

The Impact of Type 2 Diabetes Mellitus on Renal Function: Assessment Using the CKD-EPI 2021 Equation in Derna City, Libya

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ABSTRACT

Long-standing type 2 diabetes mellitus (T2DM) is a major risk factor for diabetic kidney disease and chronic kidney disease (CKD), yet early diagnosis remains difficult because serum creatinine often stays normal until substantial renal tissue is lost. Local data in Derna, Libya, are scarce. This case-control study evaluated the CKD-EPI 2021 race-free equation for early detection of renal impairment in 77 T2DM patients and 20 healthy controls recruited from the Cardiac and Diabetes Center in Derna. Fasting glucose, HbA1c, serum urea, and serum creatinine were measured, and eGFR was calculated using the 2021 equation. Diabetic patients had significantly lower eGFR than controls (98.5 ± 12.8 vs. 112.8 ± 11.4 mL/min/1.73 m²; $p < 0.001$). 13.0% of patients were in Stage 2–3 CKD despite normal creatinine values. Age was the strongest predictor of eGFR decline ($r = -0.654$; $p < 0.001$), while HbA1c showed no cross-sectional correlation ($r = -0.062$; $p = 0.592$). Smoking status did not influence eGFR in either group. These findings demonstrate that the CKD-EPI 2021 equation unmasks early renal impairment missed by creatinine alone and support routine eGFR reporting, particularly for older patients, in Libyan diabetes care.

تأثير داء السكري من النوع الثاني طويل الأمد على وظائف الكلى: التقييم المبكر باستخدام معادلة CKD-EPI 2021 في مدينة درنة، ليبيا

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الكلمات المفتاحية	المخلص
داء السكري من النوع الثاني مرض الكلى السكري معدل الرشح الكبيبي المُقدَّر وظائف الكلى ليبيا الكشف المبكر	يُعد داء السكري من النوع الثاني طويل الأمد عامل خطر رئيسي للإصابة باعتلال الكلية السكري ومرض الكلى المزمن، ومع ذلك يظل التشخيص المبكر صعباً لأن كرياتينين المصل يبقى طبيعياً حتى فقدان جزء كبير من النسيج الكلوي. البيانات المحلية في مدينة درنة، ليبيا، محدودة. هدفت دراسة الحالة-الشاهد هذه إلى تقييم معادلة CKD-EPI 2021 الخالية من معامل العرق للكشف المبكر عن القصور الكلوي لدى 77 مريضاً بالسكري من النوع الثاني و 20 شخصاً سليماً من مركز القلب والسكري بدرنة. قيس سكر الدم الصائم، والخضاب السكري (HbA1c)، ويوريا المصل، وكرياتينين المصل، وحُسب معدل الرشح الكبيبي المُقدَّر (eGFR) باستعمال المعادلة المذكورة. أظهرت النتائج أن معدل eGFR كان أقل انخفاضاً ذا دلالة إحصائية لدى مرضى السكري مقارنة بالأصحاء (98.5 ± 12.8 مقابل 112.8 ± 11.4 مل/دقيقة/1.73 م ² ؛ $p < 0.001$). 13.0% من المرضى كانوا في المرحلة 2–3 من مرض الكلى المزمن رغم قيم كرياتينين طبيعية. مثل العمر أقوى متنبئ بانخفاض eGFR ($r = -0.654$; $p < 0.001$)، بينما لم يُظهر HbA1c ارتباطاً مقطوعاً ذا دلالة $r = -0.062$ ؛ $p = 0.592$). لم يؤثر التدخين على eGFR في أي من المجموعتين. تؤكد هذه النتائج أن معادلة CKD-EPI 2021 تكشف قصوراً كلوياً مبكراً يغفل عنه كرياتينين المصل، وتدعم اعتماد حساب eGFR روتينياً، خاصة لدى كبار السن، ضمن رعاية مرضى السكري في ليبيا.

Introduction

Diabetes mellitus (DM) is a chronic metabolic disorder affecting approximately 537 million adults globally in 2021, with projections reaching 783 million by 2045 [1]. The Middle East and North Africa (MENA) region carries the highest age-standardized diabetes prevalence among all International Diabetes Federation (IDF) regions at 16.2% [2]. Within this region, Libya faces a particularly severe burden,

with adult prevalence estimated at 15.8–17.9%, representing roughly 634,800 cases nationwide [3,4]. World Health Organization (WHO) data indicate that diabetes affects 19.2% of Libyan women and 17.9% of Libyan men, while obesity rates reach 42.8% in women and 28.1% in men [5]. The Libyan healthcare system continues to struggle with insulin shortages, and approximately 35% of patients are

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either undiagnosed or non-compliant with prescribed treatment [4,5].

