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Research Article

Comparative Analysis of Renal Function and Lipid Profile in Diabetic Patients Across Gender, Age, and Glycemic Control: A Cross-sectional Study in Basrah, Iraq

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Abstract
Background: Poor glycemic control adversely affects lipid and renal function; however, the modifying roles of age and sex have not been sufficiently characterized, particularly among Middle Eastern countries. ***Objective***: To evaluate the associations between glycemic control and renal and lipid biomarkers in adults with type 2 diabetes (T2DM) and characterize the independent and combined modulating effects of age and sex. ***Methods***: A cross-sectional comparative study was conducted during 12 months on 4767 subjects attending an outpatient clinic in Basrah, Iraq (4421 with diabetes and 346 with prediabetes). They were grouped according to glycemic control (good: HbA1c<7.0%, suboptimal: 7.0-8.9%, poor: ≥9.0%), age (<40, 40-59, ≥60 years), and gender. Renal function and lipid indexes were analyzed using rank-based tests and regression analysis. ***Results***: Median levels of urea, creatinine, low-density lipoprotein, and triglycerides were significantly higher in the poorly controlled group, whereas HDL levels were lower (p<0.001). Aging is directly related to kidney injury, mainly reduction in eGFR, while male sex is associated with a more atherogenic lipid profile and higher values of renal biomarkers. Multivariate analysis revealed that the impact of age and sex might be disproportionate to, if not greater than, that of HbA1c. ***Conclusions***: In T2DM, the relationship between renal and lipid abnormalities is sex asymmetrical, age-dependent, and glycemic-control-influenced. A personalized, demography-integrated strategy for complication assessment should be adopted to improve diabetic care.
Keywords: Diabetes mellitus; Diabetic nephropathies; Dyslipidemias; Glycated hemoglobin A.

دراسية تحليلية مقارنة لوظائف الكلى والملف الدهني لدى مرضى السكري تبعًا للجنس والعمر ومستوى السيطرة على سكر الدم

الخلاصة
الخلفية: يُعدّ داء السكري مرضًا استقلابيًا مزمنًا وأحد الأسباب الرئيسة للمراضة والوفيات عالميًا. يؤثر ضعف السيطرة السكرية سلبًا في مستويات الدهون ووظائف الكلى، إلا أن الأدوار المعدِّلة للعمر والجنس لم تُوصَف بشكل كافٍ، لاسيما في مجتمعات الشرق الأوسط. **الهدف**: تقييم العلاقة بين السيطرة السكرية والمؤشرات الحيوية الكلوية والدهنية لدى البالغين المصابين بداء السكري من النوع الثاني، مع توصيف التأثيرات المعدِّلة المستقلة والمجتمعة لكل من العمر والجنس. **الطرائق**: أُجريت هذه الدراسة المقطعية المقارنة لمدة اثنا عشر شهرًا على 4767 مراجعًا لعيادة خارجية في البصرة، العراق (4421 مصابًا بالسكري و346 في مرحلة ما قبل السكري). تم تصنيف المشاركين وفق مستوى السيطرة السكرية والعمر والجنس. تم تحليل مؤشرات وظائف الكلى والملف الدهني باستخدام اختبارات الرتب والتحليل الانحدار. **النتائج**: كانت القيم الوسيطة لليوريا والكرياتينين والبروتين الدهني منخفض الكثافة والدهون الثلاثية أعلى بشكل معنوي في مجموعة السيطرة الضعيفة، في حين كانت مستويات البروتين الدهني عالي الكثافة أقل (p<0.001). ارتبط التقدم في العمر مباشرةً بحدوث إصابة كلوية، خاصة بانخفاض معدل الترشيح الكبيبي المقدر، بينما ارتبط الجنس الذكري بملف دهني أكثر ميلاً لتصلب الشرايين وقيم أعلى للمؤشرات الكلوية. وأظهر التحليل متعدد المتغيرات أن تأثير العمر والجنس قد يكون مساويًا، إن لم يكن أكبر، من تأثير مستويات السيطرة سكر الدم. **الاستنتاجات**: في داء السكري من النوع الثاني، تتسم العلاقة بين اضطرابات الكلى والدهون بعدم تماثل بين الجنسين، واعتمادها على العمر، وتأثرها بمستوى السيطرة السكرية. ويوصى باعتماد استراتيجية تقييم مخصصة ومتكاملة مع الخصائص الديموغرافية لتحسين رعاية مرضى السكري.

