(IJUSE) 2026, Vol. No. 13, Issue 1, Jan-Dec **e-ISSN: 2454-759X, p-ISSN: 2454-7581**

Sex Differences in the Triglyceride–Glucose Index and Creatinine-Based Renal Markers Across Glycaemic Control in Type 2 Diabetes

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[1]*Date of Receiving: 30 September 2026; Date of Acceptance: 31 October 2026; Date of Publication: 17 November 2026*

Abstract

Cross-sectional comparative study was done to identify the existence of any differences between sex regarding insulin resistance and creatinine-related renal markers among T2DM patients. 150 patients (75 males, 75 females) and 75 healthy controls (38 males, 37 females) in Maysan, Iraq, were included in the study. Patients were categorized according to their HbA1c level (<7%, 7-9%, >9%). The TyG index, serum creatinine, BUN/Cr ratio and eGFR were compared using non-parametric statistical methods, two-way ANCOVA adjusted for age, multiple linear regression and ROC curve analysis. TyG was found to be significantly elevated in the patient group when compared to the control group (9.95 ± 0.69 versus 8.40 ± 0.22 for males, 9.81 ± 0.89 versus 8.37 ± 0.18 for females, $p < 0.001$) and it increased with HbA1c level ($F = 20.44$, $p < 0.001$, $\eta p^2 = 0.222$).Females with T2DM had lower serum creatinine (0.52 ± 0.18 mg/dL; group by sex interaction $p = 0.001$) and higher BUN/creatinine ratio (27.99 ± 12.04 compared to 21.58 ± 6.95 in males; $p < 0.001$); elevated BUN/creatinine ratio (> 20) was noted in 73.3% of females and in 54.7% of males (OR 2.28, 95% CI 1.15-4.52). The eGFR was mostly unchanged but positively correlated with HbA1c (B = 1.61 per 1%; $p = 0.034$), reflecting increased filtration rate. Therefore, females exhibited increased TyG gradient and low-creatinine and high-BUN/creatinine profile, which indicates reduced muscle mass. TyG above 10.6 in females indicates poor glycemic control with high specificity.

Keywords: *Diabetes Mellitus Type 2; Insulin Resistance; Triglyceride–Glucose Index; Creatinine; Glomerular Filtration Rate; Sex Characteristics*

1. Introduction

Insulin resistance is the major pathophysiological defect associated with type 2 diabetes mellitus (T2DM), with an approximate global prevalence of 537 million adults in 2021 [1]. There are sex differences in its clinical presentation, whereby women tend to present with T2DM having a heavier burden of risk factors and a reduction in their cardiometabolic advantage when compared to men [2]. Due to the unavailability of the hyperinsulinaemic-euglycaemic clamp technique in daily practice, the TyG index derived from fasting triglyceride and glucose levels was introduced [3, 4] and found to be highly correlated with insulin sensitivity obtained via clamp technique [5, 6].

It is also one of the major organs affected by the metabolic dysregulation described above. Early T2DM is associated with increased proximal sodium and glucose reabsorption, afferent vasodilation and a consequent glomerular hyperfiltration which precedes the development of albuminuria and subsequent kidney dysfunction [7, 8]. The sex differences in T2DM affect kidney complications through hormonal, haemodynamic and body composition effects [9, 10]. Body composition also influences the use of creatinine as an indicator of kidney function because serum creatinine levels depend on muscle mass [11, 12] and low creatinine was found to be connected with T2DM [13, 14].

[1] How to cite the article: Al-Hameedawi A.K.J.; (November 2026); Sex Differences in the Triglyceride–Glucose Index and Creatinine-Based Renal Markers Across Glycaemic Control in Type 2 Diabetes; *International Journal of Universal Science and Engineering*; Vol 13, 170-182

(IJUSE) 2026, Vol. No. 13, Issue 1, Jan-Dec **e-ISSN: 2454-759X, p-ISSN: 2454-7581**

Most studies on TyG have been done in general or mixed populations where diabetes has been considered as a single entity, as well as in chronic and diabetic kidney disease [16, 17]. There is a significant correlation between TyG and HbA1c in T2DM patients [18]; however, it is unknown how TyG varies depending on the increase in HbA1c in the already existing disease, and whether this difference is consistent among men and women. In addition, there are few data available on TyG in Iraqi population. In the database of more than 12,000 patients from Basrah, only 13.8% had HbA1c<7%, and being a woman was one of the factors associated with poor glycemic control [19]; TyG cut-off values for metabolic syndrome in male and female have been reported from Baghdad [20]; however, no TyG cut-off for poor glycemic control or renal function markers have been described. This study aims at comparing TyG index, serum creatinine, the ratio of BUN to creatinine, and eGFR between patients with T2DM and controls stratified by HbA1c levels and sex.

