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Serum glucagon-like peptide-1 and G-protein-coupled receptor levels are associated with albuminuria and kidney function in type 2 diabetes: A cross-sectional study

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Abstract. *The relationship of serum glucagon-like peptide-1 (GLP-1) and G-protein-coupled receptor (GPCR) with kidney-related outcomes continues to be poorly studied. The purpose of this study was to determine whether serum GLP-1 and GPCR are related to urinary albumin-to-creatinine ratio (uACR), estimated glomerular filtration rate (eGFR), and cystatin C in patients with type 2 diabetes mellitus (T2DM).*

Methods. A total of 150 participants were included in this cross-sectional study and divided into three groups: the healthy subjects (Control group), T2DM patients with albuminuria stage A1 (T2DM-A1 group), and T2DM patients with albuminuria stage A2/A3 (T2DM-A2/A3 group). There were 50 subjects in each group. The clinical information was collected: fasting glucose, HbA1c, insulin, urea, creatinine, eGFR, uACR, cystatin C, GLP-1, and GPCR values. Serum GLP-1, GPCR, and cystatin C were measured using sandwich ELISA kits. Groups were compared using non-parametric testing. Analysis of Spearman correlation was utilized in the diabetic cohort. Linear regression adjusted for age, BMI, diabetes duration, and HbA1c was conducted to identify independent associations of GLP-1 and GPCR with uACR and eGFR.

Results. GLP-1 and GPCR concentrations were gradually increasing from Control group to group T2DM-A1 and group T2DM-A2/A3. Within the diabetic cohort, GLP-1 and GPCR were positively correlated with uACR and cystatin C and negatively correlated with eGFR. After adjustment for covariates, GLP-1 was associated with higher log-transformed uACR (standardized = 0.529, $p < 0.001$) and lower eGFR (standardized = -0.415, $p < 0.001$). Similarly, GPCR also showed a positive correlation with log-transformed uACR (standardized = 0.319, $p = 0.002$) and a negative correlation with eGFR (standardized = -0.365, $p = 0.002$).

Conclusions. Circulating GLP-1 and GPCR levels were associated with higher albuminuria and lower eGFR in T2DM. GLP-1 demonstrated a stronger association with albuminuria, while GPCR displayed a comparable negative association with kidney function. The study's findings offer evidence for a cross-sectional GLP-1-GPCR kidney-related biomarker profile that characterizes the albuminuric T2DM phenotype and call for longitudinal studies to confirm the clinical utility of these markers.

Key words: *diabetes mellitus type 2, diabetic nephropathies, albuminuria, glomerular filtration rate, cystatin C, glucagon-like peptide 1, receptors, G-protein-coupled, biomarkers.*

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Сироваткові рівні глюкагоноподібного пептиду-1 та рецепторів, сполучених з G-білком, асоційовані з альбумінурією та функцією нирок у пацієнтів з цукровим діабетом 2 типу: одномоментне поперечне дослідження

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Резюме. *Зв'язок сироваткових рівнів глюкагоноподібного пептиду-1 (ГПП-1) та рецепторів, сполучених з G-білком (GPCR), з показниками ураження нирок залишається недостатньо вивченим. Метою дослідження було визначити зв'язок сироваткових рівнів ГПП-1 і GPCR з альбумін-креатиніновим співвідношенням сечі (АКС), розрахунковою швидкістю клубочкової фільтрації (рШКФ) та рівнем цистатину С у пацієнтів з цукровим діабетом 2 типу (ЦД2).*