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INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic disease in which the glucose level in the blood is high, either because the pancreas does not produce enough insulin or cells do not respond to the insulin produced [1,2]. Globally, the prevalence of DM continues to rise every year because of population growth, urbanization, physical inactivity, and obesity [3,4]. Beyond dysregulation of glucose metabolism, diabetes mellitus contributes to many other complications, such as lipid abnormalities and kidney dysfunction that predispose the patient to the sustained risk of chronic kidney disease (CKD) and cardiovascular diseases (CVD) [5,6]. Dyslipidemia is often associated with abnormal glucose metabolism and is usually defined by high serum levels of triglycerides (TG) and low-density lipoprotein (LDL) and reduced high-density lipoprotein (HDL) [7,8]. The dysregulated profile is attributed to insulin abnormality, disturbing lipid metabolism by increasing the flux of free fatty acid between tissues, as well as TG synthesis in the liver [9,10], thereby accelerating atherosclerosis and worsening the prognosis of diabetic patients [11]. Diabetic kidney disease (DKD) is one of the most common and substantial microvascular complications of DM and is a leading global cause of chronic kidney disease (CKD). Despite its prevalence, it has a silent

course with minimal clinical indices until end-stage renal damage has already occurred. Persistent hyperglycemia triggers the initiation and perpetuation of renal injury through complicated hemodynamic and metabolic pathways related to free radicals, advanced glycation end products, and stimulation of the renin-angiotensin system, resulting in progressive structural changes through increasing the thickness of the glomerular basement membrane and mesangial expansion, reflected clinically by raised albumin in the urine with an eventual reduction in glomerular filtration and increased urea and creatinine levels, emphasizing the importance of monitoring renal function among diabetic patients [12,13]. Several studies have reported that poor glycemic control, as presented by the hemoglobin A1c (HbA1c) level, is significantly correlated with the deterioration of lipid and renal function, whereas adequate glycemic control decelerates complications [14]. However, the extent to which age and sex can affect these complications has not been adequately defined [15-20]. Although the preceding studies have explored the relationships between glycemic status and metabolic markers, many of these studies have been limited by small sample sizes, binary categorization of glycemic control, and a focus on single outcome evaluations of either lipid or renal parameters; isolated demographic contributions have been examined without considering their collective influence. The current study aims to evaluate the associations between glycemic control and renal and lipid biomarkers in adults with type 2 diabetes (T2DM) and characterize the independent and combined modulating effects of age and sex.

METHODS

Study design and participants

This was a 1-year cross-sectional comparative study carried out between October 2024 and October 2025 in an outpatient clinic in Basra City/Iraq. The study looked at the kidney and lipid profiles of 4421 adults with type 2 diabetes and of 346 adults with prediabetes who were being followed up in routine visits. Patients aged 18 years or older with a diagnosis of T2DM for more than 6 months were eligible, while those with type I or gestational diabetes, end-stage renal failure on renal replacement therapy, primary dyslipidemia, acute illness, and recent hospital admission were excluded. The participants were categorized according to glycemic control based on HbA1c values as follows: good control (< 7.0%), suboptimal control (7.0-8.9%), and poor control (≥ 9.0%). Age was stratified into three categories (< 40, 40-59, and ≥ 60 years). Diabetic individuals were also stratified by sex (2649 females and 1772 males).

Sample collection and laboratory measurement

The data collected included demographic data (age, sex); glycemic control data (glycated hemoglobin (HbA1c) and randomly measured blood sugar); renal functions (serum creatinine, urea, and eGFRs); and lipid profiles (total cholesterol (TC), TG, LDL, and HDL). Four milliliters of venous blood were collected per participant via the standard phlebotomy procedure and then transferred into sterile vacutainer gel- and ethylenediaminetetraacetic acid (EDTA)-containing tubes. The gel tubes were allowed to clot at room temperature and then centrifuged at 4000 rpm for approximately 5 minutes using the ROTOFIX 32A centrifuge (Andreas Hettich GmbH & Co.KG, Tutt Lingen, Germany). The lipid indicators were measured via enzymatic colorimetric assays (homogeneous for LDL & HDL), such as for the glucose enzymatic hexokinase method, using the commercial reagent kit supplied by Roche Diagnostics (GmbH, Mannheim, Germany) on the COBAS Integra 400 PLUS analyzer (Roche Diagnostics). The D-10TM system, an ion-exchange high-performance liquid chromatography (HPLC) from Bio-Rad Laboratories, Inc., Hercules, CA, US, was employed for HbA1c measurement in a whole blood sample. The level of albumin in urine was not routinely measured in an outpatient setting during the study period. Therefore, the albumin-to-creatinine ratio was not included; renal function was assessed via serum urea, creatinine, and the estimated glomerular filtration rate (eGFR). The CKD-EPI 2021 creatinine-based equation was applied for GFR estimation, adjusted for sex and age without race correction, to account for possible overestimation of kidney function at extremely low creatinine levels, particularly in women with low muscle mass. eGFRs were cautiously reviewed in the hyperfiltration range. All the instruments were used according to the manufacturer's instructions, with quality control procedures performed as recommended to ensure accurate results.