2. Materials and methods

2.1 Study design and participants

This cross-sectional comparative study, which also included control subjects, was performed at the Specialized Center for Endocrinology and Diabetes, Maysan Governorate, Iraq, during January to July 2026. T2DM patients who followed up at the Center were included in the study till 75 male and 75 female subjects were involved in the study, based on ADA criteria [21]. Seventy-five control subjects (38 male and 37 female) with fasting glucose < 100 mg/dL and HbA1c < 5.7% were also included during the same period. The exclusion criteria included type 1 or secondary diabetes, chronic kidney or liver disease, thyroid disease, pregnancy, cancer, acute illness, and recent use of nephrotoxic drugs. The number of cases was not calculated but determined by the study period, where there were 75 cases and 37-38 controls of each gender, resulting in a statistical power of 84% for detecting a standardized difference of 0.6 between patients and controls, and 86% for detecting a difference of 0.5 between men and women with T2DM ($\alpha = 0.05$ two-sided). The study conformed to the Declaration of Helsinki and was approved by Approval No. 127, Date: 22/2/2026). All participants gave written informed consent.

2.2 Laboratory measurements and derived indices

An overnight fast of 10–12 h prior to sampling, venous blood was obtained from the antecubital vein of the study subjects who were seated from 08:00 to 10:00. Two millilitres of venous blood was collected in a K2-EDTA tube for HbA1c analysis, while the rest was collected in a plain gel separator tube. The serum samples were allowed to clot for 30 min in the room temperature followed by centrifugation at 3000 rpm for 10 min. Serum samples were immediately analysed after 2 hours, but those which were found haemolysed or lipaemic were excluded from analysis. The measurement of serum glucose, TG, TC, urea and creatinine was performed with a cobas c 311 analyser (Roche Diagnostics, Mannheim, Germany) by the use of enzymatic colorimetric procedures with creatinine measured enzymatically traceable to isotope dilution mass spectrometry (IDMS).Measurement of glycated haemoglobin (HbA1c) from EDTA whole blood by fluoroimmunoassay was carried out on an ichroma™ analyzer (Boditech Med Inc., Chuncheon, Republic of Korea). Calibration of both analyzers was done based on the manufacturers' instructions. Levels of two different types of commercial control material (normal and pathological) were tested for every workday on the cobas c 311 analyzer, and only when both controls satisfied the Westgard rules (1-3s and 2-2s), results were accepted. For the ichroma™ HbA1c assay, the manufacturer's control material was tested for each day of measurement. Triglyceride – glucose (TyG) index was calculated as ln[TG (mg/dL) × glucose (mg/dL) / 2] [3, 4]. Blood urea nitrogen (BUN) was calculated by dividing the urea concentration (mg/dL) by 2.14, and the BUN/creatinine ratio was calculated as BUN divided by the serum creatinine. Calculation of eGFR was done by race-free 2021 CKD-EPI creatinine equation [22]:

$$eGFR = 142 \times \min(S_{cr}/\kappa, 1)^{\alpha} \times \max(S_{cr}/\kappa, 1)^{-1.200} \times 0.9938^{age} \times 1.012 \text{ [if female]}$$

where Scr is serum creatinine (mg/dL), κ is 0.7 for females and 0.9 for males, and α is −0.241 for females and −0.302 for males. Based on HbA1c, the patients were classified into either being "at target" (<7%) [23], "moderately controlled" (7-9%), or "poorly controlled" (>9%). For the following four cut-off values of categorization, a BUN/creatinine ratio >20; an eGFR ≥130 mL/min/1.73 m², which indicates the hyperfiltration

(IJUSE) 2026, Vol. No. 13, Issue 1, Jan-Dec **e-ISSN: 2454-759X, p-ISSN: 2454-7581**

range, a value used as a threshold despite variations in the definition of hyperfiltration [7, 8]; an eGFR <90 mL/min/1.73 m², indicating reduced filtration; and urea >45 mg/dL.

2.3 Statistical analysis

All analyses were done using IBM SPSS Statistics v26.0 (IBM Corp., Armonk, NY, USA). The Shapiro–Wilk test revealed non-normal distributions for most of the studied parameters in at least one subgroup; thus, means ± SD and medians (IQR) are presented. Comparison between groups was carried out using the Mann-Whitney U test (effect size r=|Z|/√N) and the Kruskal-Wallis test followed by Dunn's post hoc test with Bonferroni correction [24]. The group and gender effects were analyzed using two-way ANCOVA adjusting for age, with TyG as continuous and log-transformed renal markers. The effects of HbA1c stratification and gender within each patient were studied with the aid of another two-way ANCOVA adjusting for age. Correlations with HbA1c were found using Spearman's ρ. Type III sums of squares were applied; partial eta squared (ηp^2) is reported.

Comparison of categorical variables was made using the Pearson χ^2 test, or Fisher's exact test where an expected frequency was < 5; the results were presented as odds ratio (OR) with 95% confidence interval (CI). Multiple linear regression was used to establish determinants of TyG (HbA1c, sex, age, TC) and eGFR (age, sex, HbA1c, TyG); the effect modification of HbA1c slope between the sexes was evaluated through mean centered HbA1c × sex interaction; collinearity was assessed using variance inflation factor (VIF). TyG performance for classifying subjects into patients and controls, and its capability for identification of HbA1c > 9% in patients were evaluated using ROC analysis. The area under the curve (AUC) is given with 95% CI, and the optimal cut-off point was chosen by Youden index [25].

