ORIGINAL ARTICLE

# Detection of Reduced eGFR among Adults with Normal Serum Creatinine: A Cross-Sectional Study

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## ABSTRACT

**Objective:** This study aimed to determine the prevalence of reduced glomerular filtration rate (eGFR) among adults with normal serum creatinine and to compare eGFR values calculated using the Cockcroft–Gault (CG) and Modification of Diet in Renal Disease (MDRD) equations.

**Study Design:** Cross-sectional study

**Place and Duration of Study:** Department of Pathology, Services Hospital, Lahore, from 1st August 2023 to 31st October 2023.

**Materials and Methods:** A total of 180 adults aged between 45 and 70 years were enrolled in the study. To reduce potential confounding effects on renal function assessment, participants with normal serum creatinine levels were included, whereas those who were fat or malnourished were omitted. After obtaining each participant's informed written consent, data were gathered using a systematic, pre-designed Performa. Relevant demographic characteristics and clinical information were systematically recorded and subsequently analyzed. Serum creatinine was measured, and estimated glomerular filtration rate (eGFR) was calculated using the Cockcroft–Gault (CG) and MDRD equations.

**Results:** The mean serum creatinine level was 0.65 ± 0.15 mg/dL. The mean eGFR calculated using the Cockcroft–Gault equation was 117.03 ± 27.55 mL/min, whereas the mean eGFR using the MDRD equation was 112.23 ± 24.20 mL/min/1.73 m². The difference between the two equations was statistically significant ($p < 0.001$).

**Conclusion:** The findings demonstrate that reduced eGFR may occur in adults with normal serum creatinine levels. Reliance solely on serum creatinine may lead to underdiagnosis of renal impairment. Routine reporting of eGFR, particularly using the MDRD equation, may facilitate earlier detection of renal dysfunction.

**Key Words**: *Cockcroft–Gault Equation, Estimated Glomerular Filtration Rate, MDRD Equation, Renal Insufficiency, Serum Creatinine.*

## Introduction

Chronic kidney disease (CKD) is defined as the presence of kidney damage or reduced kidney function for at least three months, regardless of the underlying cause. Kidney damage may be identified through imaging findings, histopathological abnormalities, or clinical markers such as increased albuminuria or abnormal urinary sediment. Reduced kidney function is generally assessed by measuring the glomerular filtration rate (GFR), which is commonly estimated (eGFR) from serum creatinine levels. CKD is a progressive condition affecting more than 10% of the global population and is particularly prevalent among older individuals, females, and patients with diabetes mellitus or hypertension. It is also an important contributor to increased morbidity and mortality worldwide.[1,2]

Renal impairment significantly increases the risk of complications such as hypertension, cardiovascular disease, and bone mineral disorders, which may ultimately require renal replacement therapy. Early identification of renal dysfunction, therefore, allows timely interventions that can slow disease progression and reduce associated complications.[3–8]

Serum creatinine (SCr) is widely used in clinical practice as an endogenous marker to assess renal function due to its simplicity and availability. However, SCr is relatively insensitive for detecting early kidney dysfunction. Serum creatinine levels may remain within the normal range despite

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substantial nephron loss, as they are influenced by factors such as age, muscle mass, and delayed accumulation in the bloodstream. Consequently, reliance solely on serum creatinine may lead to underdiagnosis of early renal impairment.[9–11]

Glomerular filtration rate (GFR) is considered the most reliable indicator of kidney function. Direct measurement of GFR using exogenous filtration markers such as inulin clearance is regarded as the gold standard; however, this method is complex, costly, and impractical for routine clinical use.[13] Therefore, various equations have been developed to estimate GFR using serum creatinine along with demographic variables such as age and sex.[12,14]

Among these equations, the Modification of Diet in Renal Disease (MDRD) equation is widely used for estimating eGFR in clinical practice, whereas the Cockcroft–Gault (CG) equation estimates creatinine clearance and has historically been used for drug dosing adjustments in renal impairment. Although these equations are useful for estimating renal function, differences between them may influence the detection of reduced kidney function.[12,15]

According to Kidney Disease Improving Global Outcomes (KDIGO) guidelines, CKD is classified into stages based on eGFR values, ranging from normal kidney function (≥90 mL/min/1.73 m²) to end-stage renal disease (<15 mL/min/1.73 m²).[18] Reduced eGFR becomes increasingly common with advancing age due to structural and functional changes in the kidney.

