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ORIGINAL ARTICLE

Comparison of the European Renal Function Consortium Equation With Chronic Kidney Disease – Epidemiology Collaboration 2021 for Estimating Glomerular Filtration Rate Among Algerian Population With Type 2 Diabetes Mellitus

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Abstract

Introduction. Type 2 diabetes mellitus (T2D) is the leading cause of end stage renal disease. Screening for chronic kidney disease is recommended for early diagnosis and intervention. This requires assessment of renal function by computing for estimated glomerular filtration rate (eGFR) and urine albumin-creatine ratio. Several formulas have been proposed for computation of eGFR. The European Renal Function Consortium (EKFC) equation, obtained by combining the full age spectrum (FAS) and Chronic Kidney Disease – Epidemiology Collaboration 2021 (CKD-EPI) equations, has been proposed as a more universal formula for eGFR. It has the advantage of eliminating correction for ethnicity and covers a wide age range. The aim of this study is to compare the EKFC and CKD-EPI 2021 equations to assess eGFR among Algerian population with T2D.

Methodology. This is an observational, cross-sectional, analytical study. Serum creatinine levels were measured using the Cobas integra 400 Roche diagnostic device. The results were used to estimate GFR using the two formulas: CKD-EPI 2021 and EKFC.

Results. There was a statistically significant difference between the performance of the CKD-EPI 2021 and EKFC equations (p <0.001). However, there was a very good correlation (r = 0.99) even though the EKFC underestimates eGFR compared to CKD-EPI 2021 (bias: -8 ml/min/1.73 m^2).

Conclusions. The main value of the EKFC lies in its ability to provide a detailed stratification in the early stages of chronic kidney disease. Our study also represents the first attempt to establish the q-value in the Algerian population.

Key words: type 2 diabetes mellitus, estimated glomerular filtration rate, EKFC equation, CKD-EPI equation

INTRODUCTION

Chronic kidney disease (CKD) is defined as the presence of abnormalities in kidney structure or function for at least three months that have an impact on health. Diabetes mellitus is the leading cause of end-stage renal disease worldwide.[1] Approximately 30% of people with diabetes have diabetic kidney disease (DKD).[2] It is a slowly progressive complication which is unfortunately often detected late because early stages are usually asymptomatic.[3] Therefore, early detection of CKD is important and is based on two main parameters: albuminuria of at least 30 mg/g or 3 mg/mmol and estimated glomerular filtration rate (eGFR) below 60 ml/min/1.73 m^2.[4]

Screening for albuminuria is done using urine albumin-creatine ratio (uACR) which is also a marker of cardiovascular risk among people with diabetes.[5] On the other hand, eGFR is computed through several equations using serum creatinine as the most widely used biomarker.

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Glomerular filtration rate is the volume of plasma filtered by the glomeruli, in milliliters per minute[6] and is affected by the age, gender and body surface area.[7] Initially, eGFR was calculated based on enzymatic creatinine, but since the 2000s, the Jaffé methods for creatinine measurement have been recalibrated according to international standards using isotope dilution mass spectrometry (IDMS).[8] The Kidney Disease: Improving Global Outcomes (KDIGO) recommends the use of IDMS-standardized creatinine regardless of the method.[9] Previously, the most commonly used formulas to compute for eGFR were the Modification of Diet in Renal Disease (MDRD) and the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI 2012) equations.[10]

Recently, in 2021, a new equation known as the European Kidney Function Consortium (EKFC) was developed in Europe by a consortium of mathematicians, biostatisticians and nephrologists.[11] This runs in parallel with the CKD-EPI equation updated in 2021,[12] in order to estimate a more accurate and universal glomerular filtration rate by removing the ethnic variable. The differences between these two raise a crucial question: Is there a significant difference in the eGFR values using the EKFC and CKD-EPI 2021 equations in the Algerian population? Since these equations were developed based on different reference populations, this study will provide information and local validation of renal function assessment tools among the Algerian population.

The aim of our study is to assess the concordance and any clinically significant differences between the EKFC and CKD-EPI 2021 equations for eGFR in an Algerian population with T2D.