3. Results

3.1 TyG index and renal markers by group and sex

The T2DM women were significantly older than control women and T2DM men (52.6 ± 10.6 vs 42.6 ± 9.9 and 47.8 ± 12.0 years; $p < 0.001$ and $p = 0.026$; Table 1); all the between-group models, therefore, were adjusted for age. Not surprisingly, the patients had a higher fasting glucose, HbA1c, TG and TC levels than the control subjects; the glycaemic measures were comparable between male and female T2DM subjects (HbA1c 7.84 ± 1.35% vs 7.74 ± 1.45%), while the TC was a bit higher in the females. The TyG index was much higher in patients compared to the controls in both genders ($r = 0.80$ in males and 0.76 in females; ANCOVA $\eta p^2 = 0.531$) and did not differ between male and female patients (Table 2; Figure 1).

The renal biomarkers exhibited a sex-specific distribution. While serum creatinine levels were significantly reduced in diabetic females compared to female control subjects (0.52 ± 0.18 vs 0.71 ± 0.22 mg/dL; $p < 0.001$, $r = 0.40$) and male diabetic patients (0.65 ± 0.16 mg/dL; $p < 0.001$), no differences were observed between men with diabetes and male controls ($p = 0.214$); the interaction of group x sex reached statistical significance ($F = 10.91$, $p = 0.001$). No differences in urea were observed across the groups, which correlated mostly with age (ANCOVA $F = 10.82$, $p = 0.001$). This resulted in the BUN/creatinine ratio being higher in women with T2DM (27.99 ± 12.04) compared to 18.32 ± 6.41 in women in the control group ($p < 0.001$, $r = 0.46$) and 21.58 ± 6.95 in males with diabetes ($p < 0.001$). The eGFR values were also different in the study groups, showing a significant group x sex interaction ($F = 16.26$, $p < 0.001$; Table 2). For female control group, the lowest eGFR was recorded, i.e., 102.9 ± 21.6 mL/min/1.73m2, which was consistent with their highest serum creatinine, 0.71 mg/dL, among the four groups, while mean eGFR for male and female patients exceeded 110 mL/min/1.73 m2. In the case of the CKD-EPI equation, there is no need to interpret age and sex because they are already part of the equation.

(IJUSE) 2026, Vol. No. 13, Issue 1, Jan-Dec **e-ISSN: 2454-759X, p-ISSN: 2454-7581**

Table 1. Age, glycaemic and lipid profile, TyG index and renal markers by group and sex.

Variable	Control men (n = 38)	Control women (n = 37)	T2DM men (n = 75)	T2DM women (n = 75)
Age (years)	48.0 ± 10.0	42.6 ± 9.9	47.8 ± 12.0	52.6 ± 10.6
	47.0 (40.8–56.5)	43.0 (37.0–49.5)	48.0 (40.0–58.0)	53.0 (45.0–60.0)
TyG index	8.40 ± 0.22	8.37 ± 0.18	9.95 ± 0.69	9.81 ± 0.89
	8.36 (8.25–8.55)	8.33 (8.23–8.51)	9.91 (9.58–10.40)	9.63 (9.20–10.32)
Fasting glucose (mg/dL)	87.0 ± 5.2	88.4 ± 5.4	253.3 ± 103.1	216.6 ± 95.9
	88.0 (83.8–90.0)	88.0 (86.0–91.0)	254.1 (173.0–321.2)	194.6 (143.1–274.2)
HbA1c (%)	5.07 ± 0.31	5.11 ± 0.26	7.84 ± 1.35	7.74 ± 1.45
	5.10 (4.88–5.30)	5.10 (4.90–5.30)	7.80 (6.80–8.90)	7.40 (6.80–8.50)
Triglycerides (mg/dL)	105.0 ± 25.8	99.4 ± 19.0	200.8 ± 103.6	226.1 ± 165.8
	97.5 (89.0–121.5)	93.0 (85.5–109.0)	182.6 (122.2–245.2)	166.6 (122.5–265.1)
Total cholesterol (mg/dL)	159.5 ± 9.3	162.0 ± 7.8	186.3 ± 41.3	201.4 ± 62.1
	161.0 (151.5–166.2)	164.0 (154.0–169.0)	187.2 (156.8–216.1)	202.5 (160.9–232.0)
Urea (mg/dL)	24.89 ± 6.19	25.95 ± 6.65	28.74 ± 8.30	28.00 ± 8.42
	24.50 (19.75–28.00)	24.00 (20.50–32.00)	27.85 (22.40–33.30)	26.43 (22.42–32.07)
Serum creatinine (mg/dL)	0.69 ± 0.18	0.71 ± 0.22	0.65 ± 0.16	0.52 ± 0.18
	0.70 (0.57–0.79)	0.69 (0.54–0.86)	0.65 (0.51–0.77)	0.50 (0.37–0.66)
BUN/creatinine ratio	18.22 ± 6.91	18.32 ± 6.41	21.58 ± 6.95	27.99 ± 12.04
	16.94 (12.73–22.25)	16.99 (14.47–20.19)	21.37 (16.44–24.83)	25.89 (19.75–34.17)
eGFR (mL/min/1.73 m²)	115.5 ± 15.4	102.9 ± 21.6	118.2 ± 13.6	112.5 ± 15.1
	116.7 (105.6–124.2)	111.1 (86.3–119.9)	117.7 (109.1–124.4)	113.1 (103.4–122.0)

Values are mean ± SD (first line) and median (IQR) (second line). BUN, blood urea nitrogen; eGFR, estimated glomerular filtration rate (CKD-EPI 2021); HbA1c, glycated haemoglobin; IQR, interquartile range; TC, total cholesterol; TG, triglycerides.