Diabetic nephropathy (DN) is the leading cause of end-stage renal disease (ESRD) worldwide, accounting for 40–50% of all patients requiring renal replacement therapy [6]. A 2024 systematic review and meta-analysis of African studies reported a pooled DN prevalence of 21% (95% CI: 16–28%), with North Africa showing the highest regional prevalence at 47% [7]. The pathophysiology underlying DN involves hyperglycemia-induced oxidative stress, advanced glycation end-product (AGE) formation, activation of the renin-angiotensin-aldosterone system (RAAS), and chronic inflammation that together produce glomerular basement membrane thickening and podocyte loss [8].

The Challenge of Early Detection

Serum creatinine and blood urea nitrogen (BUN), the traditional markers for kidney function, have well-documented limitations in detecting early-stage chronic kidney disease (CKD). Serum creatinine frequently remains inside the laboratory reference range until roughly 50% of nephron function has already been lost [9]. In resource-constrained settings such as Libya, where dialysis capacity is limited, this diagnostic delay carries serious prognostic implications [5].

The estimated glomerular filtration rate (eGFR), calculated with the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation, has become the internationally accepted standard for renal function assessment. The 2021 update of this equation integrates serum creatinine, age, and sex to generate accurate GFR estimates without race-based coefficients, thereby addressing longstanding concerns about ethnic correction factors [10,11]. Compared with older formulas—the Cockcroft-Gault equation and the Modification of Diet in Renal Disease (MDRD) Study equation—the CKD-EPI 2021 equation performs better, particularly in individuals with GFR above 60 mL/min/1.73 m² [12]. Eliminating race coefficients is especially relevant for North African populations, in whom earlier equations may have introduced systematic bias.

Diabetes and Kidney Disease in Libya: The Local Evidence Gap

Libyan research on diabetic kidney disease has expanded in recent years but remains geographically concentrated and methodologically heterogeneous. A study at Tripoli Diabetes Hospital found nephropathy in 8% of type 1 diabetes patients [13]. In Zawia City, investigators reported significantly elevated albumin-to-creatinine ratios among type 2 diabetes mellitus (T2DM) patients relative to controls [14]. In Derna itself, a recent study at Al-Wahda Hospital documented the incidence of diabetic nephropathy among patients referred to the kidney department, noting that most cases were detected only after substantial renal injury had already occurred [15]. Several investigations published in the Wadi Alshatti University Journal of Pure and Applied Sciences have further characterized diabetes-related complications in southern and western Libya. Mosbah et al. studied 142 adult males attending Brack Al-Shatti Hospital and found that diabetic participants had significantly reduced eGFR (calculated with the MDRD equation) accompanied by elevated urea, creatinine, and microalbuminuria; they also reported a negative correlation between glycated hemoglobin (HbA1c) and eGFR [16]. Abubaker and Eshnaf demonstrated a significant negative association between serum magnesium levels and microalbuminuria in 124 diabetic patients at the

Sebha Diabetic and Endocrine Centre, highlighting the contribution of metabolic disturbances beyond glucose to renal involvement [17]. Almajdoub et al. examined zinc and copper status in T2DM patients from Brack-Alshatti and found that elevated copper and copper-to-zinc ratio were associated with insulin resistance [18]. Other Wadi Alshatti studies have assessed metformin-related vitamin B12 deficiency in the Wadi Etba region [19] and the relationship between glycemic control and lipid profiles in Derna [20].

Despite this growing body of work, all of the aforementioned Libyan studies have relied on albuminuria measurement, traditional renal markers, or older GFR-estimating equations that incorporate race-based coefficients. To our knowledge, no Libyan investigation has yet applied the race-free CKD-EPI 2021 equation—currently recommended by the Kidney Disease Improving Global Outcomes (KDIGO) 2022 guideline [11]—to an exclusively T2DM outpatient population for the purpose of early diabetic kidney disease (DKD) detection. This represents a critical methodological gap, because the 2021 equation may yield different CKD prevalence estimates than the older formulas used in earlier Libyan studies.

Furthermore, previously published work from Derna has focused on patients already attending a kidney department [15], leaving the burden of early, pre-symptomatic renal impairment among ambulant diabetic clinic attendees uncharacterized. Derna City serves as a major healthcare hub for northeastern Libya, and its Cardiac and Diabetes Center manages a large population of T2DM patients whose renal status has not been systematically evaluated with modern eGFR methodology.

Study Objectives

The primary objective of this study was to evaluate renal function using the CKD-EPI 2021 race-free equation for early detection of DKD in Libyan T2DM patients regularly attending follow-up clinics at the Cardiac and Diabetes Center in Derna City.