Методи. До одномоментного поперечного дослідження включено 150 учасників, яких розподілили на три групи: здорові особи (контрольна група), пацієнти з ЦД2 та альбумінурією категорії А1 (група ЦД2-А1) і пацієнти з ЦД2 та альбумінурією категорій А2/А3 (група ЦД2-А2/А3). Кожна група складалась з 50 осіб. Визначали рівні глюкози натще, глікованого гемоглобіну (HbA1c), інсуліну, сечовини, креатиніну, цистатину С, ГПП-1 та GPCR, а також розраховували ШКФ і АКС. Сироваткові рівні ГПП-1, GPCR і цистатину С визначали методом імуноферментного аналізу. Для порівняння груп застосовували непараметричні статистичні методи. У когорті пацієнтів із ЦД2 зв'язки між показниками оцінювали за допомогою кореляційного аналізу Спірмена. Для визначення незалежного зв'язку ГПП-1 і GPCR з АКС та рШКФ застосовували лінійний регресійний аналіз з поправкою на вік, індекс маси тіла, тривалість ЦД2 та рівень HbA1c.

Результати. Концентрації ГПП-1 і GPCR поступово зростали від контрольної групи до груп ЦД2-А1 та ЦД2-А2/А3. Серед пацієнтів із ЦД2 рівні ГПП-1 і GPCR позитивно корелювали з АКС і цистатином С та негативно — з рШКФ. Після поправки на коваріати вищий рівень ГПП-1 був асоційований з вищим логарифмічно трансформованим АКС (стандартизований $\beta = 0{,}529$; $p < 0{,}001$) та нижчою рШКФ (стандартизований $\beta = -0{,}415$; $p < 0{,}001$). Аналогічно, вищий рівень GPCR був незалежно пов'язаний з вищим логарифмічно трансформованим АКС (стандартизований $\beta = 0{,}319$; $p = 0{,}002$) та нижчою рШКФ (стандартизований $\beta = -0{,}365$; $p = 0{,}002$).

Висновки. Вищі концентрації ГПП-1 і GPCR у сироватці пацієнтів з ЦД2 асоційовані з більш вираженою альбумінурією та нижчою рШКФ. ГПП-1 продемонстрував сильніший зв'язок з альбумінурією, тоді як для GPCR визначено співставний негативний зв'язок з функцією нирок. Отримані результати свідчать про наявність профілю ниркових біомаркерів ГПП-1—GPCR, характерного для фенотипу ЦД2 з альбумінурією. Для визначення клінічного значення цих маркерів необхідні подальші проспективні дослідження.

Ключові слова: *цукровий діабет 2 типу, діабетична хвороба нирок. Альбумінурія, швидкість клубочкової фільтрації. цистатин С, глюкагоноподібний пептид-1, рецептори, сполучені з G-білком, біомаркери.*

Introduction. One of the main consequences of type 2 diabetes mellitus (T2DM) is diabetic kidney disease (DKD) and an important contributor to chronic kidney disease (CKD) [1, 2]. Albumin-to-creatinine ratio in urine (uACR) and estimated glomerular filtration rate (eGFR) are two standard measures of kidney injury in patients with diabetes. However, they capture advanced changes and do not always fully represent early biological changes that are present before manifest kidney dysfunction [3, 4]. For this reason, additional circulating markers may help to describe different kidney-risk phenotypes in T2DM patients.

Albuminuria is a key marker of diabetic kidney damage. However, diabetic kidney disease is heterogeneous. Some patients develop albuminuria, while others show reduced kidney function with little or no albuminuria [2, 4]. For this reason, additional circulating markers may help to describe different kidney-risk phenotypes in T2DM patients.

Cystatin C is a useful complementary marker for GFR estimation, and current evidence supports using cystatin C together with creatinine when available to improve GFR assessment, especially in diabetes, where creatinine may be less sensitive in early dysfunction [2]. Recent studies also show that cystatin C can help detect early DKD in T2DM [5, 6].

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Blood glucose is controlled by the incretin hormone glucagon-like peptide-1 (GLP-1). GLP-1 signalling is biologically relevant in DKD [7]. Large clinical studies and recent reviews show renal benefit with GLP-1 receptor agonists in T2DM and CKD, although these treatment effects cannot be directly equated with endogenous circulating GLP-1 concentrations [8]. A recent review also notes that GLP-1RAs reduce renal outcomes and microalbuminuria in pooled analyses [9].