METHODOLOGY

Study setting

This is an observational, analytical study conducted at the Rouïba Public Hospital, Department of Medical Biology, Biochemistry Laboratory in collaboration with the Nephrology Department of Mustapha Bacha University Hospital from February 2, 2024 to September 29, 2025. A cross-sectional method comparison study was conducted to evaluate agreement between EKFC and CKD-EPI 2021 in measuring eGFR.

Patients

Recruitment was carried out among patients hospitalized in various departments of the hospital as well as outpatient department. Only those with T2D, aged over 35, with a fasting blood glucose level above 1.26 g/L and/or a glycated hemoglobin (HbA1c) level above 6.5% were included. Pregnant women, cancer patients and people who had participated in another study were excluded. During recruitment, we completed an information sheet for each patient with the following details: age, gender, weight, height, personal and familial history, duration of diabetes, T2D and blood pressure treatment, use of statin and presence of chronic complications.

The sample size was determined in accordance with the sample size for binary classifiers (SFBC) protocol. This recommends a cohort of at least 40 samples to obtain a reliable estimate of agreement.[13] Our sample initially consisted of 110 patients. After excluding patients with missing data, the final number was 83 patients. The sample size included in our study was significantly larger than the minimum number recommended by the SFBC protocol.

The population of presumed healthy subjects was used to determine q-value. They consisted of 275 adults recruited from among the staff of the nephrology department at Mustapha University Hospital, as well as kidney donors (prior to donation) and individuals with a single anatomical or functional kidney. All subjects were over 18 years of age, healthy with no kidney disease or chronic pathology and had normal kidney function (eGFR >60 ml/min/m²). The following were excluded from the study: pregnant women, subjects who had experienced an episode of acute renal failure and those who had taken nephrotoxic drugs in the month prior to inclusion.

All participants gave informed consent. The study was approved by the local ethical committee of the hospital. There were no confounding factors**.**

Sample collection

Samples were collected from patients after fasting for at least 8 hours, using lithium heparin tubes as an anticoagulant for blood glucose and creatinine analysis and EDTA tubes as an anticoagulant for HbA1c measurement. The heparinized tubes were analyzed immediately or stored at -20°C after plasma separation for later analysis. The EDTA tubes were analyzed on the same day without centrifugation. If necessary, the sample was stored at +4°C for 7 days.[14]

Material

Blood glucose and creatinine levels were measured by spectrophotometric technique using the Cobas Integra 400 Plus (Roche Diagnostic, Switzerland). The Jaffé method for creatinine measurement was recalibrated according to IDMS. The HbA1c was determined using high-performance liquid chromatography (HPLC) of D-10 Automate dual program (BIO-RAD, USA).

Methodology

The eGFR was estimated using the EKFC and CKP-EPI 2021 equations based on blood creatinine level as shown in Tables 1 and 2, respectively.

Table 1. European Renal Function Consortium Equation for estimating eGFR[12]

Age (years)	Scr/Q	Equation for eGFR
2–40	<1	$107.3 \times (Scr/Q)^{-0.232}$
2–40	≥1	$107.3 \times (Scr/Q)^{-1.132}$
>40	<1	$107.3 \times (Scr/Q)^{-0.232} \times 0.990^{(Age-40)}$
>40	≥1	$107.3 \times (Scr/Q)^{-1.132} \times 0.990^{(Age-40)}$

Scr – serum creatinine. Q value for ages 2–25: Men: Ln (Q) = 3.200 + 0.259xAge – 0.543 x ln (Age) – 0.00763 x Age^2 + 0.0000790xAge^3, Women: Ln (Q) =3.080+ 0.177 Age-0.223xln (Age)-0.00596 x Age^2+ 0.0000686xAge^3. Q value for ages >25 years correspond to the median Scr values for the age and sex specific populations.[15]

Table 2. Chronic Kidney Disease – Epidemiology Collaboration 2021 equation for estimating eGFR[16]

Gender	SCr (mg/dL)	Equation (age in years)
Female	≤0.7	$DFG = 142 \times (Scr / 0.7)^{-0.241} \times (0.9938)^{Age} \times 1.012$
Female	>0.7	$GFR = 142 \times (Scr / 0.7)^{-1.200} \times (0.9938)^{Age} \times 1.012$
Male	≤0.9	$GFR = 142 \times (Scr / 0.9)^{-0.302} \times (0.9938)^{Age}$
Male	>0.9	$GFR = 142 \times (Scr / 0.9)^{-1.200} \times (0.9938)^{Age}$