Table 2. Sex-stratified Mann–Whitney comparisons and age-adjusted two-way ANCOVA.

Variable	Mann–Whitney U, p (r)			Two-way ANCOVA, F; p; ηp²		
	T2DM vs controls, men	T2DM vs controls, women	T2DM men vs women	Group	Sex	Group × sex
TyG index	<0.001 (0.80)	<0.001 (0.76)	0.091 (0.14)	249.42; <0.001; 0.531	0.78; 0.377; 0.004	0.19; 0.665; 0.001
Urea	0.014 (0.23)	0.226 (0.11)	0.512 (0.05)	3.22; 0.074; 0.014	0.03; 0.863; 0.000	2.50; 0.115; 0.011

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Variable	Mann–Whitney U, p (r)			Two-way ANCOVA, F; p; ηp²					
	T2DM vs controls, men	T2DM vs controls, women	T2DM men vs women	Group		Sex		Group × sex	
Serum creatinine	0.214 (0.12)	<0.001 (0.40)	<0.001 (0.36)	19.57; <0.001; 0.082		6.94; 0.031	0.009;	10.91; 0.047	0.001;
BUN/creatinine ratio	0.009 (0.25)	<0.001 (0.46)	<0.001 (0.29)	28.33; <0.001; 0.114		6.13; 0.027	0.014;	2.93; 0.013	0.088;
eGFR	0.516 (0.06)	0.064 (0.18)	0.027 (0.18)	28.21; <0.001; 0.114		25.91; <0.001; 0.105		16.26; <0.001; 0.069	

ANCOVA adjusted for age (df = 1, 220); TyG on the original scale and renal markers log-transformed. r = |Z|/√N; ηp², partial eta squared.

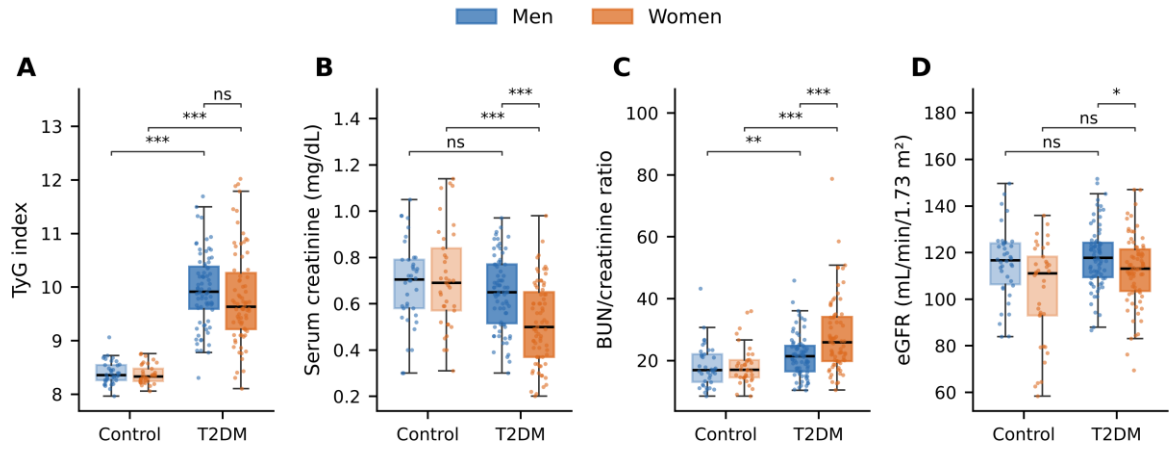


Figure 1. TyG index (A), serum creatinine (B), BUN/creatinine ratio (C) and eGFR (D) by group and sex. Boxes show the median and IQR, whiskers 1.5 × IQR and dots individual participants; lighter boxes are controls. Brackets show Mann–Whitney results: ***p < 0.001, **p < 0.01, *p < 0.05; ns, not significant.

3.2 Prevalence of renal patterns

BUN/creatinine ratio > 20 was seen in 64.0% of patients and 32.0% of controls (OR 3.78, 95% CI 2.10–6.81; p < 0.001). In the patient group, it occurred more often in females than in males (73.3% vs 54.7%; OR 2.28, 95% CI 1.15–4.52; p = 0.017); while in the control group the percentages were 27.0% and 36.8% (Table 3), respectively. Lower eGFR (< 90 mL/min/1.73 m²) was rare (2.7% in males and 6.7% in females), and the eGFR hyperfiltration range was observed in 17.3% of males and 10.7% of females (p = 0.239).