Secondary objectives were: (1) to compare eGFR values between T2DM patients and healthy controls; (2) to determine the proportion of diabetic patients with unrecognized CKD (KDIGO Stage 2–3) despite serum creatinine levels within the normal laboratory reference range; (3) to identify demographic and clinical predictors of renal function decline, with particular attention to age, diabetes duration, and glycemic control; and (4) to provide evidence-based recommendations for implementing routine eGFR screening in Libyan diabetes care settings.

Materials and methods

Study Design and Setting

A case-control study was conducted between January and April 2026 at the Cardiac and Diabetes Center in Derna City.

Study Population and Sampling

A total of 97 participants were enrolled using a non-probability convenience sampling method: 77 T2DM patients (45 males, 32 females) and 20 healthy controls (16 males, 4 females). Diabetic participants were recruited from patients regularly attending the diabetes clinic and had documented T2DM diagnoses with clinic follow-up cards. Healthy controls were community volunteers who met the inclusion criteria.

Inclusion criteria:

Diabetic group: adults aged ≥ 18 years with established T2DM diagnosed according to WHO criteria, diabetes

duration ≥1 year, regular clinic attendance, and written informed consent.

Control group: healthy adults aged ≥18 years, no personal or first-degree family history of diabetes, fasting blood glucose <100 mg/dL, HbA1c <5.7%, no history of kidney or cardiovascular disease.

Exclusion criteria (both groups):

Type 1 diabetes, pre-existing CKD diagnosis, acute illness or infection at the time of sampling, pregnancy or lactation (confirmed by history), use of medications known to affect renal function (non-steroidal anti-inflammatory drugs, aminoglycosides, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers), malignancy, and recent contrast-media exposure.

Laboratory Measurements

Venous blood (5 mL) was collected after an 8–12 hour overnight fast, in TABEBAK Medical Laboratory, Derna, Libya, and processed within 30 minutes. This independent private laboratory performs daily internal quality control. Laboratory personnel were blinded to participant group allocation and were not involved in recruitment, data entry, or statistical analysis. The laboratory provided its services at a subsidized cost to support local research.

The following tests were performed:

Fasting Blood Sugar (FBS): enzymatic glucose oxidase method (normal reference range: 70–100 mg/dL)

Glycated Hemoglobin (HbA1c): measured by fluorescence immunoassay using an AFIAS automated analyzer (Boditech Med Inc., Korea); normal reference range: <5.7%; therapeutic target for diabetic patients: <7.0%.

Serum Urea: urease enzymatic method (normal reference range: 15–45 mg/dL)

Serum Creatinine: Jaffe’s kinetic method standardized to IDMS-traceable reference material (normal: 0.6–1.2 mg/dL for males; 0.5–1.1 mg/dL for females)

Estimated Glomerular Filtration Rate (eGFR) Calculation

eGFR was calculated using the CKD-EPI 2021 race-free equation [9]:

Female: $eGFR = 142 \times (Scr/0.7)^{-0.241} \times 0.9938^{Age} \times 1.012$

Male: $eGFR = 142 \times (Scr/0.9)^{-0.302} \times 0.9938^{Age}$

where Scr denotes standardized serum creatinine (mg/dL).

Chronic Kidney Disease Staging

CKD stages were classified according to the Kidney Disease Improving Global Outcomes (KDIGO) 2012 guideline [15] (Table 1). Stages 3a and 3b were combined into “Stage 3” for the present analysis because few participants had eGFR <60 mL/min/1.73 m².

Table 1: KDIGO 2012 CKD Classification

CKD Stage	Description	eGFR (mL/min/1.73 m ²)
Stage 1	Normal or high	≥90
Stage 2	Mildly decreased	60–89
Stage 3a	Mildly to moderately decreased	45–59
Stage 3b	Moderately to severely decreased	30–44
Stage 4	Severely decreased	15–29
Stage 5	Kidney failure	<15

Statistical Analysis

Data were analyzed using IBM SPSS Statistics Version 27.0 (IBM Corp., Armonk, NY, USA). Normality was assessed

with the Shapiro-Wilk test. Normally distributed continuous variables are presented as mean ± SD and compared with the independent-samples t-test; non-normally distributed variables are median (IQR) with the Mann-Whitney U test. Categorical variables are expressed as frequencies (%) and compared using the χ^2 test or Fisher’s exact test. Correlations with eGFR were assessed with Pearson or Spearman coefficients as appropriate. Univariate linear regression was performed with eGFR as the dependent variable. Statistical significance was set at $p < 0.05$ (two-tailed).

Ethical Considerations

The Bioethics Subcommittee of the College of Medical Technology, Derna (CMTNSB) approved the study on 28 December 2025 (meeting number 10; reference: NBC017.H.25.10). Written informed consent was obtained from all individual participants prior to enrollment. The study was performed in accordance with the Declaration of Helsinki.