SCr – serum creatine

Statistical tools

Statistical analysis was performed using Microsoft Excel (Microsoft, 2023) software on Windows and R version 4.4.2 (R Core Team (2024). R: A Language and Environment for Statistical Computing. R Foundation for Statistical Computing, Vienna, Austria. Available at: https://www.R-project.org/). Qualitative variables were expressed as percentages, while quantitative variables were expressed as means ± standard deviation (SD) or medians. The statistical tests applied were: Shapiro-Wilk normality test, T-student test to compare means and U-Man Whitney test to compare medians, χ^2 - test for comparing qualitative variables, and the Pearson correlation test, Passing and Bablock regression and Bland and Altman plot to compare the two methods. The acceptable difference was fixed at ±5 units.

The specific R packages used in the analysis were:

```
bland.altman.plot(
 ekfc,
 ckd_epi,
 graph.sys = "ggplot2",   # joli graphique
 conf.int = 0.95,        # IC 95%
 xlab = "Moyenne (EKFC + CKD-EPI)/2",
 ylab = "Différence (EKFC - CKD-EPI)"
)
 passig.bablock.plot
# ekfc = méthode test
# ckd_epi = méthode de référence

model <- mcreg(
x = ckd_epi, # référence
y = ekfc, # méthode testée
method.reg = "PaBa", # Passing-Bablok
method.ci = "analytical"
)
```

The level of statistical significance α (*p-value*) was set at 0.05. There was no need to carry out tests to adjust the significance level.

Table 3. Demographic characteristics by glycemic status and sex

Variable	T2DM, (N = 83)	Healthy subjects, (N = 275)	*p*-value (T-test)
Male	**48**	**120**	
Age (years), Mean ± SD	65.89 ± 2.05	39.03 ± 11.10	<0.01
BMI (kg/m^2), Mean ± SD	24.52 ± 4.33	26.13 ± 3.54	0.453
Female	**35**	**155**	
Age (years), Mean ± SD	61.11 ± 1.12	42.93 ± 15.23	<0.01
BMI (kg/m^2), Mean ± SD	28.03 ± 5.12	27.65 ± 4.18	0.789
Sex ratio	**1.37**	**0.77**	

SD – standard deviation, BMI – body mass index

Table 4. Clinical characteristics of subjects with type 2 diabetes mellitus

Characteristic	Results (N = 83)
Duration of diabetes	<5 years (25.6%) 5-10 years (44.9%) >10 years (29.5%)
Associated hypertension	Yes (51.80%)
Family history of diabetes	Yes (30.12%)
Smoking status	Yes (18.1%)
Treatment of T2D	OAD only (84%) OAD + Insulin (15%) Lifestyle and dietary measures (1%)
Dyslipidemia treatment	Yes (31%)
Treatment of hypertension	Yes (49%)
Chronic complications of T2D	Yes (8.43%) *(4 cases of macroangiopathy and 3 cases of microangiopathy)*

OAD – oral antidiabetic drugs, T2D – type 2 diabetes

RESULTS

Description of the study population

A total of 83 T2D and 275 healthy subjects were included in this study. The demographic characteristics of the overall study population and the clinical characteristics of T2D subjects are presented in Tables 3 and 4, respectively.

As show in Table 3, the two populations studied (T2D vs. healthy) were comparable in terms of BMI distribution but not in terms of age. As expected, majority of those with T2D were elderly while majority of healthy subjects recruited to determine the median in the Algerian population (the q) were younger. Regarding sex, the difference between the two populations constitutes a limitation of our study due to random recruitment.

Majority of the studied population had diabetes for more than 5 years. Nearly half of them had hypertension. Majority were on oral antidiabetic agents (OADs) alone and 8.43% had diabetic complications.

The age, gender and BMI distribution by sex based on WHO classification of the subjects with T2D is shown in Figures 1 and 2, respectively.

Biochemical measurements and eGFR calculation

To determine the q-value in the Algerian population, it was necessary to calculate the median creatinine level in healthy subjects of both sexes (Table 5).