Clinical variables

Body mass index (BMI), blood pressure (BP), and smoking status data were gathered from the patients' clinical records at the time of visit. BMI was calculated from the measured body weight and height and is expressed as kg/m², with obesity defined as a BMI ≥30 kg/m². Blood pressure readings were obtained from the most recent resting measurement documented at the same visit; hypertension was defined as a systolic pressure ≥140 mmHg and diastolic blood pressure ≥90 mmHg or a previously documented diagnosis of hypertension. Self-reports were used to determine smoking status. Clinical data, such as the duration of diabetes and the use of lipid-lowering agents, were not consistently documented in the outpatient records.

Ethical considerations

The study protocol was approved by the Institutional Review Board of Al-Zahraa College of Medicine, University of Basrah (Number: E/T/64). All participants gave written, informed consent before participation, as approved by the review board, and in line with local regulations.

Statistical analysis

Data analysis was done using SPSS software version 31 (IBM Corp., NY, USA). Continuous variables are presented as medians because of their non-normal distribution, and frequencies and percentages are reported for categorical variables. Group comparisons were performed via the Mann–Whitney U test and the Kruskal–Wallis H test, followed by a post hoc pairwise comparison test. In addition to demographic and biochemical data, selected clinical variables (BMI, BP, and smoking) were available for only a subset of participants and, therefore, were not included in the adjusted analysis. Those variables were presented descriptively in the table where available. Following the initial comparative analysis, multivariable association was tested using a Gamma generalized linear model; accordingly, the regression analysis was limited to age, sex, and HbA1c as predictors, which were available for the entire study population. Multivariate analysis of covariance (MANCOVA) was conducted to evaluate the combined influence of metabolic and demographic factors on renal and lipid parameters. For descriptive purposes, the percentage of patients with low eGFR (< 60 ml/min/1.73 m²) was calculated across glycemic control classes. A *p*-value less than 0.05 was regarded as statistically significant.

RESULTS

The study population encompassed 4421 diabetics and 346 prediabetic patients. The mean age was comparable between the two groups, with an average of 55 years in diabetic patients and 53 years in prediabetic patients, with a female predominance in both groups (Table 1).

Table 1: Demographic and biochemical characteristics of participants

Variable	Diabetic (n=4421)	Pre-Diabetic (n=346)
Age (years)	55(15)	53(16)
Female gender	2649(59.72)	222(64.16)
Male gender	1772 40.27)	124(35.8)
Urea (mg/dL)	30.69(14.61)	28.775(12.23)
Creatinine (mg/dL)	0.76 (0.32)	0.74(0.262)
HDL-cholesterol (mg/dL)	41.92(14.75)	44.85(11.15)
LDL-cholesterol (mg/dL)	81.60(57.71)	80.305(51.552)
Total Cholesterol (mg/dL)	149.86(65.18)	142.38(59.51)
Triglyceride (mg/dL)	158.38(125)	127.9(109.98)
Hemoglobin A1c (%)	8.00(2.6)	6.0(0.4)
Glucose (mg/dL)	191.20(137.93)	130.14(31.13)
eGFR mL/min/1.73 m²	95(27.1)	101(19.8)

Data are presented as the median (interquartile range; IQR) or number (%); eGFR, estimated glomerular filtration rate.

