Research Article

Impact of creatinine-eGFR equations on chronic kidney disease stratification in a Ghanaian Tertiary Care Setting

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Article Info

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Abstract

Kidney diseases disproportionately affect people of African descent, yet current estimated glomerular filtration rate (eGFR) equations lack accuracy in African populations. The widely used the race-adjusted Modification of Diet in Renal Disease (MDRD) equation underestimates GFR in African individuals with kidney disease, while newer race-agnostic equations, such as the 2021 CKD-EPI and European Kidney Function Consortium (EKFC) equations, require further validation in these populations. This study evaluated five creatinine-based eGFR equations in a Ghanaian population to assess their impact on chronic kidney disease (CKD) stratification.

The study utilized the MDRD, MDRD without race coefficient (MDRDnr), CKD-EPI 2009 and 2021, and EKFC equations, to compare stratification into GFR stages per KDIGO guidelines using creatinine results from adult patients seen at the University of Ghana Medical Centre (January 2021–December 2023).

Among 10,864 creatinine results from 6172 females (56.8%) and 4692 males (43.2%), the MDRDnr yielded the lowest median eGFR (76.4 mL/min/1.73 m²), while MDRD had the highest. The MDRDnr identified the highest prevalence of reduced eGFR (<60 mL/min/1.73 m²) at 19.9%, followed by EKFC (14.8%), 2021 (11%), CKD-EPI 2009 (10.6%), and MDRD (8.8%). Notably, one-third of individuals with reduced eGFR (per EKFC) were under 60 years old. The EKFC equation identified more cases of reduced eGFR than both CKD-EPI equations.

The MDRDnr and EKFC equations detected the highest proportion of reduced eGFR. However, the EKFC has been shown in other studies to be more accurate. Further validation and adoption of the EKFC equation are recommended for improved CKD diagnosis in Ghana.

Introduction

Kidney diseases are the third fastest leading cause of mortality globally and are projected to be the 5th leading cause of death by 2040 [1,2]. The majority of the 850 million people globally affected by kidney diseases reside in low- and middle-income countries (LMICs) [3]. While certain risk factors for kidney disease such as diabetes and hypertension, are common in these regions, the higher prevalence of infectious diseases, environmental factors (use of herbal medicines) and genetic factors (predispositions to sickle cell disease and APOL[1] risk alleles), further exacerbate the progressive kidney disease burden among African populations [4,5]. Chronic Kidney Disease (CKD) increases the risk of end-stage renal disease (ESRD), cardiovascular disease, and mortality, underscoring the importance of early diagnosis and therapeutic intervention. Unfortunately, a significant proportion of those affected are unaware of their disease status in LMICs partly due to the clinically silent nature of CKD, and lack of access to screening facilities [6]. This ensuing late diagnosis is further complicated by the limited to non-
existent access to renal replacement therapy (RRT, dialysis and transplantation) in LMICs like Ghana where ~13% of the population has CKD [7–9].

Creatinine-based estimation of glomerular filtration rates (Cr-eGFR) are widely used for kidney disease assessments given the resource-intensive gold-standard methodologies for measuring GFR (mGFR) [10]. Several Cr-eGFR equations exist, including the 2006 Modification of Diet in Renal Disease (MDRD 2009 and 2021), Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI 2009 and 2021), and 2021 European Kidney Function Consortium (EKFC). These equations exhibit varying degrees of accuracy and bias relative to mGFR, impacting clinical decision-making differently [11,12]. Of these equations, the MDRD and 2009 CKD-EPI utilize racial coefficients, which contribute to racial disparities in kidney care globally [13,14]. However, the 2021 CKD-EPI and EKFC equations have been developed to be race-neutral although EKFC estimations are more accurate if population specific factors (Q values) are incorporated [15]. While the 2021 CKD- EPI equation has shown promise in improving equity in kidney care in the U.S. where it was developed and has been primarily validated, emerging evidence suggests that the EKFC may provide more accurate GFR estimates across diverse populations, including Africans [9-11].

The 2024 Kidney Disease Improving Global Outcomes (KDIGO) Clinical Practice guidelines recommend the use of a validated, race-free creatinine-based eGFR alone or in combination with cystatin C measurement for evaluating patients at risk for CKD as well as for disease staging within a region [10]. Nonetheless, in many settings, including Ghana, the older MDRD equation with the race coefficient remains widely used, partly due to its simplicity and lack of robust validation of the newer eGFR equations in African populations [16]. Furthermore, alternative methods for estimating kidney function, such as those based on cystatin C, are currently not readily available or affordable in resource-limited settings despite improved race-agnostic performance [17].

Selecting an appropriate eGFR equation requires rigorous population and/or region- specific validation to ensure accuracy and clinical relevance [10]. In the absence of such validation in Ghana and given the critical need for early CKD diagnosis to prevent complications, this study aims to retrospectively compare absolute eGFR values obtained using the 2021 EKFC equation with those obtained using the 2006 MDRD and three other creatinine-based eGFR equations (2006 MDRD (no race, MDRDnr), 2009 CKD-EPI, and 2021 CKD-EPI). Furthermore, we will estimate the prevalence of reduced eGFR as a surrogate for CKD prevalence in the Ghanaian adult population visiting a tertiary healthcare facility. Finally, we will assess the impact of these different equations on the re-stratification of individuals across CKD stages.

Methods

Study subjects

This retrospective study utilized data from adults aged 18 years and above who visited the University of Ghana Medical Center (UGMC), a tertiary healthcare facility in Accra, Ghana, between January 2021 to December 2023 and had creatinine measured. We applied a stringent criterion to exclude data from inpatients, pregnant women, and those with acute conditions, including those seen at the ER, surgery, and nephrology departments, generating a data set representative of outpatient visits. Entries with missing data on creatinine results, department, age, or sex were also excluded. For patients with multiple creatinine measurements, the first available measurement was used. UGMC Institutional Review Board approval was obtained before the commencement of the study.