The mean of blood glucose, serum creatinine and HbA1c and the eGFR using the two equations, EKFC and CKD-EPI 2021, among T2D are shown in Table 6.

The mean fasting blood glucose and HbA1c were both above targets. The average renal function as estimated by the two formulas was preserved with a normal average creatinine and a GFR >60 ml/min/1.73 m^2.

Comparison of the two methods for estimating GFR

To visualize the differences between the two equations for estimating GFR in our population, we draw a regression line using the Passing-Bablock plot as shown in Figure 3.

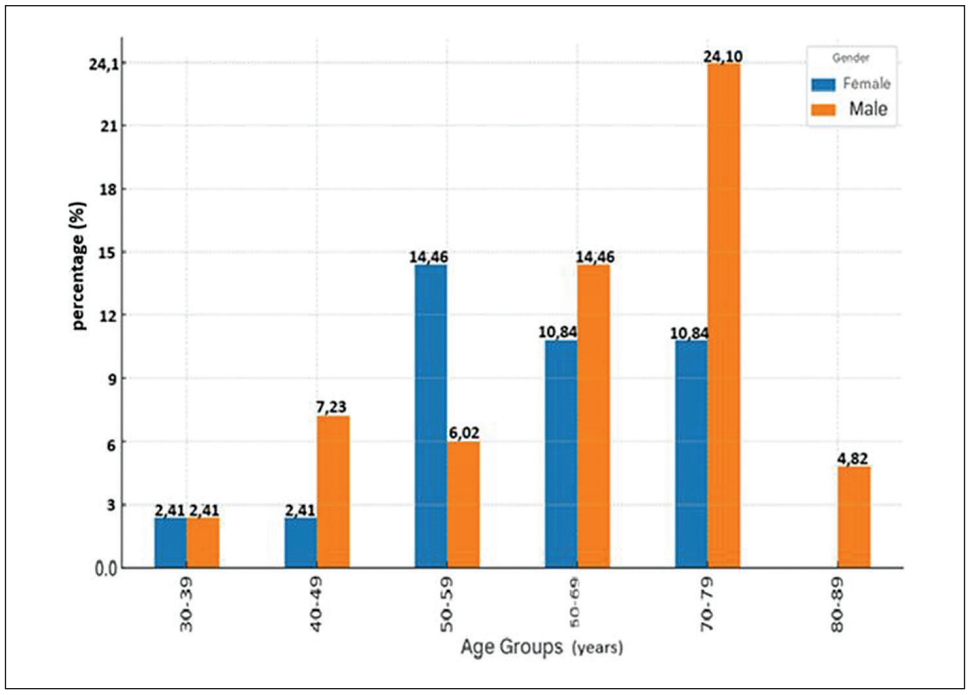

Figure 1. Distribution of patients with type 2 diabetes mellitus by age and gender.