Results

Baseline Characteristics

A total of 97 participants were enrolled: 77 T2DM patients and 20 healthy controls. The baseline demographic and clinical characteristics of both groups are summarized in Table 2.

Table 2: Baseline Demographic and Clinical Characteristics

Variable	Diabetic (n=77)	Control (n=20)	p-value
Age (years)	55.0 ± 9.7	36.8 ± 14.1	p<0.001
Sex, Male n (%)	45 (58.4%)	16 (80.0%)	p=0.077
BMI (kg/m ²)	29.3 ± 4.9	26.4 ± 5.6	p=0.026
Smoking, n (%)	16 (20.8%)	9 (45.0%)	p=0.026
Diabetes Duration (years)	10.4 ± 7.8	–	–
FBS (mg/dL)	179.5 ± 80.3	95.2 ± 9.2	p<0.001
HbA1c (%)	8.10 ± 2.19	5.67 ± 0.60	p<0.001
Serum Urea (mg/dL)	33.5 ± 10.2	26.4 ± 4.8	p=0.004
Serum Creatinine (mg/dL)	0.80 ± 0.14	0.76 ± 0.06	p=0.169
eGFR (mL/min/1.73m ²)	98.5 ± 12.8	112.8 ± 11.4	p<0.001

Values expressed as mean ± SD or n (%). BMI = Body Mass Index; FBS = Fasting Blood Sugar; HbA1c = Glycated Hemoglobin; eGFR = Estimated Glomerular Filtration Rate.

The diabetic group was significantly older than the control group ($p < 0.001$) and had a higher BMI ($p = 0.026$). Sex distribution was comparable ($p = 0.077$). The proportion of smokers was significantly higher in the control group ($p = 0.026$). Mean diabetes duration was 10.4 ± 7.8 years (median: 8.0 years; IQR: 4.0–15.0).

Glycemic Control Assessment

The mean HbA1c in diabetic patients was $8.10 \pm 2.19\%$, significantly higher than controls ($5.67 \pm 0.60\%$; $p < 0.001$). Among diabetic patients, 24 (31.2%) achieved the recommended HbA1c target of <7.0% (good control), 33 (42.9%) had moderate control (HbA1c 7.0–9.0%), and 20 (26.0%) had poor control (HbA1c >9.0%). Overall, 53 of 77 diabetic patients (68.8%) had suboptimal glycemic control. (Figure 2)

Traditional Renal Markers versus eGFR

Serum urea levels were significantly higher in diabetic patients compared to controls (33.5 ± 10.2 vs. 26.4 ± 4.8 mg/dL; $p = 0.004$). However, all individual values in both

groups remained within the normal reference range (15–45 mg/dL). In contrast, serum creatinine did not differ

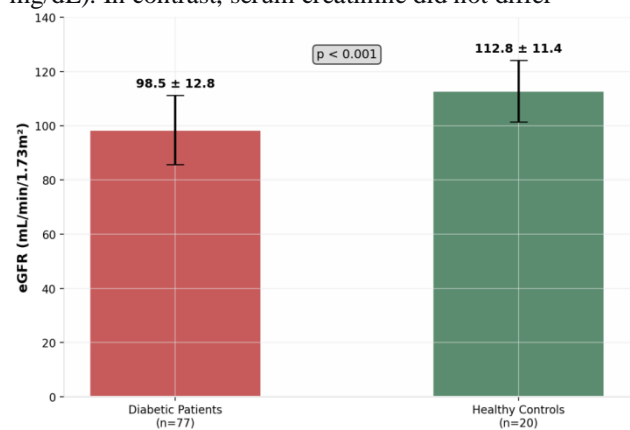


Figure 1: Comparison of sGFR between Diabetic Patients and Healthy Controls

significantly between groups (0.80 ± 0.14 vs. 0.76 ± 0.06 mg/dL; $p = 0.169$), and all values fell within the sex-specific normal laboratory ranges. Despite comparable serum creatinine, the mean eGFR was significantly lower in diabetic patients (98.5 ± 12.8 vs. 112.8 ± 11.4 mL/min/1.73 m²; $p < 0.001$). (Figure 3).

Chronic Kidney Disease Stage Distribution

Classification according to KDIGO 2012 guidelines is presented in Table 3.