Creatinine Measurements

All serum creatinine measurements were completed in accordance with standard clinical laboratory practice using the MINDRAY (Shenzhen. China) IDMS-traceable creatinine sarcosine oxidase assay and assayed on the Mindray Bs-480 analytical instrument.

eGFR calculations staging kidney function

Five creatinine-based eGFR equations were utilized in this study: MDRD, MDRD (without race, MDRDnr), 2009 CKD-EPI, 2021 CKD-EPI, and EKFC (21) (Supplementary Table 1). The 2021 EKFC utilized Q values (0.72 for females, 0.96 for males) generated from a small cohort of Africans from Cote-D'Ivoire and the Democratic Republic of Congo [15]. Comparison of CKD classifications using the 2021 EKFC with the African-Q-value versus a race-free Q-value (EKFCrf: 0.73 for females, 0.99 for males) is provided in the Supplementary [15]. CKD staging was done in accordance with KDIGO guidelines [10]. In brief, G^1 (GFR ≥90 ml/min/1.73m^2), G^2 (GFR 60-89 ml/min/1.73m^2), G^3a (GFR 45-59 ml/min/1.73m^2),

G^3b (GFR 30- 44 ml/min/1.73m^2), G^4 (GFR 15-29 ml/min/1.73m^2), and G^5 (GFR <15 ml/min/1.73m^2).

Statistical analysis

All participants were stratified into seven age groups: 18–29, 30–39, 40–49, 50–59, 60–69, 70-79 and ≥ 80 years old. Excel and GraphPad Prism V[10].4.0 were used for all data analysis and graphing. Descriptive statistics are presented as median and interquartile range (IQR). ANOVA and Wilcoxon paired rank sum tests were used to compare quantitative eGFRs values (Table 1) between equations. Chi-Square tests were used to identify differences in categorical data between equations (i.e. low eGFR prevalence groupings).

Results

Demographic and Clinical Characteristics

Our dataset was composed of 10,864 creatinine results, each representing a unique patient. Males comprised 4692 (43.2%) while females comprised 6172 (56.8%). The median age was 47.5 (28.6) years, (Table 2).

Of the five eGFRs, median eGFR values were lowest with the MDRDnr at 76.4 (28) mL/min/1.73 m^2 and highest with the MDRD at 92.4 (33.8) mL/min/1.73 m^2. The 2009 CKD-EPI, 2021 CKD- EPI and EKFC had median eGFRs of 92.2 (40.1), 89.8(32.1), and 80.6(30) (mL/min/1.73 m^2), respectively. A statistically significant difference in absolute eGFR values between the equations was observed (p<0.001).

The highest prevalence of decreased eGFR (i.e. G^3a to G^5, <60 mL/min/1.73 m^2) was observed with the MDRDnr at 19.9%, followed by the EKFC (14.8%), 2021 CKD-EPI (11%), 2009 CKD- EPI (10.6%) and the MDRD (8.85%). The difference in prevalence observed between the equations was statistically significant (p<0.0001).

Table 1: Baseline characteristics of study population.

Characteristics	Data
Age, year (median, IQR)	47.5 (28.6)
Age group (n, %)	
18 to 29 years	1461 (13.5)
30 to 39 years	2448 (22.5)
40 to 49 years	1921 (17.7)
50 to 59 years	1676 (15.4)
60 to 69 years	1780 (16.4)
70 to 79 years	1128 (10.4)
>80 years	450 (4.1)
Sex (n, %)	
Male	4692 (43.2)
Female	6172 (56.8)
Serum Cr (mg/dL, median, IQR)	0.91 (0.35)

Characteristics	Data
Median eGFR ((mL/min/1.73 m^2, IQR)	
MDRD	92.4 (33.8)
MDRDnr	76.4 (28.0)
2009 CKD-EPI	92.2 (40.1)
2021 CKD-EPI	89.8 (32.1)
EKFC	80.6 (30)
eGFR <60 mL/min/1.73 m^2, CKD ≥ G^3a (n, %)	
MDRD	961 (8.8)
MDRDnr	2164 (19.9)
2009 CKD-EPI	1148 (10.6)
2021 CKD-EPI	1194 (11.0)
EKFC	-14.8