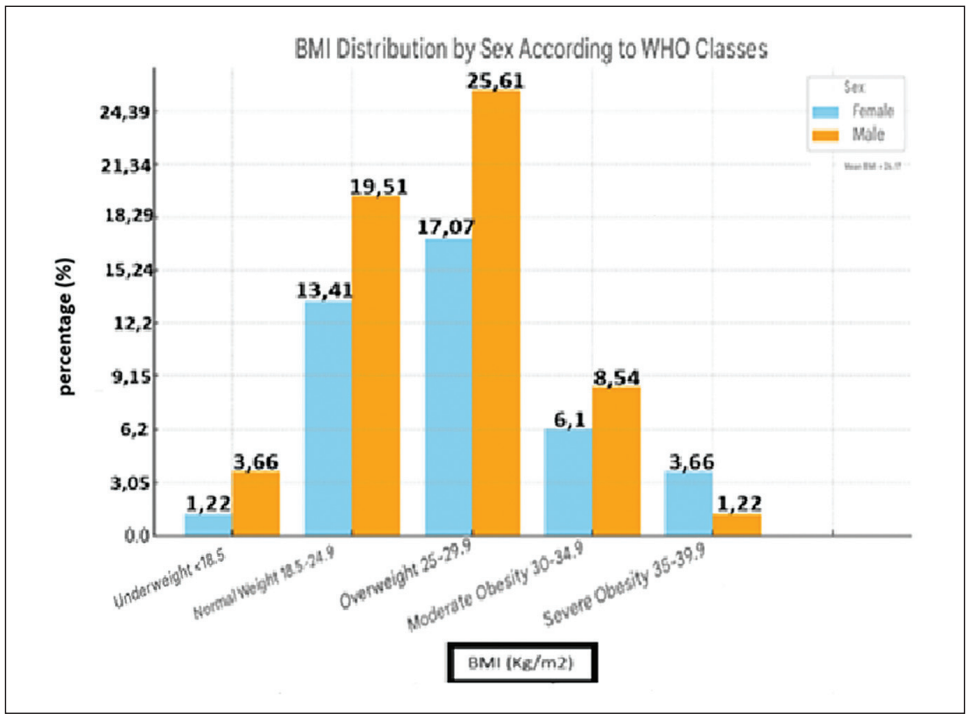

Figure 2. Distribution of patients with type 2 diabetes mellitus by body mass index.

Table 5. Median creatinine levels in healthy volunteers by gender

Parameter	Serum créatinine (mg/dL)			
	Mean ± SD	Médian (Q)	Min-max	*p*-value (T-test)
Female	0.76 ± 0.12	0.8	0.5-1.0	<0.001
Male	0.99 ± 0.15	1.0	0.5-1.5	

The eGFR using EKFC and CKD-EPI 2021 were strongly correlated (r ≈ 0.99 p <0.0001). However, the Passing–Bablock regression indicates a slope less than 1 (0.93; 95% CI 0.89–0.97), suggesting that there was a proportional bias, with EKFC increasing less rapidly than CKD-EPI and an intercept representing the negative systematic bias (−2.6; 95% CI −5.4 to −0.079).

There was a statistically significant difference between eGFR values from the two equations (Table 6: p <0.001), but with a good correlation (r = 0.99) (Figure 3). To confirm these results, the Bland-Altman plot is shown in Figure 4.

The difference between the EKFC and CKD-EPI 2021 values shown on the y-axis were generally below 0, confirming that EKFC underestimates eGFR compared to the CKD-EPI 2021 equation.

The mean difference (red line) was around -8. This means that EKFC values were 8 ml/min/1.73 m² lower than CKD-EPI 2021. Ninety-five percent of the results were within the agreement limit (-1.25, -15). Only one case had a difference greater than 0 (+0.26), with a low eGFR of 9 ml/min/1.73 m² by CKD-EPI and 9.26 ml/min/1.73 m² by EKFC. Another case of an 83-year-old individual had a difference below -15 (-16 ml/min/1.73 m²) with eGFR of 76.99 ml/min/1.73 m² using EKFC and 93 ml/min/1.73 m² with the CKD-EPI 2021 formula. Since the acceptable difference was fixed at ±5 units the difference of -8 units (range: -15, -1.25, was considered unacceptable.

The body mass index (BMI) appears to influence eGFR. The median eGFR in our population according to BMI is shown in Table 7.

Table 6. Laboratory results and estimated glomerular filtration rate using EKFC and CKD-EPI 2021 among subjects with type 2 diabetes mellitus

Parameters	Results (mean ± SD)	Minimum-maximum	Standards	*p* value (T-test)
Blood glucose (g/L)	1.90 ± 0.11	0.72 – 8	0.7-1.25	/
Blood creatinine (mg/L)	10.23 ± 0.83	2.3 – 73.7	Men: 6-13 Women: 5-12	/
HbA1c (%)	8.44 ± 0.23	6.1 – 13	<6.5	/
eGFR-EKFC (mL/min/1.73 m²)	73 ± 2.43	9.26 – 118.42	>90	<0.0001
eGFR-CKD-EPI (mL/min/1.73 m²)	81.41 ± 2.53	9 – 124	>90	

SD – standard deviation, eGFR – estimated glomerular filtration rate
Reference standards for HbA1c and eGFR are based on KDIGO guidelines[4]