Table 3. Renal patterns in patients with T2DM by sex.

Criterion	Men, n (%)	Women, n (%)	χ^2	p	OR (95% CI), women vs men
BUN/creatinine ratio > 20	41 (54.7)	55 (73.3)	5.67	0.017	2.28 (1.15–4.52)
eGFR ≥ 130 mL/min/1.73 m²	13 (17.3)	8 (10.7)	1.38	0.239	0.57 (0.22–1.47)
eGFR < 90 mL/min/1.73 m²	2 (2.7)	5 (6.7)	1.35	0.442[a]	2.61 (0.49–13.88)
Urea > 45 mg/dL	5 (6.7)	4 (5.3)	0.12	1.000[a]	0.79 (0.20–3.06)

[a] Fisher's exact test (expected count < 5). OR, odds ratio; CI, confidence interval.

(IJUSE) 2026, Vol. No. 13, Issue 1, Jan-Dec **e-ISSN: 2454-759X, p-ISSN: 2454-7581**

3.3 TyG and renal markers across HbA1c strata

The stratification of HbA1c levels did not differ between the genders (χ^2 p = 0.806). TyG index positively correlated with worsening glycaemic control in both genders (Table 4; Figure 2), with the strong effect of the stratum after the adjustment for age (F = 20.44, p < 0.001, ηp^2 = 0.222; Table 5). The correlation was stronger in women: from median 9.34 in HbA1c < 7% to 10.83 in HbA1c > 9%, compared to 9.64 to 10.19 in men, although the interaction term sex by stratum did not reach the statistical significance (p = 0.075). Post hoc tests showed that in men TyG index increased in the < 7% to higher strata and did not change significantly beyond 9% (7-9% vs > 9%, p = 0.715), whereas in women the increase continued in the highest stratum (7-9% vs > 9%, p = 0.031).

For women, the BUN-to-creatinine ratio increased with increasing severity (means for strata were 19.86, 26.67 and 30.14; p = 0.005), but not for men (p = 0.119); age adjusted stratum effect on all patients was significant (F = 9.07, p < 0.001, ηp^2 = 0.113). For all patients, creatinine level was reduced (ρ = −0.20, p = 0.013) and the eGFR was increased (ρ = 0.25, p = 0.002) by HbA1c; the latter relationship was strongest for men (ρ = 0.32, p = 0.005).

Table 4. TyG index and renal markers across HbA1c strata in patients with T2DM: median (IQR).

Variable	Sex	HbA1c < 7%	HbA1c 7–9%	HbA1c > 9%	Kruskal–Wallis p	Spearman ρ with HbA1c (p)
TyG index	Men	9.64 (9.04–9.95)	10.09 (9.66–10.51)	10.19 (9.88–10.47)	0.004	0.41 (<0.001)
	Women	9.34 (9.00–9.59)	9.72 (9.34–10.23)	10.83 (9.68–11.81)	<0.001	0.46 (<0.001)
Serum creatinine (mg/dL)	Men	0.68 (0.62–0.84)	0.65 (0.47–0.72)	0.56 (0.50–0.70)	0.073	−0.29 (0.011)
	Women	0.57 (0.49–0.70)	0.46 (0.33–0.64)	0.46 (0.36–0.66)	0.218	−0.20 (0.080)
BUN/creatinine ratio	Men	19.67 (12.68–23.64)	21.94 (17.91–25.06)	19.62 (17.42–25.34)	0.119	0.21 (0.068)
	Women	19.86 (16.58–27.14)	26.67 (22.40–35.69)	30.14 (19.93–38.97)	0.005	0.28 (0.015)
eGFR (mL/min/1.73 m²)	Men	112.9 (105.6–122.6)	119.6 (111.6–125.2)	123.8 (116.3–136.4)	0.065	0.32 (0.005)
	Women	111.2 (102.1–119.2)	112.8 (102.3–124.4)	114.5 (108.0–122.3)	0.644	0.18 (0.116)

Men: n = 24, 40 and 11; women: n = 23, 38 and 14 in the three strata, respectively. Dunn–Bonferroni pairwise comparisons (< 7% vs 7–9%, < 7% vs > 9%, 7–9% vs > 9%): TyG in men, p = 0.023, 0.008 and 0.715; TyG in women, p = 0.037, < 0.001 and 0.031; BUN/creatinine ratio in women, p = 0.005, 0.077 and 1.000.

Table 5. Two-way ANCOVA of HbA1c stratum and sex in patients with T2DM, adjusted for age.

Outcome	HbA1c stratum, F(2, 143); p; ηp^2	Sex, F(1, 143); p; ηp^2	Stratum × sex, F(2, 143); p; ηp^2	Age, F(1, 143); p; ηp^2
TyG index	20.44; <0.001; 0.222	0.12; 0.729; 0.001	2.64; 0.075; 0.036	0.08; 0.784; 0.001
ln serum creatinine	3.83; 0.024; 0.051	19.42; <0.001; 0.120	0.05; 0.949; 0.001	0.34; 0.560; 0.002

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Outcome	HbA1c stratum, F(2, 143); p; ηp²	Sex, F(1, 143); p; ηp²	Stratum × sex, F(2, 143); p; ηp²	Age, F(1, 143); p; ηp²
ln BUN/creatinine ratio	9.07; <0.001; 0.113	10.24; 0.002; 0.067	0.56; 0.574; 0.008	7.64; 0.006; 0.051
ln eGFR	2.17; 0.118; 0.029	1.33; 0.252; 0.009	0.08; 0.926; 0.001	83.36; <0.001; 0.368

Type III sums of squares; ηp², partial eta squared.