Population distribution of eGFR and CKD stages

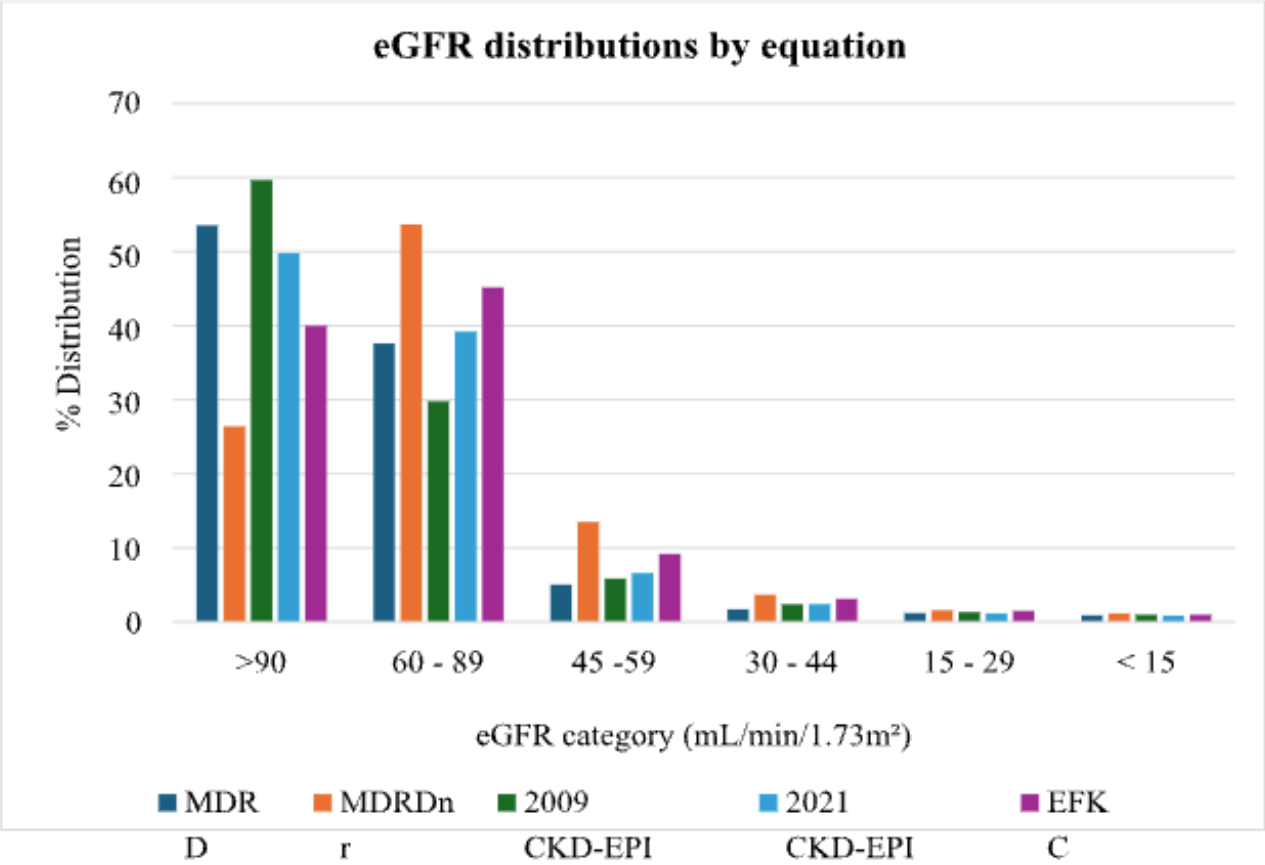
The distribution of eGFR categories varied significantly across the different eGFR equations (Figure 1, Table 3). The MDRD, 2009 CKD-EPI, and 2021 CKD-EPI equations predominantly categorized individuals in G^1 (eGFR > 90 mL/min/1.73m²), with 54%, 60%, and 50% of values falling within this range, respectively, whereas the MDRDnr and the EKFC predominantly classified individuals into G^2 (eGFR: 60 and 90 mL/min/1.73m²), with 58% and 45% of values falling within this range, respectively. The proportion of individuals classified with reduced eGFR (stages 3a-5) varied significantly across the different eGFR equations. The MDRD equation identified the lowest proportion of individuals with reduced eGFR (8.8%, 961 individuals). In contrast, the MDRDnr identified the highest proportion (19.9%, 2164 individuals). The 2009 CKD-EPI, 2021 CKD-EPI, and 2021 EKFC equations identified 10.6% (1148), 11% (1194), and 14.8% (1607) individuals with reduced eGFR, respectively.

Within the reduced eGFR categories, CKD stage 3a was the most prevalent across all equations, accounting for 57% (547 individuals) with the MDRD, 68% (1466 individuals) with the MDRDnr, 56% (638 individuals) with the 2009 CKD-EPI, 60% (713 individuals) with the 2021 CKD-EPI, and 62% (998 individuals) with the 2021 EKFC.

CKD stage 3b accounted for 19% (186 individuals), 18% (400 individuals), 23% (260 individuals), 22% (262 individuals), and 21% (337 individuals) of cases, respectively, across

the different equations. CKD stage 4 comprised 14% (130 individuals), 8% (172 individuals), 12% (142 individuals), 11% (126 individuals), and 10% (164 individuals) of cases, respectively. Finally, CKD stage 5 comprised 10% (98 individuals), 6% (126 individuals), 9% (108 individuals), 8% (93 individuals), and 7% (108 individuals) of cases, respectively, across the MDRD, MDRDnr, 2009 CKD-EPI, 2021 CKD-EPI and EKFC equations. These differences were statistically significant (Chi square, p<0.0001).

Figure 1: Distribution of eGFR by equations.



The left y-axis represents the percent distribution of the population for each of the equation. The x-axis represents the eGFR category (G^1, G^2, G^3a, G^3b, G^4 and G^5).

Table 2: Equation-based eGFR staging (counts).

	G^1	G^2	G^3a	G^3b	G^4	G^5
MDRD	5818	4085	547	186	130	98
MDRDnr	2870	5830	1466	400	172	126
2009 CKD-EPI	6482	3234	638	260	142	108
2021 CKD-EPI	5411	4259	713	262	126	93
EKFC	4347	4910	998	337	164	108