Therefore, this study aimed to determine the prevalence of reduced eGFR among adults with normal serum creatinine and to compare eGFR values calculated using Cockcroft–Gault and MDRD equations.

## Materials and Methods

After obtaining approval from the institutional review board (IRB Num # IRB/2023/1144/SIMS), this cross-sectional study was conducted in the Department of Pathology, Services Hospital Lahore, over a three month period from 1st August 2023 to 31st October 2023.

The sample size of 180 participants was calculated using a 95% confidence level , 7% margin of error, and an expected prevalence of moderate renal impairment of 21% based on previously published literature. A consecutive non-probability sampling (Convenient Sampling) technique was used.

Adult Pakistani patients aged 45-70 years attending the outpatient department with normal serum creatinine levels (male ≤ 1.3 mg/dL and female ≤ 1.1 mg/dL) were included in the study. Patients on dialysis and those with obesity or malnutrition were excluded to minimize confounding due to altered muscle mass affecting serum creatinine and eGFR estimation.

Information regarding risk factors such as diabetes mellitus and hypertension was obtained through patient history. During clinical assessment, participants' weight and height were measured, and body mass index (BMI) was calculated using the formula weight (kg)/height (m²).

Serum samples were collected from all participants for the estimation of serum creatinine. A fully automated chemistry analyzer (Beckman Coulter AU480) was used to measure serum creatinine using the Jaff kinetic technique (photometric measurement) following standard laboratory quality control procedures.

In our study, renal function was determined using the MDRD equation and CG formula, and eGFR of all patients was calculated using both equations.

According to KDIGO guidelines, renal function was classified based on eGFR values as follows:
G1 ≥90 mL/min/1.73 m² (normal),
G2 60–89 mL/min/1.73 m² (mild decreased),
G3a 45–59 mL/min/1.73 m², (mild to moderately decreased)
G3b 30–44 mL/min/1.73 m²,(moderately to severely decreased
G4 15–29 mL/min/1.73 m² (severely decreased).[19, 20]

Data analysis was performed using SPSS version 28. Quantitative variables like age, height, weight, BMI, and Serum Creatinine were presented as mean ± standard deviation, while categorical variables like ethnicity, gender, hypertension, diabetes, obesity, and family history, were presented as frequency or percentages. Stratification was performed for potential effect modifiers, and the Chi-square test was applied for comparison of categorical variables. P-value <0.05 considered statistically significant.

## Results

In our study, 38.33% (n=69) were female and 61.67% (n=111) male. The mean age was 52.40 ±5.35 years, with a range of ages between 45 and 70. In this study, 106 (59%) hypertensive and 74 (41%) non-hypertensive patients were enrolled, with 53 (29.44%) diabetic and 127 (70.56%) non-diabetic patients, as shown in Fig. 1. The mean body mass index (BMI) was 26.47 ± 3.48. The serum creatinine estimated was 0.65 ± 0.15mg/dl.

The mean eGFR by the C-G equation was 117.03 ± 27.55 ml/min and 112.23 ± 24.20 ml/min/1.73$m^2$ by the MDRD equation. Patients falling in G1, G2, and G3a stages of renal insufficiency were 146 (81.1%), 31 (17.2%), and 3 (1.7%), respectively, by C-G formula (Table I). Patients with renal insufficiency in stages G1, G2, and G3a were 154 (85.6%), 24 (13.3%), and 2 (1.1%), respectively, by the MDRD equation (Table II). A comparison of both equations according to stages by chi square is given in Table III.