Compared with prediabetics, diabetic participants presented higher median TG and total cholesterol values, whereas HDL values were lower. However, renal function markers were modestly different, with diabetic individuals having slightly lower median eGFRs than prediabetic individuals. Subgroups were formed with respect to glycemic control, sex, and age to explore the potential differences in lipid and renal indicators among the diabetic population. This stratification is also clinically meaningful since it was intended to reveal patterns that might be used to guide more individualized and effective approaches for the management of diabetes, which may improve the long-term outcomes of diabetes management. Based on glycemic status, the diabetic patients were categorized as group I (good control; HbA1c < 7%), group II (suboptimal; HbA1c 7-8.9%), and group III (poor control; HbA1c ≥ 9%), to investigate the influence of the severity of hyperglycemia on organ and metabolic functions. Since the data were skewed, a nonparametric Kruskal–Wallis H test was applied. The results revealed significant differences in all metabolic and renal parameters (Kruskal–Wallis H test, $p < 0.05$ for all) (Table 2).

Table 2: Comparison of biochemical parameters across glycemic control groups

Variable	Group I (n=976)	Group II (n=1928	Group III (n=1517)	Prediabetic (n=346)	*p*-value
Age	55	56	53	53	< 0.001
Urea	30.47	31.66	35.92	28.98	< 0.001
Creatinine	0.75	0.77	0.80	0.74	0.0153
HDL cholesterol	43.18	42.39	40.36	43.74	< 0.001
LDL cholesterol	70.8	75.59	103.16	80.59	< 0.001
Total cholesterol	135.82	143.82	173.76	142.59	< 0.001
Triglyceride	129.72	150.48	189.7	129.8	< 0.001
HbA1c	6.5	7.8	10.4	6	< 0.001
Glucose	131.57	175.64	292.82	127.41	< 0.001
eGFR	101.1	100.0	95	102.0	< 0.001
Low eGFR (%)	5.3	9.4	8.0	1.7	
Current smoker (%)	9.4	10.4	16.0	7.6	
Obesity (%)	30.3	40.0	54.9	27.0	
Hypertension (%)	40.9	54.6	73.6	35.5	
Female (%)	63.0	59.6	58.3	63.9	
Male (%)	37.0	40.4	41.7	36.1	

Data are presented as median or percentage. Kruskal–Wallis test with post hoc pairwise comparisons. Percentages were calculated using the number of participants with available data.

Patients with poor control had the highest median values of TG, LDL, and total cholesterol compared to those with good and suboptimal control and prediabetes. HDL cholesterol showed a decreasing trend as the control worsened. Although median eGFR values were relatively close among the groups, the percentage of individuals with low eGFRs (< 60 mL/min/1.73 m²) varied across the groups, being more frequent among diabetic patients with suboptimal and poor glycemic control, with the lowest proportion (1.7%) observed among prediabetics (Table 2). The prevalence of smoking was low across all groups, with a slightly greater proportion observed among those with poor control. Obesity and hypertension demonstrated a clear progressive increment with worsening control. Compared with diabetic patients, prediabetic patients presented lower frequencies of these clinical variables.

Table 3: Sex-based comparison of biochemical parameters in patients with T2DM

Variable	Male (n=1772)	Female (n=2649)	*p*-value
Creatinine	0.88	0.67	<0.001
HDL cholesterol	40.185	43.09	<0.001
LDL cholesterol	97.02	74.84	<0.001
Urea	31.53	29.74	<0.001
Total cholesterol	168.02	141.37	<0.001
HbA1c	10.1	7.3	<0.001
Triglyceride	187.015	141.39	<0.001
Glucose	275.1	160.14	<0.001
Age	53	56	<0.001
eGFR	100.6	101.2	0.293

Data are presented as median; comparisons were performed using the Mann–Whitney U test.

These findings indicate a greater cardiometabolic burden in those with poor control. Based on gender, the diabetic patients were divided into two subgroups: female and male. The data were skewed rather than normally distributed. Thus, the Mann–Whitney U nonparametric test was used. Males and females differed significantly in most biochemical variables (Mann–Whitney test, $p< 0.001$ for all except eGFR; Table 3). This uniform pattern of very low p-value is a positive indicator for gender-derived trends in these crucial health parameters. The diabetic males in this cohort demonstrated significantly higher values for urea and creatinine ($p< 0.001$). Men had a lipid profile that was more likely to cause atherosclerosis (higher TG, LDL, and TC) and worse glycemic control, while women had higher HDL cholesterol levels. No significant difference in eGFR was detected between sexes. Based on age, diabetic patients were classified into three age-defined groups (group I < 40, group II 40-59, and group III ≥ 60). The analysis illustrated statistically significant differences across all renal, glycemic, and lipid biomarkers ($p< 0.001$). Aging was associated with a progressive increment in urea and creatinine with a marked reduction in eGFR (121.0 → 105.5 → 86.4 mL/min/1.73 m²), whereas HbA1c showed a modest age-associated reduction. Lipid markers demonstrated a heterogeneous age-related pattern: LDL and total cholesterol showed a progressive decline with age, while TG value peaked in the middle-aged strata (Table 4).