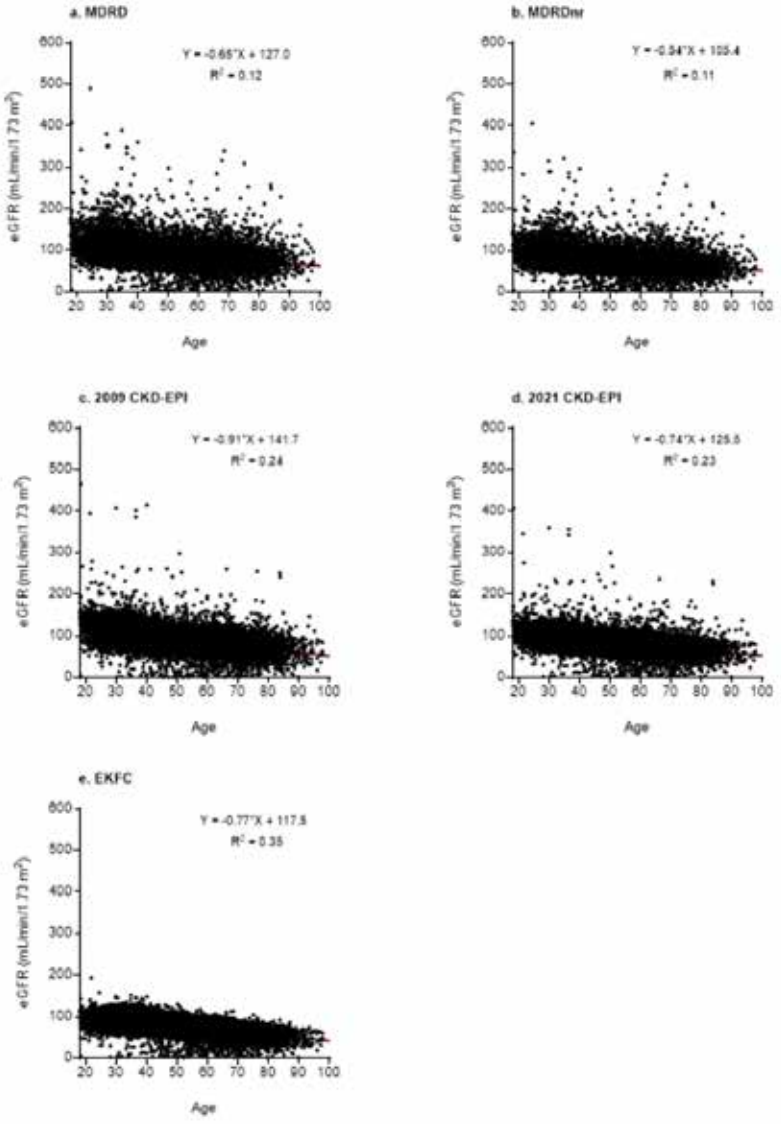
Age and sex distribution of eGFR and CKD stages

The absolute eGFR values, regardless of the equation used, decreased with age (Figure 2). This decline showed a weak to moderate negative correlation, as measured by Pearson's r. The strongest negative correlation was observed with the EKFC equation (r = -0.59, 95% CI: -0.60 to -0.58, p<0.0001), while the weakest was with the MDRDnr equation (r = -0.34, 95% CI: -0.35 to -0.32, p<0.0001). Also, the slope, representing the constant decline in eGFR per year of age, was -0.65 (95% CI: - 0.68 to -0.61) for MDRD, -0.54 (95% CI: -0.57 to -0.51) for MDRDnr, -0.91 (95% CI: -0.94 to -0.86) for 2009 CKD-EPI, -0.74 (95% CI: -0.76 to -0.71) for 2021 CKD-EPI, and -0.77 (95% CI: -0.79 to -0.75) for EKFC

The distribution of eGFR categories per age group was also influenced by choice of eGFR equation (Figure 3). For the 18-29 age group, eGFR values above 60 mL/min/1.73m² ranged from 96% (MDRDnr) to 99% (MDRD, and 2009 and 2021 CKD-EPI). In the 30-39 age group, this range was 92% to 98%. Subsequent age groups showed a decreasing trend in the proportion of individuals with eGFR > 60 mL/min/1.73m²: 84% to 94% for 40-49 years, 76% to 90% for 50-59 years, 68% to 85% for 60-69 years, 61% to 81% for 70-79, and 44% to 73% for those 80 years and above. A critical consideration of reduced eGFR categories per age groups influenced by equation revealed concerning statistics. Of the proportion of patients identified by both the MDRD and EKFC as having reduced eGFR, a significant proportion were patients less than 60 years of age, who are still in their productive years. They made up 40.6%, 24.75%, 44.6% and 55% for stages G^3a, G^3b, G^4, G^5 respectively for the MDRD (Table 3), and 31.3%, 32.1%, 30.8% and 52% of those with stages G^3a, G^3b, G^4, and G^5 respectively for the EKFC (Table 4).