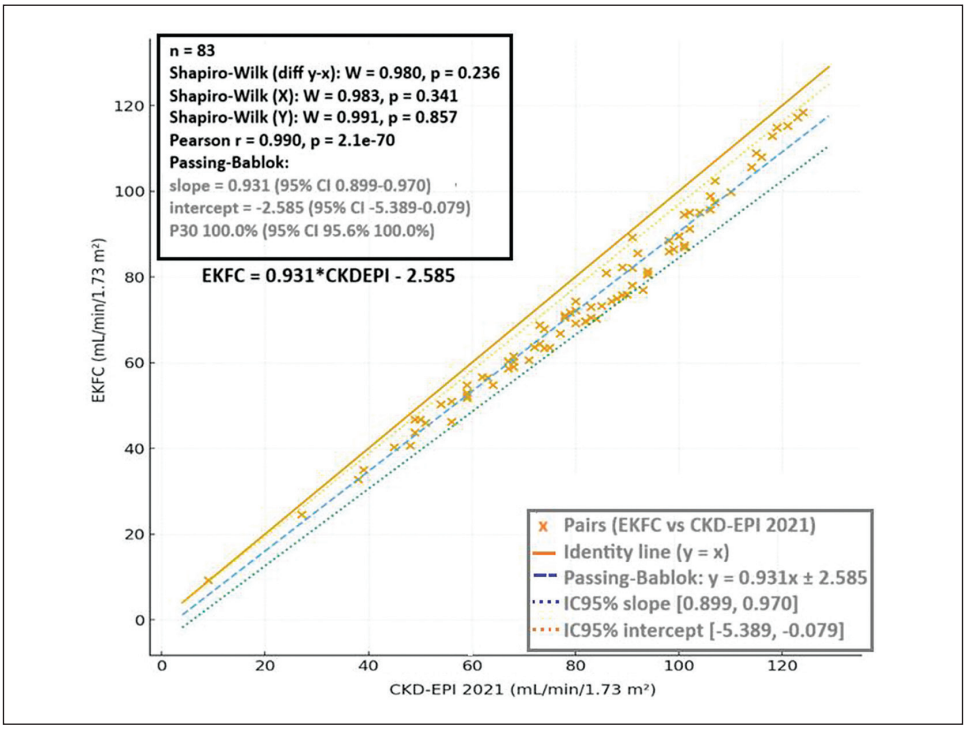

Figure 3. Passing-Bablock regression.

Table 7. The median estimated glomerular filtration rate based on the two methods according to body mass index among the population with type 2 diabetes mellitus[17]

BMI class (WHO)	N	Median eGFR EKFC (ml/min/1.73 m²)	Median eGFR CKD-EPI 2021 (ml/min/1.73 m²)	*p* value (U-Man Whitney)
Underweight <18.5	4	57	65	0.053
Normal weight 18.5-25	27	74	85	0.027
Overweight 25-29.9	36	70.06	79	0.023
Moderate and severe obesity ≥30	16	84.90	96	<0.001

BMI – body mass index, eGFR – estimated glomerular filtration rate

Table 8. Distribution of the population with type 2 diabetes mellitus (n = 83) according to the KDIGO classification based on eGFR[4]

KDIGO stage (eGFR: ml/min/m²)	Number according to EKFC	Number according to CKD-EPI 2021	*p* value (χ^2 test)
G1(>90)	17 (20.48%)	33 (40.24%)	0.0013
G2 (60-89)	45 (54.21%)	34 (40.96%)	0.045
G3a (45-59)	15 (18.07%)	13 (15.66%)	0.945
G3b (30-44)	5 (6.02%)	2 (2.40%)	0.063
G4 (15-29)	0 (0.00%)	0 (0.00%)	/
G5 (<15)	1 (1.20%)	1 (1.20%)	0.865