Table 4: Comparison of biochemical parameters across age clusters in diabetic patients

Variable	Group I <40 (n=438)	Group II 40–<60 (n=2458)	Group III ≥60 (n=1525)	*p*-value
Urea	23.97	28.49	36.48	<0.001
Creatinine	0.68	0.74	0.83	<0.001
HDL cholesterol	42.51	41.75	43.09	<0.001
LDL cholesterol	101.39	85.175	72.86	<0.001
Total cholesterol	167.42	153.6	142.025	<0.001
Triglyceride	149.07	169.225	145.675	<0.001
HbA1c	8.5	8.1	7.9	<0.001
Glucose	205.05	194.68	184.115	<0.001
eGFR	121.0	105.5	86.4	<0.001

Data are presented as median. Kruskal–Wallis test was used for data analysis.

eGFR exhibited a noticeable age-related decline across participants (Kruskal–Wallis H=1537, $p< 0.001$). The median eGFR was 121 (IQR 11.3) ml/min/1.73 m² among young individuals, whereas those aged 40-59 years had 105.5 (17.9) and 86.4 (30.4) among those in their sixties and above. The participants demonstrated a consistent predominance of females in all age categories, as shown in Table 5, with the most profound discrepancy noted in the elderly group, where females outnumbered the males by nearly double.

Table 5: Distribution of diabetic patients by age group and sex

Age group	Female	Male
Group I (<40 years)	251	187
Group II (40–59 years)	1388	1070
Group III (≥60 years)	1010	515

Data are presented as the number of participants.

To minimize the gender imbalance, age- and sex-stratified analysis was performed (Tables 6 and 7). A stratified Mann-Whitney U test was conducted to examine sex-based differences within the same age group. Notably, urea and creatinine were consistently greater in males than in females across all age groups ($p< 0.001$), supporting a well-established difference in muscle mass, whereas HDL was consistently higher among females, supporting the role of estrogen in cardiovascular protection. While young males and females showed no significant difference in total cholesterol, significant variation was reported in middle-aged and elderly individuals, with females presenting significantly higher TC values than did males of the same age (Table 6), and although the earlier pooled analysis (Table 3) revealed a statistically significant male–female difference in LDL values, the stratified analysis did not reveal a sex difference within the same age group. Age-based differences within the same sex (comparing females separately across age groups and males separately across age groups) were performed in an attempt to reduce possible confounding and permit more exact education of true age-associated biological differences. When analyzed separately by sex, both genders demonstrated a significant age-related increase in urea and creatinine with a reduction in eGFR ($p< 0.001$) (Table 7). Interestingly, the initial pooled analysis (Table 4) revealed statistically significant variation in HDL and glucose by age group, whereas reanalysis following sex stratification showed the age-related differences in

HDL and glucose were significant among males but not among females (Table 7), indicating that the initial difference is possibly due to the unequal distribution of sexes across age groups rather than an actual age-related biological outcome.

Table 6: Sex-based differences within the same age group

Variable	Group I (<40)	Group II (40 – <60)	Group III (≥60)	*p*-value
Urea	Female: 21.12 Male: 26.82	Female: 27.6 Male: 29.68	Female: 35.83 Male: 37.72	Group I: < 0.001 Group II: < 0.001 Group III: 0.007
Creatinine	Female: 0.57 Male: 0.79	Female: 0.63 Male: 0.87	Female: 0.75 Male: 0.98	Group I: < 0.001 Group II: < 0.001 Group III:< 0.001
HDL	Female: 46.32 Male: 38.22	Female: 44.34 Male: 37.42	Female: 45.4 Male: 38.92	Group I: < 0.001 Group II: < 0.001 Group III: < 0.001
LDL	Female: 104.43 Male: 100.06	Female: 83.88 Male: 87.72	Female: 74.35 Male: 70.59	Group I: 0.559 Group II: 0.248 Group III: 0.247
Total cholesterol	Female: 163.96 Male: 162.2	Female: 155.06 Male: 152.45	Female: 145.1 Male: 135.61	Group I: 0.362 Group II: 0.036 Group III: < 0.001
Triglyceride	Female: 141.39 Male: 159.65	Female: 157.68 Male: 184.47	Female: 145.24 Male: 148.24	Group I: 0.026 Group II: < 0.001 Group III: 0.778
HbA1c	Female: 8.2 Male: 8.9	Female: 8.05 Male: 8.15	Female: 7.9 Male: 7.8	Group I: 0.198 Group II: 0.157 Group III: 0.929
Glucose	Female: 196.83 Male: 231.7	Female: 187.69 Male: 203.41	Female: 183.06 Male: 188.61	Group I: 0.02 Group II: 0.005 Group III: 0.337