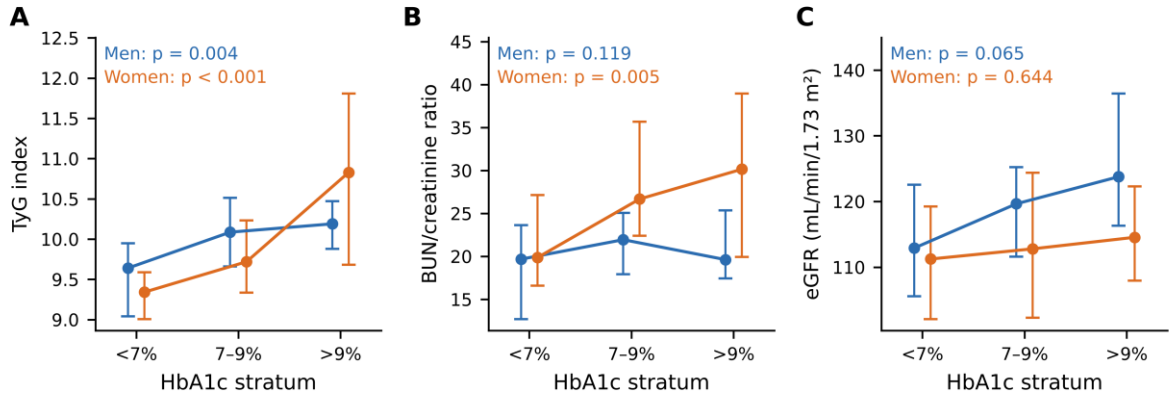


Figure 2. TyG index (A), BUN/creatinine ratio (B) and eGFR (C) across HbA1c strata in men (blue) and women (orange) with T2DM. Points show the median and bars the IQR; p values are from the Kruskal–Wallis test within each sex.

3.4 Independent determinants of TyG and eGFR

In patients, TyG increased by 0.252 per 1% rise in HbA1c (95% CI 0.173–0.331; p < 0.001) and with TC, independently of sex and age (R^2 = 0.304; Table 6). The HbA1c slope was 0.296 (95% CI 0.180–0.412) in women and 0.199 (0.089–0.309) in men, but the interaction was not significant (p = 0.174). After adjustment for age, sex and TyG, eGFR increased by 1.61 mL/min/1.73 m² per 1% HbA1c (95% CI 0.12–3.09; p = 0.034), whereas TyG itself was not associated with eGFR (Table 7); the age coefficient mainly reflects the age term built into the CKD-EPI equation.

Table 6. Multiple linear regression of the TyG index in patients with T2DM (n = 150).

Predictor	B	SE	95% CI	β	p	VIF
Constant	7.1508	0.4516	6.2582 to 8.0434	–	<0.001	–
HbA1c (%)	0.2518	0.0400	0.1728 to 0.3309	0.444	<0.001	1.04
Male sex (ref. female)	0.1608	0.1133	−0.0630 to 0.3847	0.102	0.158	1.07
Age (years)	−0.0008	0.0049	−0.0104 to 0.0089	−0.011	0.878	1.05
Total cholesterol (mg/dL)	0.0037	0.0011	0.0016 to 0.0058	0.251	0.001	1.05

R^2 = 0.304; adjusted R^2 = 0.285; F(4, 145) = 15.87, p < 0.001. Interaction model (HbA1c mean-centred): HbA1c × male sex B = −0.108, SE = 0.079, p = 0.174. Sex-specific HbA1c slopes (women 0.296; men 0.199) were estimated in separate models for each sex adjusted for age and TC, so their difference does not equal the interaction coefficient exactly. B, unstandardised coefficient; β, standardised coefficient; VIF, variance inflation factor.

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Table 7. Multiple linear regression of eGFR in patients with T2DM (n = 150).

Predictor	B	SE	95% CI	β	p	VIF
Constant	145.0110	12.4254	120.4528 to 169.5693	–	<0.001	–
Age (years)	−0.7747	0.0813	−0.9353 to −0.6141	−0.613	<0.001	1.05
Male sex (ref. female)	1.8553	1.8696	−1.8398 to 5.5505	0.064	0.323	1.05
HbA1c (%)	1.6097	0.7515	0.1244 to 3.0949	0.154	0.034	1.32
TyG index	−0.4289	1.3273	−3.0524 to 2.1945	−0.023	0.747	1.32

$R^2 = 0.431$; adjusted $R^2 = 0.415$; $F(4, 145) = 27.45$, $p < 0.001$.