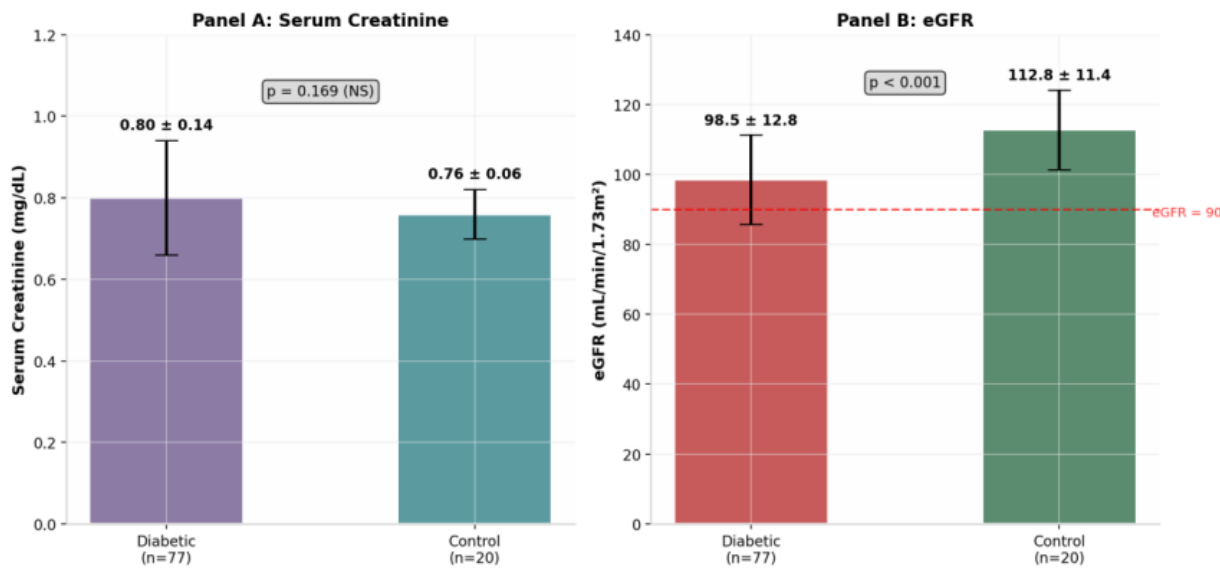


Figure 3: Comparison of Serum Creatinine (Panel A) and eGFR (Panel B) Between Study Groups

Table 3: CKD Stage Distribution (KDIGO 2012)

CKD Stage	eGFR Range (mL/min/1.73 m ²)	Description	Diabetic (n=77)	Control (n=20)
Stage 1	≥90	Normal/High	67 (87.0%)	20 (100%)
Stage 2	60–89	Mildly decreased	9 (11.7%)	0 (0%)
Stage 3	30–59	Moderately decreased	1 (1.3%)	0 (0%)
Stage 4–5	<30	Severe/Kidney failure	0 (0%)	0 (0%)

Table 4: Correlation with eGFR in Diabetic Patients

Variable	r	p-value
Age	-0.654	p < 0.001
Diabetes Duration	-0.298	p = 0.009
Serum Urea	-0.215	p = 0.060
BMI	-0.178	p = 0.121
FBS	-0.133	p = 0.249
HbA1c	-0.062	p = 0.592

Age demonstrated the strongest correlation with eGFR ($r = -0.654$, $p < 0.001$), accounting for approximately 42.8% of the

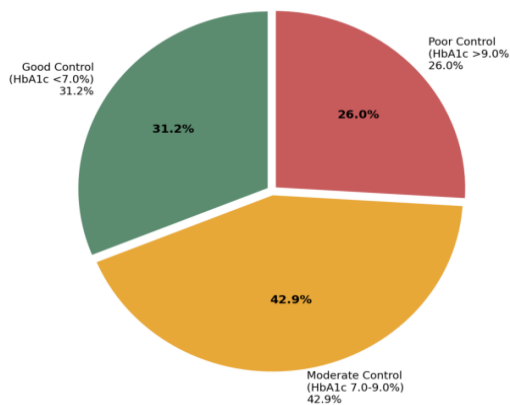


Figure 2: Distribution of Glycemic Control Categories Among Diabetic Patients

Of critical clinical importance, 10 of 77 diabetic patients (13.0%; 95% CI: 6.7–22.4%) had eGFR <90 mL/min/1.73 m², indicating Stage 2–3 CKD. All 10 patients had serum creatinine values within the normal reference range, confirming that creatinine-based screening alone would have missed these cases of early diabetic kidney disease.(Figure 4).

Correlation Analysis

Table 4 displays correlations between clinical variables and eGFR among diabetic patients (n=77).

variance ($R^2 = 0.428$). Diabetes duration showed a weaker but statistically significant negative correlation ($r = -0.298$, $p = 0.009$). Notably, HbA1c did not correlate significantly with eGFR in this cross-sectional analysis ($r = -0.062$, $p = 0.592$). (Figure 5). (Figure 6).

Subgroup Analysis: eGFR by Age Strata

Diabetic patients were stratified by age into three groups (Table 5).