Data are presented as median. Comparisons within age groups were performed using the Mann–Whitney U test.

Table 7: Age-based differences within the same sex group

Variable	Group I (< 40)	Group II (40 – <60)	Group III (≥ 60)	*p*-value
Urea	Female: 21.12 Male: 26.82	Female: 27.6 Male: 29.68	Female: 35.83 Male: 37.72	Female: <0.001 Male: <0.001
Creatinine	Female: 0.57 Male: 0.79	Female: 0.63 Male: 0.87	Female: 0.75 Male: 0.98	Female: <0.001 Male: <0.001
HDL-cholesterol	Female: 46.32 Male: 38.22	Female: 44.34 Male: 37.42	Female: 45.4 Male: 38.92	Female: 0.131 Male: <0.001
LDL-cholesterol	Female: 104.43 Male: 100.06	Female: 83.88 Male: 87.72	Female: 74.35 Male: 70.59	Female: <0.001 Male: <0.001
Total cholesterol	Female: 172.96 Male: 162.2	Female: 155.06 Male: 152.45	Female: 145.1 Male: 135.61	Female: <0.001 Male: <0.001
Triglyceride	Female: 141.39 Male: 159.65	Female: 157.68 Male: 184.47	Female: 145.24 Male: 148.24	Female: 0.003 Male: <0.001
HbA1c	Female: 8.2 Male: 8.9	Female: 8.05 Male: 8.15	Female: 7.9 Male: 7.8	Female: 0.007 Male: <0.001
Glucose	Female: 196.83 Male: 231.7	Female: 187.69 Male: 203.41	Female: 183.06 Male: 188.61	Female: 0.149 Male: 0.001

Data are presented as median. Kruskal–Wallis test applied separately within each sex.

Multivariable regression analysis was conducted to examine the independent effects of demographic (age and sex) and metabolic (HbA1c) predictors on renal and lipid markers. While the former comparative analysis allowed for capturing the difference across groups, they do not consider possible confounding or interaction among variables. A generalized linear model (GLM) with gamma distribution was applied. We assessed the magnitude and direction of influence for each predictor (Table 8); the model demonstrated a consistent and significant association between high HbA1c and unfavorable renal function with a more atherogenic profile. Age emerged as an independent determinant of renal indices, with each 1-year aging being associated with an approximately 1% rise in creatinine. In contrast, age showed a weaker or non-significant association with lipid parameters, and although the former comparative analyses demonstrated significant differences in HDL and triglyceride levels across age clusters, the association did not hold statistical significance in regression after adjusting for covariates, suggesting that these differences may be imposed by confounding rather than a real independent effect. Gender was a significant predictor for renal and lipid parameters; females were found to have significantly lower creatinine, total cholesterol, and triglyceride levels as compared to males. Considering the biological interconnection, multivariate analysis of covariance (MANCOVA) was employed to evaluate the collective influence of HbA1c, age, and gender on renal and lipid profiles. The model obtained a significant combined effect for all predictors ($p< 0.001$), with sex having the most pronounced multivariate impact (21%), followed by age (14.7%) and HbA1c (12.1%) (Table 9).