3.5 Diagnostic performance of TyG

The TyG test classified the patients against the control group with an area under the curve (AUC) of 0.979 (95% CI 0.961–0.997) at a cutoff of 8.76 (Table 8, Figure 3). This is because TyG incorporates glucose, and the controls have been selected based on their normal glucose values. In patients, the TyG test identified HbA1c> 9% with an AUC of 0.806 (0.658–0.953) in women and a cut off of 10.59, with a sensitivity of 64.3% and specificity of 88.5%.

Table 8. ROC analysis of the TyG index.

Discrimination task	Subgroup	AUC (95% CI)	Cut-off (Youden)	Sensitivity (%)	Specificity (%)
T2DM vs controls	All	0.979 (0.961–0.997)	8.76	96.0	98.7
	Men	0.988 (0.970–1.000)	8.75	98.7	97.4
	Women	0.971 (0.940–1.000)	8.76	93.3	100.0
HbA1c > 9% within T2DM	All	0.762 (0.659–0.865)	9.82	84.0	59.2
	Men	0.692 (0.556–0.828)	9.81	100.0	48.4
	Women	0.806 (0.658–0.953)	10.59	64.3	88.5

AUC, area under the curve; CI, asymptotic 95% confidence interval.

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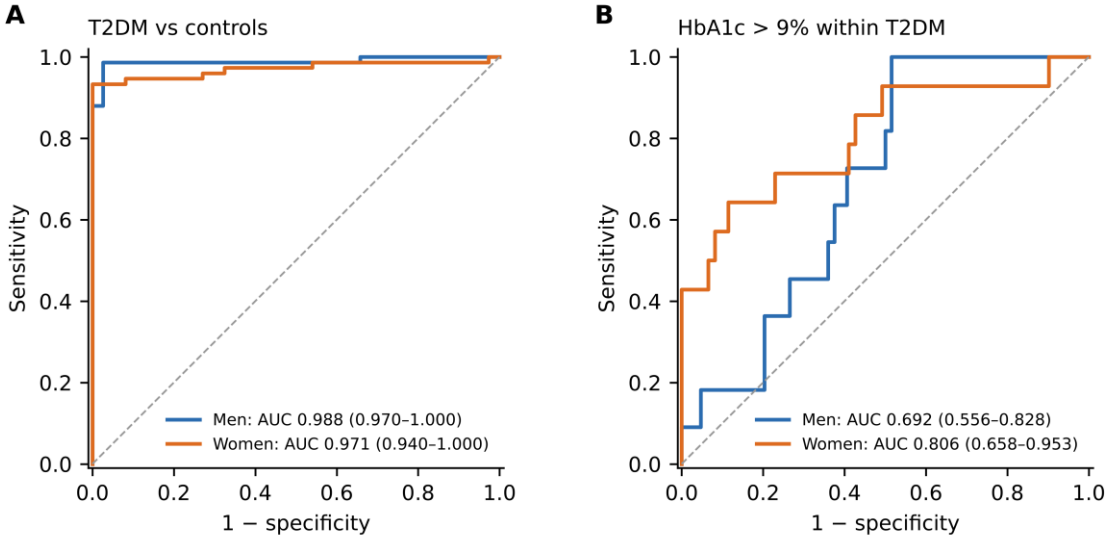


Figure 3. ROC curves of the TyG index in men and women for distinguishing patients with T2DM from controls (A) and for identifying HbA1c > 9% among patients (B). AUC values are given with 95% CI.

4. Discussion

Three sex-specific associations were found regarding sex characteristics in patients with T2DM. Female subjects had a steeper slope for TyG according to the glycemic categories, the lowest serum creatinine levels and the highest BUN/creatinine ratio, whereas in both sexes an increase in eGFR correlated positively with HbA1c.

The TyG index was created as an approximation of clamp-determined insulin resistance [3, 5], and in the current study, it followed the trend of the glycemic state in both males and females as it was previously described in T2DM [18]. Since TyG is a combination of glucose and triglyceride components, the steeper slope among females could be explained by a greater importance of the second one, taking into account existing sex differences in lipoprotein metabolism [26] and the worsening of lipids profile during the menopause transition [27]. It might be a reason why the TyG index detected poor glycemic control better in female (AUC 0.806) than in male patients (0.692). Clinically, in a female patient with T2DM, a high TyG level of more than 10.6 suggested the presence of poor control with a specificity of 88.5%.A near-total differentiation of the two groups cannot be overstated due to the role of glucose in the index.

Urea levels did not differ between the groups, so the BUN/creatinine ratio was elevated in females with T2DM because of low creatinine. Creatinine is a product of skeletal muscle, and low serum creatinine level indicates low muscle mass [11, 12], which has been linked to T2DM in the cohort studies and a meta-analysis [13, 14]. The skeletal muscle is the primary location for insulin-mediated glucose uptake [28], and low muscle mass and T2DM complement each other [29], which explains the finding. Thus, the ratio > 20 in such patients is not a reliable indicator of pre-renal azotaemia. The increased BUN/creatinine ratio could be caused by volume depletion, osmotic diuresis, and protein catabolism [15], yet low muscle mass is the easiest cause to consider and measure directly.