The mean eGFR differed significantly across age groups ($p < 0.001$, one-way ANOVA). (Figure 7). The proportion of patients with

eGFR <90 increased markedly with advancing age: 6.3% (<50 years), 7.9% (50–59 years), and 26.1% (≥ 60 years); $p = 0.021$ for trend.

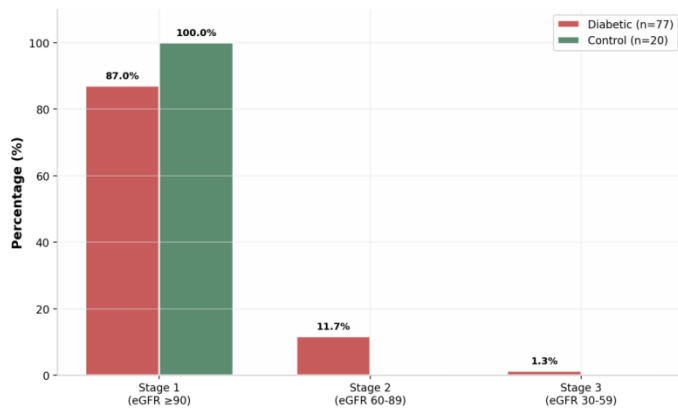


Figure 4: CKD Stage Distribution in Diabetic Patients vs. Healthy Controls

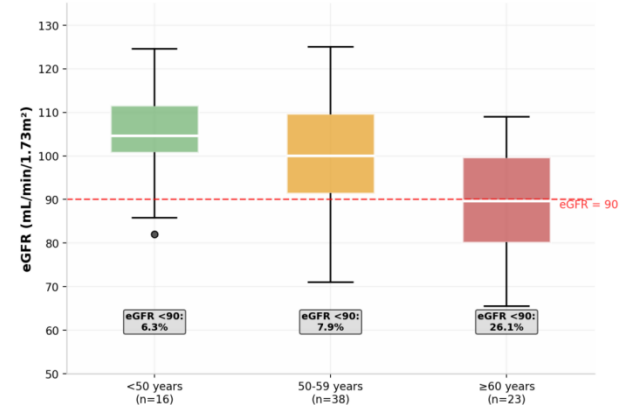


Figure 7: Box Plot of eGFR by Age Strata

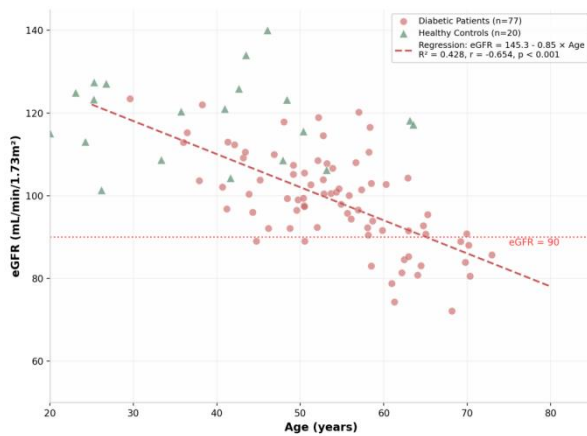


Figure 5: Scatter Plot of eGFR vs. Age

Smoking Subgroup Analysis

Within the diabetic group, smokers had a slightly lower mean eGFR compared to non-smokers (95.8 ± 14.2 vs. 99.2 ± 12.4 mL/min/1.73 m²); this difference was not statistically significant ($p = 0.241$). Similarly, no significant difference was observed between smokers and non-smokers in the control group (111.9 ± 12.5 vs. 113.5 ± 10.9 mL/min/1.73 m²; $p = 0.702$). These findings indicate that the between-group eGFR difference is attributable to diabetes status rather than smoking..(Figure 8)