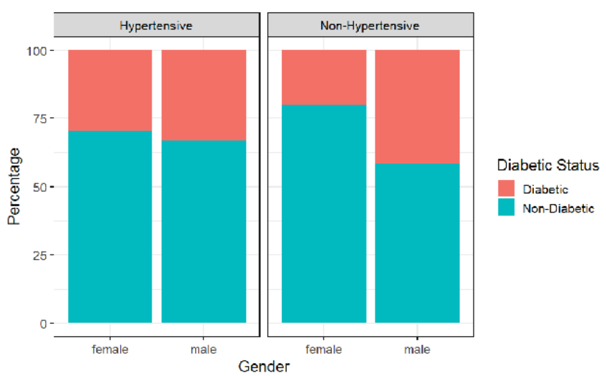


**Figure 1. Prevalence of Hypertension and Diabetes Across Gender Groups**

**Table I: Frequency of Renal failure by CG Formula (N= 180)**

| | G1 n(%) | G2 n(%) | G3a n(%) | G3b n(%) | G4 n(%) | P-Value |
|---|---|---|---|---|---|---|
| **Male** | 60 (87%) | 9 (13%) | 0 (0%) | 0 (0%) | 0 (0%) | 0.528 |
| **Female** | 94 (84.7%) | 15 (13.5%) | 2 (1.8%) | 0 (0%) | 0 (0%) | |
| **Total** | 154 (85.6%) | 24 (13.3%) | 2 (1.1%) | 0 (0%) | 0 (0%) | |

**Table II: Frequency of Renal failure by MDRD Equation (N= 180)**

| | G1 n(%) | G2 n(%) | G3a n(%) | G3b n(%) | G4 n(%) | P-Value |
|---|---|---|---|---|---|---|
| **Male** | 55 (79.7%) | 13 (18.8%) | 1 (1.4%) | 0 (0%) | 0 (0%) | 0.892 |
| **Female** | 91 (82%) | 18 (16.2%) | 2 (1.8%) | 0 (0%) | 0 (0%) | |
| **Total** | 146 (81.1%) | 31 (17.2%) | 3 (1.7%) | 0 (0%) | 0 (0%) | |

**Table III: Comparison of Renal Failure by CG and MDRD Equation (N= 180**

| CKD Stages | CG n (%) | MDRD n (%) | P-Value |
|---|---|---|---|
| **G1** | 146 (81.11%) | 154 (85.56%) | <0.001 |
| **G2** | 31(12.22%) | 24(13.33%) | |
| **G3a** | 3 (1.67%) | 2(1.11%) | |
| **G3b** | 0 (0%) | 0 (0%) | |
| **G4** | 0 (0%) | 0 (0%) | |

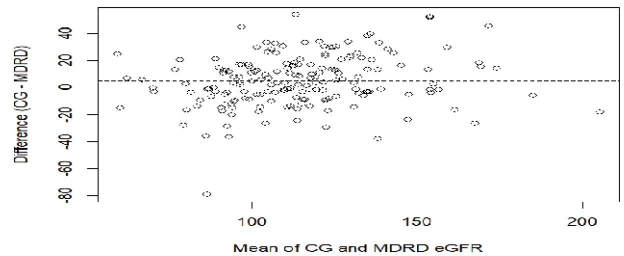


**Figure 2. Bland–Altman Plot: CG vs MDRD eGFR**

## Discussion

The early detection of any renal damage can be ensured through clinical guidelines that suggest using estimation equations like MDRD and CG formulas to estimate eGFR on the basis of SCr levels.[6] The reason why estimation equations need to be used in the detection of early-stage renal damage is because SCr levels, which by themselves are considered insensitive markers in the determination of kidney damage, can be normal even if renal impairment occurs. In view of this problem, the current study seeks to establish the prevalence of kidney insufficiency and CKD staging among adults with normal SCr levels.[20]

Our results show that the mean SCr of the patients is 0.65 ± 0.15, which aligns with the literature findings, with a mean Serum Creatinine of 0.88 ± 0.26 in patients without renal insufficiency, which displays that the serum creatinine is normal in both studies. In our study, the mean eGFR by the CG formula was 117.03 ± 27.55, and by the MDRD formula was 112.23 ± 24.20. Similar findings for $eGFR_{MDRD}$ (ml/min/1.73 $m^2$) were found in a previous study, i.e., 116.8 ± 43.5, which supported our results. However, the mean $eGFR_{CG}$ (ml/min/1.73 $m^2$) was 90.5 ± 33.1, which is different from our findings of $eGFR_{CG}$ equal to117.03 ± 27.55.[21,22]