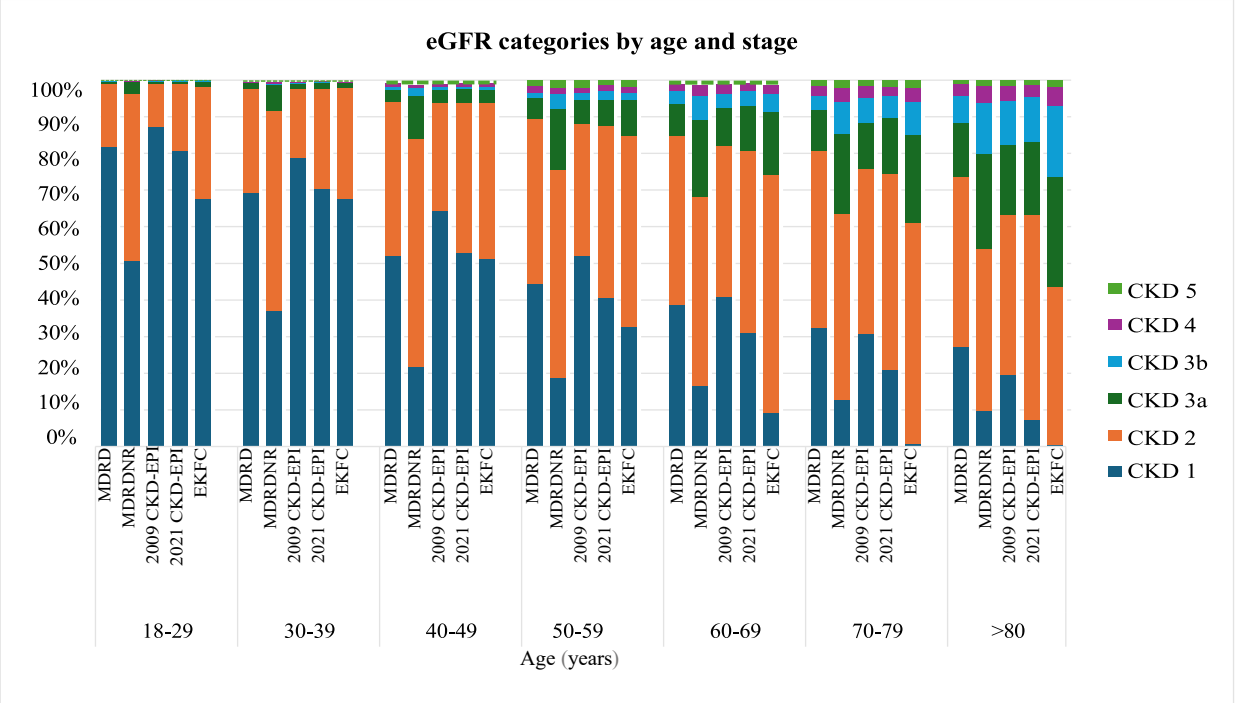
Using the MDRD equation, women aged 60 to 69 had the highest prevalence of stage G^3a, men aged 60 to 69 of stages G^3b and G^4, and women aged 50 to 59 of stage G^5. Using the 2021 EKFC, women aged 60 to 69 had the highest prevalence for stage G^3a, women aged 70 to 79 of stage G^3b, men aged 60 to 69 of G^4, and both women aged 50 to 59 and men aged 70 to 79 of G^5 . These findings highlight the significant impact of equation choice on eGFR estimates and CKD stage classification.

Figure 2: Age distribution and eGFR by the a) MDRD, b) MDRDnr, c) 2009 CKD-EPI, d) 2021 CKD-EPI, and e) EKFC.



Data points beyond 600 mL/min/1.73m² are not displayed.

Figure 3: Distribution of eGFR categories and CKD stages across different age groups, categorized by the equation used for calculation.



The left y-axis represents the percent population distribution for each equation.

Table 3: Age and sex distribution of reduced eGFR (< 60 ml/min/1.73 m^2) per the MDRD equation.

AGE	CKD 3a, n=547		CKD 3b, n=186		CKD 4, n=130		CKD 5, n=98	
	Females n=282	Males n=265	Females n=86	Males n=100	Females n=57	Males n=73	Females n=48	Males n=50
18–29 Years	26 (4.75%)	5 (0.91%)	1 (0.54%)	2 (1.08%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (2.04%)
30–39 Years	22 (4.02%)	13 (2.38%)	1 (0.54%)	2 (1.08%)	2 (1.54%)	2 (1.54%)	6 (6.12%)	6 (6.12%)
40–49 Years	32 (5.85%)	32 (5.85%)	5 (2.69%)	10 (5.38%)	8 (6.15%)	11 (8.46%)	9 (9.18%)	7 (7.14%)
50–59 Years	42 (7.68%)	50 (9.14%)	14 (7.53%)	11 (5.91%)	13 (10.00%)	18 (13.85%)	15 (15.31%)	11 (11.22%)
60–69 Years	112 (20.48%)	77 (14.08%)	27 (14.52%)	37 (19.89%)	12 (9.23%)	19 (14.62%)	11 (11.22%)	9 (9.18%)
70–79 Years	68 (12.43%)	60 (10.97%)	20 (10.75%)	24 (12.90%)	11 (8.46%)	18 (13.85%)	5 (5.10%)	13 (13.27%)
80 and above	39 (7.13%)	28 (5.12%)	18 (9.68%)	14 (7.53%)	11 (8.46%)	5 (3.85%)	2 (2.04%)	2 (2.04%)

Table 4: Age and sex distribution of reduced eGFR (< 60 ml/min/1.73 m^2) using the EKFC equation.

AGE	CKD 3a, n=1204		CKD 3b, n=410		CKD 4, n=182		CKD 5, n=115	
	Female (n=646)	Male (n=558)	Female (n=209)	Male (n=201)	Female (n=79)	Male (n=103)	Female (n=56)	Male (n=59)
18–29 Years	13 (1.08%)	18 (1.50%)	2 (0.49%)	3 (0.73%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (1.74%)
30–39 Years	29 (2.41%)	23 (1.91%)	3 (0.73%)	2 (0.49%)	2 (1.10%)	2 (1.10%)	6 (5.22%)	6 (5.22%)
40–49 Years	44 (3.65%)	46 (3.82%)	8 (1.95%)	8 (1.95%)	8 (4.40%)	14 (7.69%)	9 (7.82%)	7 (6.09%)
50–59 Years	104 (8.64%)	94 (7.81%)	19 (4.63%)	26 (6.34%)	13 (7.14%)	17 (9.34%)	17 (14.78%)	13 (11.30%)
60–69 Years	189 (15.70%)	183 (15.20%)	52 (12.68%)	56 (13.66%)	20 (10.99%)	34 (18.68%)	12 (10.43%)	10 (8.70%)
70–79 Years	172 (14.29%)	133 (11.05%)	69 (16.83%)	63 (15.37%)	19 (10.44%)	24 (13.19%)	7 (6.09%)	17 (14.78%)
80 and above	95 (7.89%)	61 (5.07%)	56 (13.66%)	43 (10.49%)	17 (9.34%)	12 (6.59%)	5 (4.35%)	4 (3.48%)

Comparison of eGFR equations (agreement and concordance)

We then assessed the agreement in GFR categorization as a surrogate for CKD stages using the different Cr-eGFR equations (Figure 3). The MDRD showed 58% agreement with the MDRDnr, 87% with 2009 CKD-EPI, 87% with 2021 CKD-EPI, and 77% with EKFC. Notably, the MDRD significantly underestimated CKD stage compared to the MDRDnr (42%), 2009 CKD-EPI (5%), 2021 CKD-EPI (10%), and EKFC (22%).