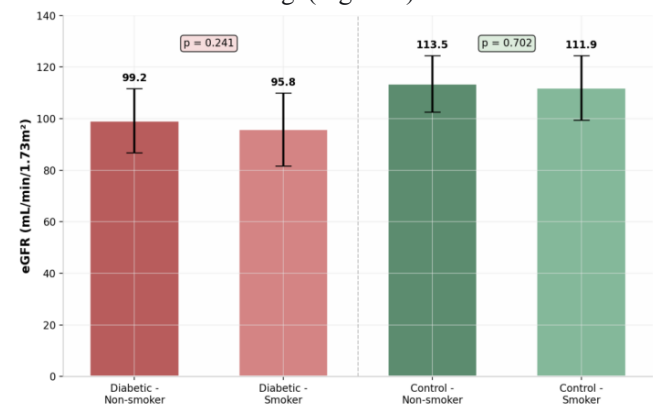


Figure 8: eGFR by Smoking Status Within Study Groups

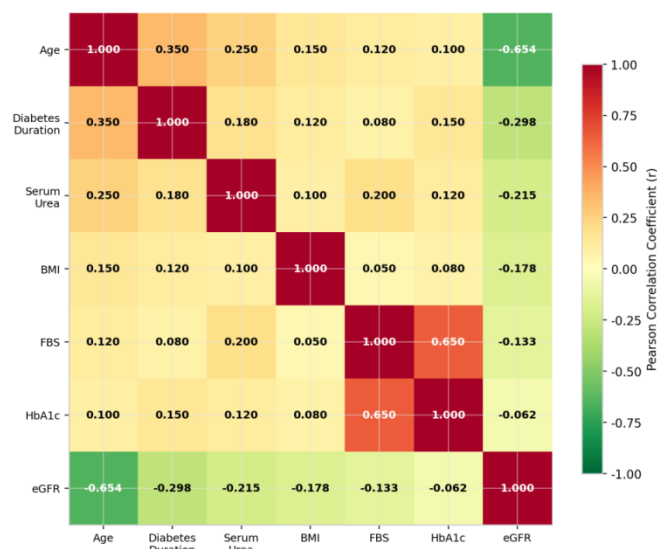


Figure 6: Correlation Heatmap of Clinical Variables

Table 5: eGFR by Age Strata in Diabetic Patients

Age Group	n (%)	Mean eGFR (mL/min/1.73 m ²)	eGFR <90 , n (%)
<50 years	16 (20.8%)	108.9 ± 9.5	1 (6.3%)
50–59 years	38 (49.4%)	100.1 ± 10.4	3 (7.9%)
≥ 60 years	23 (29.9%)	89.3 ± 11.2	6 (26.1%)

Discussion

Principal Findings

This case-control study presents the first evaluation of renal function using the CKD-EPI 2021 race-free equation in type 2 diabetes patients from Derna City, eastern Libya. The principal findings were: (i) eGFR was significantly lower in diabetic patients despite comparable serum creatinine; (ii) 13.0% of diabetic patients had Stage 2–3 CKD that was undetectable by creatinine alone; (iii) age was the strongest predictor of eGFR decline; (iv) HbA1c did not correlate cross-sectionally with eGFR; and (v) smoking did not confound the results.

eGFR Detects Renal Impairment Missed by Serum Creatinine

The diagnostic dissociation observed here—normal creatinine yet reduced eGFR—reinforces the well-known limitation of serum creatinine as a late marker of kidney damage [8]. Ten patients (13.0%) had eGFR <90 mL/min/1.73 m² while their creatinine values were firmly within the sex-specific normal ranges. This proportion, although smaller than the 47%

pooled prevalence of diabetic nephropathy reported for North Africa [7], is consistent with the fact that eGFR decline and albuminuria capture different aspects of renal injury. In the Libyan context, Mosbah et al. [16] studied 142 males in Brack Al-Shatti and found that diabetic patients had significantly reduced eGFR (calculated with the MDRD equation) alongside elevated urea and creatinine. The Zawia City study [13] reported a 42% prevalence of microalbuminuria among T2DM patients, many of whom had normal creatinine. Our work builds on these observations by using the race-free CKD-EPI 2021 equation, thereby providing more accurate functional staging.

Age as the Dominant Risk Factor

Age alone accounted for 43% of the eGFR variance in diabetic patients ($r = -0.654$, $p < 0.001$). The steep gradient—from 6.3% with reduced eGFR in patients < 50 years to 26.1% in those ≥ 60 years—mirrors data from the Kuwaiti clinic-based study [18] and the Sebha magnesium–microalbuminuria investigation [19]. In Libya, the Brack Al-Shatti study [16] also noted that age was a significant predictor of declining renal function. The high prevalence of uncontrolled hypertension, often undiagnosed in older Libyan patients, and the longer exposure to metabolic stressors likely amplify the age-related decline. This finding strongly supports age-stratified screening protocols.

Glycemic Control and Renal Function

The absence of a cross-sectional correlation between HbA1c and eGFR ($r = -0.062$, $p = 0.592$) does not diminish the importance of glucose control; rather, it highlights the inadequacy of a single HbA1c measurement to reflect the multi-year pathogenesis of DKD. A similar pattern was observed in the Sebha study [19], where HbA1c was linked to microalbuminuria but not to eGFR. The evaluation of glycemic and lipid profiles in Derna by other investigators [20] further indicates that metabolic disturbances beyond glucose contribute to renal risk. Almajdoub et al. [21] demonstrated that elevated copper and copper-to-zinc ratio—markers of oxidative stress and insulin resistance—were associated with poor metabolic control in Brack-Alshatti patients, reinforcing the multifactorial nature of diabetic kidney injury.