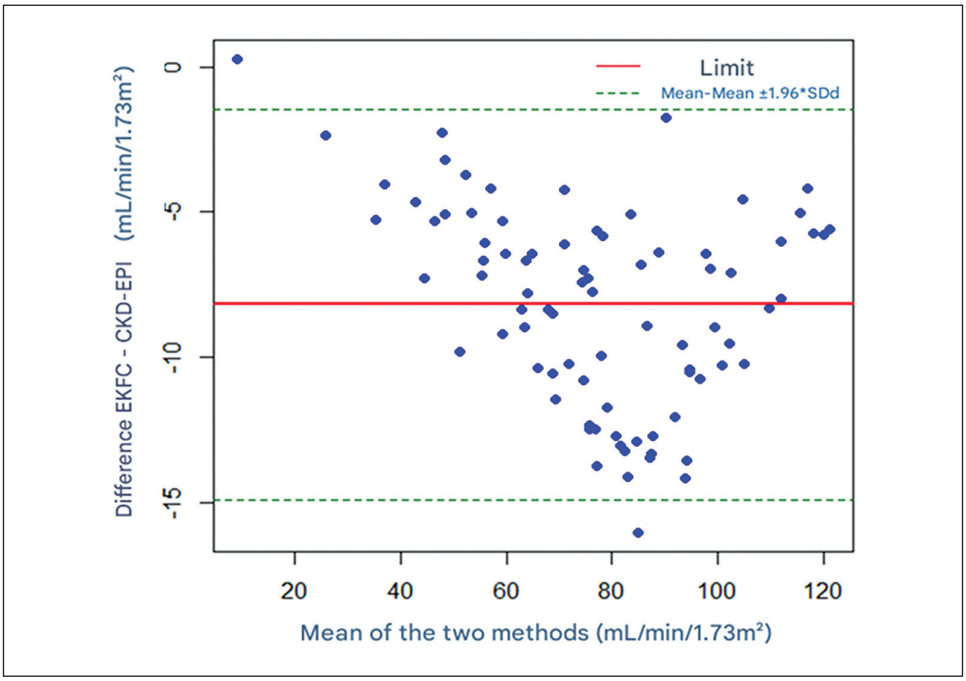

Figure 4. Bland-Altman difference diagram.

In our adult population, eGFR gradually decreases in normal-weight and overweight individuals, then increases among those with BMI >30 with an eGFR of 85 and 96 ml/min/1.73 m² according to the EKFC and CKD-EPI, respectively. The lack of concordance of the eGFR in the underweight compared to the other categories was probably due to a sample size that was too small (n = 4). The number of individuals per kidney disease stage according to KDIGO criteria based on the two methods are shown in Table 8.

The results showed a significant rate of reclassification of patients from KDIGO stage G1 to stage G2 (33 - 17 = 16 patients reclassified) when using the EKFC equation. This proves the presence of a clinical difference.

DISCUSSION

This is the first study to compare the EKFC and CKD-EPI 2021 equations among Algerian population with T2D. There was a significant difference between the eGFR using the two equations but with a strong correlation (r=0.99). The EKFC equation yielded lower eGFR compared to CKD-EPI 2021 with a difference or bias of -8 ml/min/1.73 m². Thus, the added value of the EKFC lies mainly in the fine stratification of the early stages of CKD which may help in early detection and prevention of kidney disease progression.

The result of our study is consistent with the findings of Lu et al.[18] They also demonstrated that EKFC underestimates eGFR compared to CKD-EPI 2021. The Bland-Altman diagram from the latter study showed that EKFC underestimated GFR compared to CKD-EPI 2021 in the GFR range below 120 ml/min/1.73 m^2. However, EKFC overestimated GFR in the range above 150 ml/min/1.73 m^2, results not observed in our cohort. Lu et al. also showed a bias or mean difference of -5.5 based on Bland-Altman plot and a limit of agreement in a range of -11to 0. In our study, the bias was -8 with limits of agreement of -15; to 1.25.

In an Asian study by Lee et al. conducted in 2024, the bias was -8.8.[19] This means that the eGFR by CKD-EPI is on average 8.8 ml/min/1.73 m^2/ higher than EKFC. Thus, underestimation of eGFR using EKFC was consistent with our results. The study also found a significant correlation between the GFR values estimated by the two equations, with a correlation coefficient of 0.93 (p <0.001).

In 2022, Martins et al., compared EKFC and CKD-EPI 2021 with measured glomerular filtration rate (mGFR) among 122 patients with T2D.[20] The p30 or accuracy within 30% which indicates the percentage of time an eGFR matches the patient's true value or mGFR of both methods were low at 74% (95% CI 65-81) and 64% (95% CI 56-72) for CKD-EPI and EKFC, respectively. However, in this study, neither equation achieved optimal performance in estimating GFR. This also illustrates that assessing renal function using mGFR tends to reduce the apparent performance of the two equations.