The MDRDnr demonstrated agreement rates of 56%, 66%, and 72% with the 2009 CKD-EPI, 2021 CKD-EPI, and EKFC, respectively. This equation exhibited a higher rate of overestimation compared to the MDRD, 2009 CKD-EPI, 2021 CKD-EPI and EKFC, with 44%, 34%, and 24% of individuals being classified into a more advanced CKD stage.

The 2009 CKD-EPI equation showed 83% and 74% agreement with the 2021 CKD-EPI and EKFC, respectively. It underestimated CKD stage in 13% and 25% of cases compared to the 2021 CKD-EPI and EKFC, respectively, while overestimating in only 4% and 1% of cases.

Finally, the 2021 CKD-EPI and EKFC equations demonstrated 83% agreement. The 2021 CKD- EPI overestimated CKD stage in 1% of cases and underestimated 16% of cases compared to the 2021 EKFC.

Delanaye and colleagues' proposed race-free Q-value (EKFCrf) [15] demonstrated a remarkable 97% agreement in CKD staging when used for eGFR calculation with EKFC. In comparison to the African-specific Q-value, this approach led to a minor 2.6% underestimation and 0.19% overestimation (Supplementary Table 2). This was due to higher absolute eGFRs generated by the EKFCrf ($p<0.001$).

Thus, the EKFC and MDRDnr Cr-eGFRs placed a majority of cases in higher CKD stages relative to the MDRD, 2009 CKD-EPI and 2021 CKD-EPI equations.

Figure 4: Agreement of CKD grade classification: (a) using the MDRD equation, (b) using the 2021 CKD-EPI equation and (c) using the EKFC equation.

'Underestimated' refers to cases where the CKD grade estimated by the reference equation (a, b, and c) was lower than the CKD grade estimated by each of the other equations. 'Agreement' signifies cases where the CKD grade determined by both the reference equations and the other equation matched. 'Overestimation' refers to cases where the CKD grade estimated by the reference equation was higher than the other equations.

Discussion

The best measure of kidney function is GFR. However, its direct measurement is complex and often impractical. Therefore, GFR estimates (eGFR) which incorporates factors including creatinine concentration, age, sex, and historically, race, are routinely used in clinical practice. Whereas earlier Cr-eGFRs such as the MDRD and 2009 CKD-EPI included a race- coefficient, the 2021 CKD-EPI and EKFC equations lack racial coefficients, in a bid to move towards a more equitable approach to kidney care. However, none of these equations have been properly validated in African populations, and yield varying eGFR values which potentially introduces uncertainty in clinical decision-making, and fails to accurately reflect the true burden of kidney disease in Sub-Saharan Africa [16]. This study examined how different Cr-eGFR equations affect eGFR categorization (per KDIGO guidelines), and by extension CKD staging, and also as estimates of the overall prevalence of reduced kidney function in an outpatient population at a major tertiary medical facility in Ghana. Our findings suggest that the MDRDnr and the EKFC equation (using an African

population-specific Q factor) classifies a significant proportion of individuals, the majority of whom are young, into reduced eGFR categories. However, because the MDRD and MDRDnr have reduced accuracy and precision relative to mGFR [16,18,19], we recommend further validation and potential adoption of the EKFC to replace the MDRD in routine medical practice in Ghana to facilitate early diagnosis of kidney disease.

Current Cr- eGFR equations frequently do not meet the recommended threshold of 90% accuracy within 30% of measured GFR (P^{30}) in published studies [16,20]. This discrepancy is particularly pronounced in African populations, with race-coefficients contributing substantially to this issue [19,21]. The MDRD equation, established two decades ago, is still widely utilized, in Ghana, Africa and beyond, despite lower accuracy and precision relative to the more recent Cr-eGFRs [22,23]. In our study, the MDRD identified the lowest prevalence of reduced eGFR, with higher median eGFR absolute values relative to the other Cr-eGFRs. In fact, in large African cohort studies, the MDRD was shown to grossly overestimate the prevalence of eGFR> 90 mL/min/1.73m² by 38% while grossly underestimating the prevalence of eGFR ≤ 89 mL/min/1.73m² by 37%. This significant bias and imprecision were attributed, in part, to the inclusion of the race coefficient [16]. Excluding the race variable reduced this bias, only overestimating 9% of the cohort with GFR > 90 mL/min/1.73m² and underestimating 8% of the cohort with GFR ≤ 89 mL/min/1.73m². Other studies performed without the race coefficient showed reclassification of African patients from CKD 3a to more advanced stages of kidney disease [18]. Consistent with this, in our study, removing the race coefficient from the MDRD equation yielded the highest median eGFR, identifying the highest percentage (19.9%) of individuals with reduced eGFR relative to the MDRD (8.8%), 2009 CKD-EPI (10.6%), 2021 CKD-EPI (11%) and EKFC (14.8%). Thus, eliminating the racial coefficient the MDRD may be considered in favor of identifying more at-risk patients. However, the MDRDnr still has poor accuracy relative to mGFR in individuals of African descent, particularly in those with reduced mGFR (i.e. < 60 mL/min/1.73m²). In one study of African patients, P^{30} using the MDRDnr with mGFR > 60 mL/min/1.73m² was 84.8% (95% CI: 81.3-88.3), decreasing to 31.3% (95% CI: 20.9-41.6) for those with mGFR < 60 mL/min/1.73m² [19]. Thus, the risk for kidney disease underdiagnosis and consequently delayed treatment initiation, and poorer outcomes for Africans with CKD remains. This makes the MDRD equation an inappropriate choice for kidney disease screening, diagnosis and management for the African population.