Table 8: Multivariable regression analysis of demographic and glycemic predictors on lipid and renal biomarkers

Dependent	Independent	Coef.	*p*	Interpretation
Urea	HbA1c	0.0098	<0.001	Each 1-unit increase in HbA1c → 0.97% increase in Urea
	Age	0.0126	<0.001	Each 1-year increase in age → 1.27% increase in Urea
	Gender	0.0691	<0.001	Males had approximately a 7.15% higher Urea compared to females.
Creatinine	HbA1c	0.0047	<0.001	Each 1-unit increase in HbA1c → 0.7% increase in Creatinine
	Age	0.0069	<0.001	Each 1-year increase in age → 1% increase in Creatinine
	Gender	0.2715	<0.001	Males had approximately 25.3% higher creatinine levels compared to females.
HDL-c	HbA1c	-0.011	<0.001	Each 1-unit increase in HbA1c → 1.11% decrease in HDL
	Age	0.0002	0.6513	No significant effect
	Gender	-0.148	<0.001	Males have approximately 18.3% lower HD compared to females.
LDL-c	HbA1c	0.0635	<0.001	Each 1-unit increase in HbA1c → 6.56% increase in LDL
	Age	0.0062	<0.001	Each 1-year increase in age → 0.62% increase in LDL
	Gender	0.0034	0.8072	No significant effect
Total cholesterol	HbA1c	0.04	<0.001	Each 1-unit increase in HbA1c → 4.6% increase in total cholesterol
	Age	0.0029	<0.001	Each 1-year increase in age → 0.3% increase in total cholesterol
	Gender	0.0366	<0.001	Males have approximately 4.7%higher total cholesterol compared to females.
Triglyceride	HbA1c	0.0507	<0.001	Each 1-unit increase in HbA1c →8.9% increase in Triglyceride
	Age	-0.001	0.0659	No significant effect
	Gender	0.0997	<0.001	Males have approximately 11.9% higher triglycerides

Coefficients represent the percentage change in the dependent variable for a one-unit increase in the predictor. Models adjusted for age, sex, and HbA1c.

Table 9: Multivariate analysis of covariance (MANCOVA) showing the combined effects of HbA1c, age, and sex on renal and lipid biomarkers

Predictors	Wilks' Lambda	*p*-value	Interpretation
HbA1c	0.879	<0.001	Significant combined effect. Explains ~12.1% of the variance in the outcomes.
Age	0.853	<0.001	Strong combined effect. Explains ~14.7% of the variance in renal/lipid markers.
Gender	0.79	<0.001	Strongest effect. Explains ~21% of outcome variance

DISCUSSION

This large-scale cross-sectional study provides a comprehensive evaluation of the independent and combined effects of glycemic control, age, and sex on renal and lipid biomarkers in adults with T2 DM. By integrating lipid and renal parameters within the same analytical framework and applying multilevel stratification and multivariate modeling, the findings extend previous work and offer clinically relevant insights into cardiorenal risk proofing beyond glycemic status alone. Poor glycemic control was consistently associated with an adverse lipid profile pattern (high TG, high LDL, and low HDL), which reflects the known atherogenic phenotype associated with insulin resistance and glycemic dysregulation and has been reported in previous studies of type 2 DM [21,22]. Underscoring the clinical relevance of HbA1c not only as a marker for glucose control but also as a proxy indicator of metabolic dysregulation. Impaired insulin signaling in adipose tissue fails to suppress lipolysis, leading to increased circulating free fatty acids [23,24], which in turn are taken up by the liver and incorporated into TG and subsequently released as very low-density lipoprotein (VLDL) [25,26]. Furthermore, insulin resistance, diminished lipoprotein lipase activity, and compromised clearance of TG-rich particles [27] led to the accumulation of small, dense LDLs and a reduction in HDL, contributing to an atherogenic lipid profile [28]. Renal markers exhibited a more complex relationship with glycemic status; eGFR values were largely preserved across glycemic groups, with the highest frequencies of low eGFR (< 60 ml/min/1.73 m^2) among suboptimal and poor control groups. The preserved eGFRs across groups in this outpatient cohort suggest intact global filtration capacity with the absence of advanced structural damage; the eGFR lacks the sensitivity for subtle functional alteration, particularly in the absence of data about albuminuria. A similar trend of preserved or insignificantly reduced GFR in the early and intermediate stages of dysglycemia has been mentioned in earlier studies, where hyperfiltration and variability set the scene for overt deterioration of renal function [29,30]. Sex differences were evident in both kidney function and lipid profiles. Diabetic males, those included in our cohort, showed higher levels of urea, creatinine, and more atherogenic lipids in comparison to females. These results support previous evidence that higher creatinine levels in men were likely the result of greater muscle mass and sex-specific generation of creatinine, rather than lower renal filtration [31,32], as well as the contribution of insulin resistance, visceral fat components, and delay in medical consultation for seeking treatment among males [33,34]. On the other hand, estrogen in females might have a protective effect on lipid metabolism, explaining higher levels of HDL cholesterol [35]. These findings stress the necessity of taking sex differences into account in diabetologists' practice. Although the women in our study demonstrated relatively more favorable lipid profiles, these improvements may not lower their long-term risks as estrogen levels begin to decrease after menopause. Age was identified as another important contributor to renal function, with at least as much influence as control of blood glucose levels. A stepwise increase in the serum urea and creatinine and a significant reduction in the estimated GFR with age were evident from this study. This is biologically plausible, reflecting age-related alterations in kidney function and structure, including glomerulosclerosis, a decrease in renal blood flow, and a decrease in nephron count with interstitial fibrosis, which mutually result in impaired glomerular filtration and waste excretion [36,37]. It is intriguing that in multivariable models, age was a powerful and independent determinant of