In 2020, Pottel et al., compared the differences between mGFR and eGFR using four equations: EKFC, CKD-EPI 2021, Chronic Kidney Disease in Children Study (CKID) and Full Age Spectrum (FAS) on 19,629 patients aged 2 to 90 years. They divided their population into 4 age groups: children (under 18), adults under 40, under 65 and over 65. The results showed average biases, smaller standard errors and a higher p30 in the EKFC equation than in the other equations. The p30 in the under 18 age group using the EKFC equation was 79.7%, compared to 73.2% in the CKID equation and 74.2% in the FAS equation. For adults under 40, p30 was 90%, compared to 82% and 84% in the FAS and CKD-EPI equations, respectively. Among under 65 and over 65 age groups, p30 was 89.5% and 85% for the EKFC equation, 85.9% and 83.6% for FAS, and 88.2% and 80.7% for CKD-EPI, respectively.[12] This study concluded that the EKFC equation was applicable in all age groups, while the CKD- EPI equation had a limitation in the under-18 age group. The only limitation of this study was the exclusion of black subjects.

The eGFR in our adult population showed a steady decline in both the normal weight and overweight categories, followed by an increase among those who have BMI greater than 30 and eGFR of 85 and 96 ml/min/1.73 according to EKFC and CKD-EPI, respectively. The lack of concordance of eGFR in the underweight category may be due to an inconclusive sample size (n= 4 patients). Similar to an Asian study, BMI increases while eGFR decreases, except in the group with a BMI >30 kg/m^2.[19] In a study conducted in 2008 by Chagnac et al., mGFR was 61% higher in obese individuals (BMI >30) than in the control group (BMI <25). They also demonstrated that in subjects with severe obesity, weight loss leads to a decrease in eGFR and renal plasma flow.[21]

A comparative analysis of kidney disease classification according to KDIGO criteria based on eGFR using the two equations reveals slight differences. Our data showed a significant rate of reclassification of patients from class G1 to stage G2 (16 patients), but less significant in stages G3b (3 patients) and G3a (2 patients). There were fewer individuals in stage G1 using the EKFC equation. However, the number of patients were equal in the more advanced stages (G4 and G5). Similarly, Lee et al., showed that EKFC tends to classify Asian adult population into more severe stages, moving many patients from stage G1 to stage G2 and from G2 to G3a, but with little difference in classification in the last three advance stages G3b, G4 and G5.[19] Given that the latter study was conducted on a population of 82,022 individuals and that the numbers were almost identical in G4 and G5, severe stages remain robustly identified regardless of the formula used. Thus, the added value of EKFC lies mainly in the fine stratification of the early stages. Despite the smaller number in our population, statistical significance was still observed in our study.

Limitations

We recruited subject using blind sampling method which resulted in two groups (T2D and healthy individuals) that were not comparable in terms of age and sex. The lack of comparison with mGFR was a limitation in our study due to the unavailability of the test and high cost. The mGFR is more accurate and is based on a direct measurement of glomerular filtration, whereas eGFR depends on indirect markers (creatinine in our case). Due to lack of mGFR, it was impossible to determine which of the two formulas was closer to reality, and the p30 cannot be calculated. Lastly, the sample size was insufficient to perform a subgroup analysis. This study provided preliminary data on the q-value among the Algerian population but further studies including a larger sample size is recommended.

CONCLUSION

The EKFC equation, obtained by combining the FAS and CKD-EPI 2021 equations, has been proposed as a more universal formula for computing the eGFR. It has the advantage of eliminating correction for ethnicity and covering a wide age range. The EKFC equation, due to the underestimation of GFR compared with CKD-EPI 2021, may be helpful in early detection and intervention for CKD in T2D.

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Statement of Authorship
All authors certified fulfillment of ICMJE authorship criteria.

CRediT Author Statement

Data Availability Statement
Datasets are not publicly available because participants in the study did not give written consent for their data to be shared.

Author Disclosure
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Declaration of IA
We declare the use of AI tools for the translation of the manuscript, which was subsequently revised.

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