The influence of ethnicity continues to plague the EKFC equation as population-specific Q-factors perform better in comparison to mGFR relative to race-free Q-values [15].

We assessed the impact of using a race-free Q-value in this study with a primarily African patient population [15]. We observed that 2.6% of eGFRs were classified into less severe CKD stages, as the race-free Q-value (EKFCrf) yielded higher average eGFRs compared to the EFKC using the African-specific Q-value. Thus, the outcomes of this study suggest better identification of at-risk patients using population-specific Q-values, nonetheless, further studies are certainly warranted. CKD is estimated to affect 13.3% of the Ghanaian adult population [24]. This widely referenced statistic was derived using the 2009 CKD-EPI equation, which incorporates a racial coefficient and is less accurate relative to the 2021 CKD-EPI and EKFC equations. The 2009 CKD-EPI equation is also known to overestimate mGFR ≥90 mL/min per 1.73m² while underestimating mGFR ≤89 mL/min per 1.73m² in Africans, exhibiting a P^{30} of 75% (72 to 78) [16]. In fact, studies using trained computational models have proposed a true CKD prevalence of 17% in Ghana [16]. In our study, we observed a lower prevalence of reduced eGFR using the 2009 CKD-EPI relative to the 2021 CKD-EPI and 2021 EKFC equations. Compared to the 2021 CKD- EPI and the EKFC equations, the 2009 CKD-EPI equation classified 13% and 25% into less advanced CKD stages, respectively. Additionally, it only agreed with 87% and 74% of the 2021 CKD-EPI and EKFC eGFR categorizations, respectively. We believe that race-adjusted equations like the 2009 CKD-EPI may not accurately reflect the burden of CKD in the Ghanaian population, necessitating a re-evaluation of kidney disease prevalence using more robust analytical methods and contemporary eGFR equations.

The newer 2021 CKD-EPI and EKFC equations differ from the preexisting equations by their omission of race coefficients and improved accuracy in Black populations, although they are yet to be extensively validated in African populations. In a small cohort study using participants from Cote-D'Ivoire and DR Congo, the EKFC demonstrated slight reduction in bias and increase in accuracy relative to the 2021 CKD-EPI with a P^{30} of 79.3 (75.8; 82.9) versus P^{30} of 74.4 (70.6; 78.2) respectively, increasing patient classifications within 30% of mGFR values by 8.1% [15].

Proponents of the EKFC point to its unique incorporation of a modifiable population specific Q- value (rescaled creatinine based on the population's median normal serum creatinine value) which reduces bias and increases P^{30} [15,25]. Thus, its use with the population-specific Q-Factor is currently recommended, although more robust validations are required in African populations. In our study, the EKFC exhibited lower median eGFRs than the 2021 CKD-EPI. Consequently, it identified 413 more people as having reduced eGFR than the 2021 CKD-EPI.

Age and sex significantly influence GFR. Physiological GFR declines with age, with an estimated decrease of approximately 0.87 mL/min/1.73 m² per year [26]. Consequently, older individuals typically exhibit lower mGFR, and existing eGFR equations, such as the MDRD and 2009 CKD-EPI, may exhibit

higher levels of bias in this population [26]. Furthermore, sex-based differences in CKD prevalence have been observed. Studies have shown that women are more susceptible to CKD compared to men, although men tend to experience more rapid disease progressions [5,27]. Using both the MDRD and EKFC equations in our study, the highest prevalence of reduced eGFR was observed in individuals aged 60–69 years. However, individuals under 60 years of age comprised one-third of all those classified with CKD stages 3a, 3b, and 4 according to the EKFC equation. Notably, half of the individuals with CKD stage 5 were under 60 years old—a particularly concerning finding given that this age range encompasses peak productive years. The EKFC equation identified 47% more individuals under 60 with reduced eGFR compared to the MDRD equation. This finding is consistent with other studies demonstrating variations in reduced eGFR prevalence across age groups depending on the eGFR equation used [28]. These findings underscore the importance of considering age-related variations in GFR and their potential influence on CKD stage classification when using different eGFR equations.

There is an urgent need for more accurate eGFR equations for Africans. Laudable efforts including that of the African Research on Kidney Disease (ARK) study, aimed to achieve this [29]. Some published outcomes form the ARK study have been referenced in this manuscript [16]. Unfortunately, attempts to established an eGFR using data from discrete African cohorts resulted in an equation with similar performance of existing Cr-eGFRs, prompting the need for additional work in this arena [16]. In the interim, emerging evidence suggests that, among existing Cr-eGFRs, equations, the EKFC equation may be more appropriate for use in African populations. While adopting this approach may initially strain healthcare systems in LMICs, potentially increasing the need for specialist review and RRT – resources often scarce in these settings – early diagnosis remains crucial. We acknowledge that identifying more CKD cases could initially burden healthcare systems, especially in resource-limited settings like Ghana, where access to dialysis and specialists is limited to ~9.7 hemodialysis machines and 0.44 nephrologists per million people [8]. Nevertheless, the long-term benefits of early CKD detection outweigh this initial strain. Early identification enables timely interventions, such as dietary, therapeutic and lifestyle modifications, which can be managed by adequately trained primary care clinicians, potentially preserving the renal functional reserve, delaying CKD progression, and reducing the need for resource-intense RRT. This approach necessitates increased governmental investment to strengthen primary healthcare infrastructure, create training programs for healthcare providers in CKD management and improve access to essential medications and diagnostic tools.

