | 19.5258 | 22.096 | 25.2185 | 8.762 | <0.001 | 0.528 | <0.001 |
| | Pair 2 | MDRD | 80.238 | 100 | 20.2887 | 21.893 | 27.106 | 8.077 | <0.001 | 0.45 | <0.001 |
| | Pair 3 | CG-Cr CL | 81.4239 | 100 | 26.8346 | 20.7071 | 31.39529 | 6.596 | <0.001 | 0.377 | <0.001 |
| Elective | | 24 HR Cr CL | 96.76 | 10 | 23.4835 | | | | | | |
| | Pair 1 | CKD-EPI | 82.08 | 10 | 17.2427 | 14.68 | 9.4965 | 4.888 | 0.001 | 0.937 | <0.001 |
| | Pair 2 | MDRD | 82.51 | 10 | 17.2926 | 14.25 | 9.9865 | 4.512 | 0.001 | 0.924 | <0.001 |
| | Pair 3 | CG-Cr CL | 88.048 | 10 | 22.51076 | 8.712 | 19.27077 | 1.43 | 0.187 | 0.65 | 0.042 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Emergency | | 24 HR Cr CL | 103.201 | 69 | 29.1065 | | | | | | |
| | Pair 1 | CKD-EPI | 79.826 | 69 | 18.3704 | 23.3754 | 27.838 | 6.975 | <0.001 | 0.383 | 0.001 |
| | Pair 2 | MDRD | 80.381 | 69 | 19.4445 | 22.8203 | 30.3593 | 6.244 | <0.001 | 0.268 | 0.026 |
| | Pair 3 | CG-Cr CL | 78.4075 | 69 | 25.40345 | 24.79391 | 32.10593 | 6.415 | <0.001 | 0.312 | 0.009 |
| Surgical emergency | | 24 HR Cr CL | 86.88 | 10 | 39.1336 | | | | | | |
| | Pair 1 | CKD-EPI | 69.41 | 10 | 23.7316 | 17.47 | 22.6428 | 2.44 | 0.037 | 0.852 | 0.002 |
| | Pair 2 | MDRD | 68.74 | 10 | 23.7441 | 18.14 | 22.6343 | 2.534 | 0.032 | 0.852 | 0.002 |
| | Pair 3 | CG-Cr CL | 76.451 | 10 | 33.26813 | 10.429 | 31.55659 | 1.045 | 0.323 | 0.631 | 0.051 |
| Trauma | | 24 HR Cr CL | 114.164 | 11 | 20.8498 | | | | | | |
| | Pair 1 | CKD-EPI | 89.145 | 11 | 22.2823 | 25.0182 | 19.6663 | 4.219 | 0.002 | 0.586 | 0.058 |
| | Pair 2 | MDRD | 87.727 | 11 | 22.987 | 26.4364 | 18.8262 | 4.657 | 0.001 | 0.635 | 0.036 |
| | Pair 3 | CG-Cr CL | 98.8436 | 11 | 28.69385 | 15.32 | 33.48948 | 1.517 | 0.16 | 0.114 | 0.738 |

**Table 4: Various laboratory parameters**

| | | |
|---|---|---|
| Plasma Creatinine Concentration (µmol/L) | 0.981 | 0.173901 |
| Plasma Creatinine Concentration (µmol/L) + 24hrs plasma creatinine | 0.997 | 0.148021 |
| Apache II | 9.11 | 4.607624 |
| Modified SOFA | 3.75 | 2.540083 |
| ICU Stay (days) | 4.72449 | 2.99064 |
| CKD-EPI | 80.035 | 19.52579 |
| MDRD | 80.238 | 20.2887 |
| CG-Cr CL | 81.4239 | 26.8346 |
| 24 HR U Cr | 85.99 | 17.8402 |
| 24 HR Cr CL | 102.131 | 29.2996 |

**Overall**

On comparison of the mean values of 24 HR Cr CL and CKD-EPI the mean values of 24 HR Cr CL is higher with a difference of 22.096 is statistically significant with a p value of <0.001.

On comparison of the mean values of 24 HR Cr CL and MDRD the mean values of 24 HR Cr CL is higher with a difference of 21.893 is statistically significant with a p value of <0.001.

On comparison of the mean values of 24 HR Cr CL and CG-Cr CL the mean values of 24 HR Cr CL is higher with a difference of 20.7071 is statistically significant with a p value of <0.001.

**Elective**

On comparison of the mean values of 24 HR Cr CL and CKD-EPI the mean values of 24 HR Cr CL is higher with a difference of 14.68 is statistically significant with a p value of 0.001.

On comparison of the mean values of 24 HR Cr CL and MDRD the mean values of 24 HR Cr CL is higher with a difference of 14.25 is statistically significant with a p value of 0.001.