Smoking as a Potential Confounder

The higher smoking prevalence among controls (45.0% vs. 20.8%; $p = 0.026$) posed a potential confound because smoking is a recognized risk factor for renal dysfunction. However, the within-group comparisons clearly showed that eGFR did not differ significantly between smokers and non-smokers in either the diabetic group ($p = 0.241$) or the control group ($p = 0.702$). These data indicate that the between-group difference in eGFR is primarily attributable to diabetes status, not smoking. A larger sample would be needed to definitively exclude a small additive effect.

Comparison with Regional Studies

Libyan research on diabetic complications has expanded considerably in the Wadi Alshatti University Journal of Pure and Applied Sciences. Mosbah et al. [16] demonstrated that even in a young-to-middle-aged male cohort in Brack Al-Shatti, T2DM was associated with significant reductions in eGFR and with microalbuminuria. Abubaker and Eshnaf [19] showed that hypomagnesemia is prevalent in Sebha diabetic patients with microalbuminuria, while HbA1c correlated with albumin excretion but not with eGFR—exactly the pattern we observed. Almajdoub et al. [21] reported that disturbances in zinc and copper homeostasis are

associated with insulin resistance in Brack-Alshatti. Studies of metformin-related vitamin B12 deficiency in Wadi Etba [22] and superficial fungal infections in Zliten [23] illustrate the breadth of complications that accompany diabetes in Libya, and they underscore the need for comprehensive screening programs. An evaluation of HbA1c and the Atherosclerosis Index of Plasma (AIP) in Benghazi [24] found that poor glycemic control was associated with adverse lipid profiles—another pathway that can accelerate renal arteriosclerosis. Even the COVID-19 pandemic has highlighted the vulnerability of diabetic patients; a cross-sectional study in Libya [25] reported significant associations between blood glucose levels and biochemical variables including renal function markers in SARS-CoV-2-infected patients.

Finally, a study on pregnant women attending General Ubari Hospital [26] assessed hematological parameters, kidney function, and liver function, showing that pregnancy itself can alter renal function tests—a factor that must be considered when interpreting creatinine and eGFR in reproductive-age women. This reference is particularly relevant because our control group included four females, and although pregnancy was an exclusion criterion, it underscores the importance of careful demographic documentation.

The present study is the first Libyan investigation to apply the CKD-EPI 2021 equation exclusively to an outpatient T2DM cohort. The picture that emerges from the cumulative Wadi Alshatti evidence is one of widespread metabolic dysregulation, high rates of undetected end-organ damage, and the need for systematic, guideline-based screening—exactly the gap our study aims to address.

Strengths and Limitations

This is the first Libyan study to use the race-free CKD-EPI 2021 equation in a strictly outpatient T2DM population. Strengths include the use of IDMS-traceable creatinine, a focused early-detection design, and a transparent smoking subgroup analysis. Limitations include the modest sample size ($n = 97$), the significantly younger control group (which may overestimate the eGFR difference), the cross-sectional design that prevents causal inference, the absence of albuminuria measurement, and the use of convenience sampling from a single center. These factors limit generalizability to the wider Libyan population, and future multi-center prospective studies with combined eGFR and albuminuria assessment are warranted.

Conclusion

This study demonstrates that the CKD-EPI 2021 equation unmask early renal impairment in Libyan T2DM patients that would otherwise be missed by serum creatinine alone. In this cohort, 13.0% of patients had Stage 2–3 CKD despite normal creatinine. Age was the dominant predictor of eGFR decline, explaining 43% of its variance. A single HbA1c did not correlate cross-sectionally with eGFR, but glycemic control was suboptimal in 68.8% of patients—a finding that highlights the metabolic vulnerability of this population and reinforces the urgent need for intensified management.

Recommendations

Based on these findings and the broader Libyan evidence summarized above, we recommend:

1. Immediate implementation: Automatic eGFR (CKD-EPI 2021) reporting whenever a serum creatinine is ordered for a diabetic patient; this requires no additional laboratory infrastructure and zero incremental cost.

2. Age-stratified screening: Biannual eGFR and urine albumin-to-creatinine ratio for patients ≥ 60 years, annual for those aged 50–59 years, and at diagnosis for younger patients.
3. Systemic interventions: Development of a national diabetes–CKD registry, multi-center validation studies using the race-free equation, prospective cohort studies to measure actual eGFR decline rates, and cost-effectiveness analyses of routine screening.
4. Clinician and patient education: Arabic-language materials on the silent nature of DKD, and training programs for healthcare providers on KDIGO staging and eGFR interpretation.
5. Smoking and metabolic risk management: Systematic documentation of smoking status with cessation support, and routine measurement of magnesium, zinc, copper, and lipid profiles where feasible, given the emerging evidence from Libyan studies.

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