The prevalence rates for eGFR < 90 mL/min/1.73 m² were 4.7%, and that of hyperfiltration was 14.0%; in addition, there was an increase in eGFR by 1.6 per 1% increment in HbA1c regardless of age and TyG. This tendency fits into the pattern of hyperfiltration of glucose in early diabetic kidney disease [7, 8]. TyG was not related to eGFR, while the association between elevated TyG and development of CKD has been demonstrated in cohort studies [17]; the association of such type could hardly be demonstrated in patients with filtration largely preserved. The low muscle mass is associated with the overestimation of creatinine-based eGFR; the lack of relation between eGFR and HbA1c in women could also be due to their low creatinine concentration. The

(IJUSE) 2026, Vol. No. 13, Issue 1, Jan-Dec **e-ISSN: 2454-759X, p-ISSN: 2454-7581**

evaluation of cystatin C-based eGFR and albuminuria recommended currently [22, 30] would clarify both points; the sex mechanisms of diabetic kidney disease have been recently reviewed [9, 10].

Since all of these indices are obtained through standard fasting testing, their results can be used in a normal practice setting; for instance, elevated TyG in a T2DM patient may mean poor glycemic control without HbA1c being checked each time, while low creatinine along with the ratio of BUN to creatinine greater than 20 must point to evaluating muscle mass and nutrition.

5. Conclusion

Among T2DM patients in Maysan, Iraq, women had a stronger TyG gradient in terms of their glycaemic control and exhibited low creatinine levels with a high BUN-to-creatinine ratio, whereas eGFR showed an increasing trend relative to HbA1c in a pattern of hyperfiltration in both men and women. The value of TyG above 10.6 was found to be a marker of poor glycaemic control among women with good specificity using the same blood test for lipids and glucose levels.

Outcomes of the study

TyG rose with HbA1c more steeply in women than in men, and a value above about 10.6 identified women with HbA1c > 9% with a specificity of 88.5%. Women with T2DM had a low-creatinine, high-BUN/creatinine profile, and eGFR increased with HbA1c in both sexes. Routine glucose, lipid and renal results are therefore better interpreted separately for men and women.

Study limitations

This single centre, cross-sectional study does not allow for any causal inference, and the results might not be applicable to other regions of Iraq. The variables albuminuria, cystatin C, body composition, body mass index, menopausal status, duration of diabetes and diabetes medications (SGLT2 inhibitors, metformin, statins and diuretics that affect creatinine, urea and lipid levels) were not measured. Women with T2DM had an older mean age than control women, and there might have been age bias even after adjusting for it. Only 25 patients had HbA1c above 9% (11 men, 14 women); therefore, the ROC curve estimates in this subgroup are unreliable, and further validation is needed for 10.6 cut-off point. Many comparisons were done without correcting for multiple comparisons, thus these analyses are exploratory. Finally, TyG is only a surrogate measure; fasting insulin, HOMA-IR or clamp data were not available.

Study rationale

Glucose, triglycerides, urea and creatinine are routinely assessed at low cost in the Iraqi diabetes clinics where there is often poor glycaemic control [19], and where insulin, cystatin C and body composition analysis are rarely performed. Differences in the behaviour of these variables according to gender could result in an inappropriate cut-off value which would either exclude women with poor glycaemic control or incorrectly assess their renal function; the aim of this study is to define these differences in the local population.

Acknowledgements:

The author would like to thank the medical and laboratory staff of the Specialized Center for Endocrinology and Diabetes in Maysan for their assistance during recruitment and sample analysis.Declarations

Ethics approval and consent to participate: This research was approved by the Institutional Ethics Committee, College of Science, University of Maysan, Iraq (Approval No. 127, Date: 22/2/2026). The research followed the principles of the Declaration of Helsinki (2013 amendment), and other guidelines concerning ethics. All subjects gave written informed consent for participation in the study after being explained its aim and purpose, ensuring total confidentiality of the data.

(IJUSE) 2026, Vol. No. 13, Issue 1, Jan-Dec **e-ISSN: 2454-759X, p-ISSN: 2454-7581**

Data availability: De-identified data are available from the corresponding author on reasonable request.

Funding: This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Conflicts of interest: The author declares no conflicts of interest.

Author contributions: Abbas Kadhim Jiheel Al-Hameedawi: conceptualisation, methodology, investigation, data curation, formal analysis, visualisation, writing – original draft, and writing – review and editing. The author read and approved the final manuscript.

Abbreviation List

ANCOVA, analysis of covariance; AUC, area under the curve; BUN, blood urea nitrogen; CI, confidence interval; CKD, chronic kidney disease; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; eGFR, estimated glomerular filtration rate; HbA1c, glycated haemoglobin; HOMA-IR, homeostasis model assessment of insulin resistance; IDMS, isotope dilution mass spectrometry; IQR, interquartile range; OR, odds ratio; ROC, receiver operating characteristic; SD, standard deviation; SGLT2, sodium–glucose cotransporter 2; T2DM, type 2 diabetes mellitus; TC, total cholesterol; TG, triglycerides; TyG, triglyceride–glucose; VIF, variance inflation factor.

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