On comparison of the mean values of 24 HR Cr CL and CG-Cr CL the mean values of 24 HR Cr CL is higher with a difference of 8.712 is statistically not significant with a p value of 0.187.

**Emergency**

On comparison of the mean values of 24 HR Cr CL and CKD-EPI the mean values of 24 HR Cr CL is higher with a difference of 23.3754 is statistically significant with a p value of <0.001.

On comparison of the mean values of 24 HR Cr CL and MDRD the mean values of 24 HR Cr CL is higher with a difference of 22.8203 is statistically significant with a p value of <0.001.

On comparison of the mean values of 24 HR Cr CL and CG-Cr CL the mean values of 24 HR Cr CL is higher with a difference of 24.79391 is statistically significant with a p value of <0.001.

**Surgical Emergency**

On comparison of the mean values of 24 HR Cr CL and CKD-EPI the mean values of 24 HR Cr CL is higher with a difference of 17.47 is statistically significant with a p value of 0.037.

On comparison of the mean values of 24 HR Cr CL and MDRD the mean values of 24 HR Cr CL is higher with a difference of 18.14 is statistically significant with a p value of 0.032.

On comparison of the mean values of 24 HR Cr CL and CG-Cr CL the mean values of 24 HR Cr CL is higher with a difference of 10.429 is statistically not significant with a p value of 0.323.

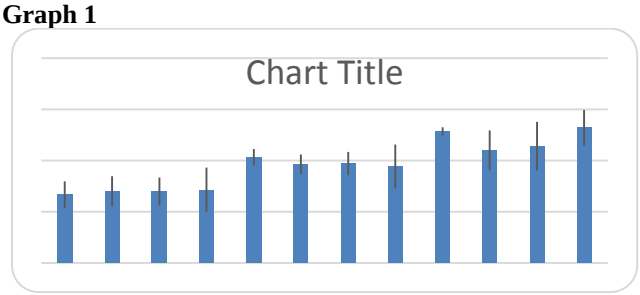
**Trauma**

On comparison of the mean values of 24 HR Cr CL and CKD-EPI the mean values of 24 HR Cr CL is higher with a difference of 25.0182 is statistically significant with a p value of 0.002.

On comparison of the mean values of 24 HR Cr CL and MDRD the mean values of 24 HR Cr CL is higher with a difference of 26.4364 is statistically significant with a p value of 0.001.

On comparison of the mean values of 24 HR Cr CL and CG-Cr CL the mean values of 24 HR Cr CL is higher with a difference of 15.32 is statistically not significant with a p value of 0.16.

**Graph 1**




## Discussion

Accurate assessment of renal function is a priority in the management of critically ill patients. Clinicians regularly utilize such information to help guide drug dosing, optimize fluid, acid–base, and electrolyte management, tailor nutritional requirements, and assess the need for renal replacement therapy (RRT). Rising plasma creatinine (CR) concentrations often trigger clinical interventions, including dose reduction of renally eliminated agents. In contrast, plasma CR concentrations within the reported reference range appear to be less useful. Normal values in the critically ill have been associated with both augmented creatinine clearance ($CL_{CR}$), and occult acute kidney injury (AKI). In ICU patients with normal serum creatinine (SCr), a state of increased renal drug excretion has been described (creatinine clearance ≥130 ml/min/1.73 m2), and named augmented renal clearance (ARC). In ICU patients, the accuracy of GFR estimates is insufficient. Currently there is a paucity of data in India as to whether examining whether eGFR could be used in place of conventional measures for such a purpose, particularly in the critical care environment.in our study titled "comparison of CKD-EPI estimated glomerular filtration rate and measured creatinine clearance in critically ill patients with normal plasma creatinine" we aimed to compare CKD-EPI eGFR with measured urinary CLCR, in recently admitted critically ill patients with normal plasma creatinine concentrations.[10]

**Admission Type**

In our study the admission type was elective 10, emergency 69, surgical emergency 10, trauma 11.

Andrew A Udy et al.[10] had Admission type, n (%) Elective 15(13.6) Emergency 33(30.0) Surgical emergency, 37(33.6) - Trauma 25(22.7).

**Need for mechanical ventilation**

16 % cases in our study needed mechanical ventilation

In a study by Stéphanie Ruizet al 270(75 %) of the patients were mechanically ventilated.

In a study by Andrew A Udy et.al Mechanical ventilation, was needed inn 63(57.3%)

**Variations of Creatinine**

Stéphanie Ruizet al[11] showed that ICU patients can exhibit important variations of their measured CrCl, despite a normal SCr with the CrCl being higher than 130 ml/min/1.73 m2 (ARC) in more than 33 % of the cases.

This finding was similar to our finding in which the ICU patients exhibit important variations of their measured CrCl, despite a normal SCr 35%. In our study on comparison of the mean values of 24 HR Cr CL and CKD-EPI the mean values of 24 HR Cr CL is higher with a difference of 22.096 is statistically significant with a p value of <0.001.