Bland-Altman plot displayed in Fig. 2 revealed the presence of a mean bias of 4.80 mL/min/1.73m2 which shows that the CG formula is somewhat biased towards an overestimation of eGFR with respect to


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MDRD formula. On the other hand, the limits of agreement were observed between -32.14 and 41.74 mL/min/1.73m2, suggesting a considerable extent of spread between the two formulas. However, the magnitude of the overall bias seems relatively low. Thus, it can be said that the CG and MDRD formulae present a fair degree of agreement and interchangeability.

Our findings shows that, according to $eGFR_{CG}$, there were 146 (81.11%) patients, and according to $eGFR_{MDRD}$, 154 (85.56%) patients were in G1 (Normal) group, while 31(12.22%) and 24(13.33%) according to CG and MDRD respectively were in G2 (Mild) stage. 3 (1.67%) patients by CG and 2 (1.11%) by MDRD in the G3a (Mild-Moderate) group. However, no patient was found in the G3b and G4 (Severe) groups. P-value was significant <0.001, making both equations significantly different as based on different formulas. Another study demonstrates that by MDRD equation with normal SCr, 21.5% of and by C-G formula, 38.2% of patients were in the mild renal impairment group. According to the MDRD and CG equations, 7.7% and 9.2% of study subjects had mild to moderate kidney dysfunction, respectively. The MDRD and CG formula found moderate renal insufficiency in 7.7% and 16.9% of patients, respectively. Additionally, 7.7% of patients had moderate to severe renal impairment despite having SCr in the reference range when eGFR was predicted by the CG formula.[23]

CG equation overestimates eGFR as body weight is used as a marker of muscle mass; in obese people, it will overestimate the eGFR value. Moreover, standardization of the Creatinine assay used in the equations is not available to reference method. Cockcroft -Gault formula has yet to be modified for body surface area. The eGFR by the MDRD equation can be calculated without body weight, and this equation is adjusted for body surface area. UK chronic kidney disease guidelines endorse it. The MDRD equation is more reliable for the calculation of eGFR as compared to the CG formula. However, the MDRD equation shows negative bias when eGFR calculated is over 60 ml/min/1.73 $m^2$.[25] A study that evaluated the MDRD equation in a sizeable, diverse population demonstrated that at eGFR less than 60 ml/min / 1.73 $m^2$, the MDRD equation had lower bias than at eGFR more than 60 ml/min / 1.73 $m^2$. The MDRD equation, therefore, provides precise and unbiased estimates when eGFR is <60 ml/min/1.73 $m^2$. Clinicians should carefully infer GFR estimates around 60 ml/min /1.73 $m^2$ to avoid erroneous CKD staging during the patient's evaluation.[26] Furthermore, in 2005, MDRD's four-factor equation (age, gender, ethnicity) was proposed for precise estimation of GFR, and this re-expressed equation has serum creatinine traceability to isotope dilution mass spectrometry (IDMS). The benefit of MDRD over CG is that it was verified against measured GFR using 125 I-iothalamate and does not require body weight because it is already corrected in the calculation.[27]

## Conclusion

Reduced eGFR can be present in adults with normal serum creatinine levels, indicating that reliance on serum creatinine alone may underestimate early renal dysfunction. Although both the Cockcroft–Gault and MDRD equations were effective in identifying reduced kidney function, significant differences were observed between the eGFR values generated by the two formulas. Routine calculation and reporting of eGFR, particularly in middle-aged and older adults, may improve early recognition of chronic kidney disease and support timely clinical intervention.

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**CONFLICT OF INTEREST**

Authors declared no conflicts of Interest.

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**DATA SHARING STATEMENT**

The data that support the findings of this study are available from the corresponding author upon request.




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