Study Strengths and Limitations

This study's strength lies in its use of stringent criteria to identify a large, representative outpatient population, enabling the comparison of reduced eGFR prevalence using five different equations. A key limitation is the absence of comparative mGFR data. While mGFR is the gold standard, it is widely unavailable and inaccessible in Ghana, precluding evaluation of eGFR accuracy and precision. Cystatin C results were also unavailable for any of the patients in this study as cystatin C testing is yet to be made available in the country. Additionally, the retrospective cohort design may have included patients with acute kidney injury, a limitation that a prospective study could mitigate.

Conflict of Interest

The authors declare no conflict of interest.

Disclosures

MM, PDS, GBK have no relevant disclosures. CLO is a member of the IFCC CETPLM, and has received travel support from the IFCC.

Ethical Approval

Ethical clearance was sought and received from the University of Ghana Medical Centre Institutional Review Board.

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Submission Declaration

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Authorship

CLO conceived the idea for this study. All authors contributed substantially to data analysis, as well as the drafting and revision of the manuscript.

Abbreviation

CKD: Chronic kidney disease IQR: Interquartile range
MDRD: Modification of Diet in Renal Disease
MDRDnr: Modification of Diet in Renal Disease, no race factor
EKFC: European Kidney Function Consortium
EKFCrf: European Kidney Function Consortium race-free
Q-value
KDIGO: Kidney Disease Improving Global Outcomes

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Supplementary Tables

Table 1: Equations for eGFR calculations.

EQUATION	FORMULA
4v-MDRD for females	eGFR = 175 × ([SCr])^-1.154 × age^-0.203 × 0.742 [if female] × 1.210 [Black race factor]. Where [SCr] is in mg/dL (IDMS-standardized assay) and age is in years.
4v-MDRD for males	eGFR = 175 × ([SCr])^-1.154 × age^-0.203 × 1.210 [Black race factor]. Where [SCr] is in mg/dL (IDMS-standardized assay) and age is in years.
4v-MDRD for females (without race)	eGFR = 175 × ([SCr])^-1.154 × age^-0.203 × 0.742 [if female]. Where [SCr] is in mg/dL (IDMS-standardized assay) and age is in years.
4v-MDRD for males (without race)	eGFR = 175 × ([SCr])^-1.154 × age^-0.203. Where [SCr] is in mg/dL (IDMS-standardized assay) and age is in years.
CKD-EPI 2009 for females	eGFR = 141 × min([SCr]/κ, 1)^α × max([SCr]/κ, 1)^-1.209 × 0.993^age × 1.018 [if female] × 1.159 [Black race factor]. Where [SCr] is in mg/dL (IDMS-standardized assay) and age is in years; κ = 0.7 for females, α = -0.329 for females. Min = minimum([SCr]/κ, 1), Max = maximum([SCr]/κ, 1).
CKD-EPI 2009 for males	eGFR = 141 × min([SCr]/κ, 1)^α × max([SCr]/κ, 1)^-1.209 × 0.993^age × 1.159 [Black race factor]. Where [SCr] is in mg/dL (IDMS-standardized assay) and age is in years; κ = 0.9 for males, α = -0.411 for males. Min = minimum([SCr]/κ, 1), Max = maximum([SCr]/κ, 1).
CKD-EPI 2021 for females	eGFR = 142 × (SCr/A)^B × 0.9938^age × (1.012 if female). Where A = 0.7, B = -0.241 if SCr ≤ 0.7; A = 0.7, B = -1.2 if SCr > 0.7.
CKD-EPI 2021 for males	eGFR = 142 × (SCr/A)^B × 0.9938^age. Where A = 0.9, B = -0.302 if SCr ≤ 0.9; A = 0.9, B = -1.2 if SCr > 0.9.

EQUATION	FORMULA
EKFC for females	eGFR = 107.3 × (sCr/Q)^−0.322 (for ages 2–40 & sCr/Q < 1); eGFR = 107.3 × (sCr/Q)^−1.132 (for ages 2–40 & sCr/Q ≥ 1); eGFR = 107.3 × (sCr/Q)^−0.322 × 0.990^(Age−40) (for >40 & sCr/Q < 1); eGFR = 107.3 × (sCr/Q)^−1.132 × 0.990^(Age−40) (for >40 & sCr/Q ≥ 1). ln(Q) = 3.080 + 0.177×age − 0.223×ln(age) − 0.00596×age² + 0.0000686×age³ (ages 2–25); Q = 62 µmol/L (ages >25).
EKFC for males	eGFR = 107.3 × (sCr/Q)^−0.322 (for ages 2–40 & sCr/Q < 1); eGFR = 107.3 × (sCr/Q)^−1.132 (for ages 2–40 & sCr/Q ≥ 1); eGFR = 107.3 × (sCr/Q)^−0.322 × 0.990^(Age−40) (for >40 & sCr/Q < 1); eGFR = 107.3 × (sCr/Q)^−1.132 × 0.990^(Age−40) (for >40 & sCr/Q ≥ 1). ln(Q) = 3.200 + 0.259×age − 0.543×ln(age) − 0.00763×age² + 0.0000790×age³ (ages 2–25); Q = 80 µmol/L (ages >25).

Table 2: Impact of race-free Q-value (EKFCrf) on CKD classifications.

EKFCrf		CKD 1	CKD 2	CKD 3a	CKD 3b	CKD 4	CKD 5
EKFC	**CKD 1**	4332	15				
	CKD 2	169	4741				
	CKD 3a		87	911			
	CKD 3b			22	315	6	
	CKD 4				158		
	CKD 5					1	107

EKFCrf: European Kidney Function Consortium race-free Q-value equation