**Drugs Given**

In a study by Andrew A Udy et al[10] the drugs given are comparable with our study Intravenous contrast administration, n (%) (n = 109) 30(27.3) Frusemide administration, n (%) 13(11.8) Mannitol administration, n (%) 4(3.6) Vasopressors, n (%) 33(30.0).

In 28 critically ill patients with normal SCr, Hoste[12] demonstrated that the Cockcroft-Gault and MDRD formulas were not adequate in assessing renal function and we have previously shown similar findings in 36 burn patients.

## Conclusion

Acute renal compromise appears to be common in intensive care critically ill patients. This study suggests the CKD-EPI equation could allow a first screening of patients with Acute renal compromise. In conclusion, this study has examined CKD-EPI eGFR in comparison to 8-hr measured CLCR in a cohort of recently admitted critically ill patients with normal plasma CR concentrations. Our results suggest poor agreement between these techniques in this population. Whether this represents a true limitation of CKD-EPI eGFR, or an intuitive discrepancy based on the problems with endogenous CLCR, remains uncertain. Notwithstanding this, until additional data are available on the utility of CKD-EPI eGFR for drug dose adjustment, particularly in identifying ARC, we would recommend clinicians consider using CLCR for this purpose.

**Conflict of Interest:** None.

## References


1. Hoste EA, Damen J, Vanholder RC, Lameire NH, Delanghe JR, Van den Hauwe K, Colardyn FA: Assessment of renal function in recently admitted critically ill patients with normal serum creatinine. *Nephrol Dial Transplant* 2005;20(4):747–53.
2. Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D: A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of diet in renal disease study Group. *Ann Intern Med* 1999;130(6):461–70.
3. Levey AS, Stevens LA, Schmid CH, Zhang YL, Castro AF 3rd, Feldman HI, Kusek JW, Eggers P, Van Lente F, Greene T, et al: A new equation to estimate glomerular filtration rate. *Ann Intern Med* 2009;150(9):604–12.
4. Matsushita K, Mahmoodi BK, Woodward M, Emberson JR, Jafar TH, Jee SH, Polkinghorne KR, Shankar A, Smith DH, Tonelli M, et al: Comparison of risk prediction using the CKD-EPI equation and the MDRD study equation for estimated glomerular filtration rate. *JAMA* 2012;307(18):1941–51.
5. White SL, Polkinghorne KR, Atkins RC, Chadban SJ: Comparison of the prevalence and mortality risk of CKD in Australia using the CKD Epidemiology Collaboration (CKD-EPI) and Modification of Diet in Renal Disease (MDRD) Study GFR estimating equations: the AusDiab (Australian Diabetes, Obesity and Lifestyle) Study. *Am J Kidney Dis* 2010;55(4):660–70.
6. Johnson DW, Jones GR, Mathew TH, Ludlow MJ, Doogue MP, Jose MD, Langham RG, Lawton PD, McTaggart SJ, Peake MJ, et al: Chronic kidney disease and automatic reporting of estimated glomerular filtration rate: new developments and revised recommendations. *Med J Aust* 2012;197(4):224–25.
7. Mathew TH, Johnson DW, Jones GR, Australasian Creatinine Consensus Working Group: Chronic kidney disease and automatic reporting of estimated glomerular filtration rate: revised recommendations. *Med J Aust* 2007;187(8):459–63.
8. Martin JH, Fay MF, Ungerer JP: eGFR–use beyond the evidence. *Med J Aust* 2009;190(4):197–99. Rodrigo E, Fernandez-Fresnedo G, Ruiz JC, Pinera C, Heras M, De Francisco AL, de Castro SS, Cotorruelo JG, Zubimendi JA, Arias M. Assessment of glomerular filtration rate in transplant recipients with severe renal insufficiency by Nankivell, Modification of Diet in Renal Disease (MDRD), and Cockroft-Gault equations. In Transplantation proceedings 2003;35(5):1671-1672. Elsevier.
9. Udy AA, Roberts JA, Shorr AF, Boots RJ, Lipman J: Augmented renal clearance in septic and traumatized patients with normal plasma creatinine concentrations: identifying at-risk patients. *Crit Care* 2013;17(1):R35
10. Bingham SA, Cummings JH. The use of creatinine output as a check on the completeness of 24-hour urine collections. Human nutrition. *Clin Nutrition* 1985;39(5):343-53.
11. Hoste EA, Damen J, Vanholder RC, Lameire NH, Delanghe JR, Van den Hauwe K, et al. Assessment of renal function in recently admitted critically ill patients with normal serum creatinine. *Nephrol Dial Transpl Off Publ European Dial Transpl Assoc European Renal Assoc* 2005;20(4):747–53.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