renal indices even after HbA1c and sex adjustments, highlighting the importance of incorporating age in the assessment of renal complications for patients with diabetes instead of using blood glucose levels alone. Lipid profiles showed heterogeneous patterns with age. Both LDL (bad) cholesterol and total cholesterol gradually decreased with age, while triglycerides peaked in middle age. This may be attributed to variations in the use of lipid-lowering drugs, age-related metabolic stress, diet, and lifestyle changes [38,39]. Clinically, these findings confirm that age-related changes are neither linear nor constant and that some variables are more sensitive than others. The study population showed a predominance of females in all age groups. Higher life expectancy and sex-based healthcare attendance behavior, with females being commonly more proactive in seeking medical care [40,41], may explain their greater representation in medical samples. Additional stratified analysis indicated that some of the deceptively age-related differences were powered by the unbalanced sex distribution across age groups; for instance, the initially noted differences in HDL and glucose in the pooled age analysis were not consistently reported when females were analyzed separately. Suggesting that gender imbalance in the dataset can obscure or exaggerate the age effect. From a clinical perspective, these findings accentuate the need to interpret the biomarker result against sex-specific reference values, even within the same age cohort, by applying a personalized diagnostic threshold to avoid misclassifying normal physiological variation as pathological, with its relevance to cardiometabolic and renal risk stratification and the construction of individual treatment plans. The multivariable regression and MANCOVA analysis offer a key contribution of this study, while HbA1c continued to be a significant predictor of adverse renal and lipid outcomes, sex and age jointly explained a greater proportion of variance in cardiorenal biomarkers. This observation has important clinical implications; for example, an elderly male patient with an acceptable HbA1c may still carry a substantial metabolic and renal risk, whereas a younger female patient with poorer glycemic control may present comparatively less adverse profiles.

Study limitations

This study has several limitations, as it is cross-sectional, the findings may reflect associations rather than causation, and it is based on a single center with parameters measured at a single point, limiting its generalizability to other populations or health care settings. The lack of albumin creatinine ratio (ACR) data for the involved cohort limits renal assessment to creatinine and eGFR, potentially underestimating early renal involvement. Clinical factors such as drug compliance and duration of diabetes were not fully controlled, and consistent data on BMI, blood pressure, and smoking status were inconsistently recorded and could not be included in the multivariable model. Some information was self-reported by the participants, which might lead to recall bias, particularly regarding their medical history and lifestyle factors that could influence renal health. Despite these drawbacks, the large sample size and the fact that we performed a detailed stratified multivariate analysis make our findings more credible and valuable for clinical practice.

Conclusion

The research indicated that renal and metabolic complications in those with T2DM are determined by more than just hyperglycemia. Atherogenic lipid profile was influenced by poor glycemic control, and kidney function was significantly associated with aging. Sex (especially male) proved to be a powerful risk factor for cardiovascular and kidney disease, as strong as or stronger than HbA1c, which is a measure of average blood glucose levels over the past two to three months. Multivariate analysis confirms the importance of demographic variables in modifying risk, beyond blood glucose values per se. Collectively, the results encourage a personalized management of diabetes that takes into account risk profiling and demographic status rather than mere HbA1c values. This policy affords an early risk estimation and enhanced monitoring in accordance with the launched term of precision medicine and tailored management for chronic diseases, especially in communities with high diabetes prevalence and diverse demographics.

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Conflict of interests

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Data sharing statement

Supplementary data can be shared with the corresponding author upon reasonable request.

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