G-protein-coupled receptor (GPCR) is an important ensemble of receptors responsible for metabolic, inflammatory, and vascular signaling [10]. Certain GPCR-related pathways, such as free fatty acid receptor 4, have been associated with fibrosis and kidney inflammation in experimental models of diabetic nephropathy [11]. However, there is a paucity of available human data on circulating GPCRs in DKD. The obvious gap in the research is apparent, then. Most studies center on classical kidney markers, albuminuria, or GLP-1 receptor agonist treatment. There are also fewer studies investigating whether GLP-1 and GPCR are associated with cystatin C, eGFR, or albuminuria in T2DM.

Therefore, the present study attempted to evaluate the relationship between GLP-1 and GPCR with kidney-related parameters depending on the existence of albuminuria in patients with T2DM.

Patients and methods. *Study design and setting*. This was a cross-sectional, single-center study that was performed at the Diabetes and Endocrinology Center, Al-Yarmouk Teaching Hospital, Baghdad, Iraq, from February 2026 until April 2026. The Medical Ethics Committee of Middle Technical University, Baghdad, Iraq, granted ethical approval for all study procedures in accordance with the Declaration of Helsinki (MEC No. 233 dated January 3, 2026). Before being enrolled, each participant provided an informed consent form.

Study participants. All adults with informed permission who were at least 18 years old were qualified for this study. The participants were divided into three equal groups: Group 1 (Control Group) included apparently healthy controls, Group 2 (T2DM-A1 Group) included patients with T2DM without albuminuria, and Group 3 (T2DM-A2/3 Group) included patients with T2DM and albuminuric DKD.

Healthy controls were eligible if they had no known diabetes or kidney disease and no acute illness at the time of sampling; they also had fasting blood glucose and HbA1c values within the non-diabetic range.

Patients in Groups 2 and 3 were eligible if they had a clinical diagnosis of

T2DM. The diagnosis was based on medical records, current antidiabetic treatment, fasting blood glucose, and HbA1c. The presence of albuminuria of 30 mg/g or above and/or an eGFR of less than 60 mL/min/1.73 m^2 was used to diagnose DKD.

Albuminuria was classified according to KDIGO categories based on uACR: A1, <30 mg/g; A2, 30–300 mg/g; and A3 >300 mg/g. These categories range from normal to slightly, significantly, and severely elevated albuminuria, respectively.

Participants with type 1 diabetes, acute kidney injury, known non-diabetic kidney disease, renal replacement therapy, kidney transplantation, or urinary tract infection were excluded from the study.

Participants who had active infection, recent antibiotic use during the previous two weeks, active inflammatory disease, malignancy, pregnancy, or severe liver disease were also excluded. Patients with known cardiovascular disease were excluded according to the original study protocol. Patients using GLP-1 receptor agonists or DPP-4 inhibitors were also excluded from the study because these medications can affect GLP-1 biology.

Sample size. This study was an exploratory cross-sectional biomarker study. There was no formal a priori determination of sample size. The number of eligible participants determined the sample size; participants were recruited during the study period. A balanced allocation across the three study groups was planned to support between-group comparisons.

Data collection and sampling. At enrolment, the data on age, sex, body weight, height, and diabetes duration were collected. Weight and height were used to calculate the body mass index and expressed as kg/m^2.

Following an overnight fast, venous blood samples were obtained from each participant. Whole blood was used for HbA1c. Serum was separated by centrifugation and used for biochemical and ELISA measurements.

HbA1c was measured by an immunoturbidimetric assay (Stanbio Laboratory, an EKF Diagnostics company, USA). An enzymatic colorimetric glucose oxidase-peroxidase technique (Randox Laboratories Limited, United Kingdom) was used to measure fasting blood glucose. Serum urea and creatinine were measured using a urease enzymatic method and a kinetic Jaffe method, respectively (Biolabo SA, Maizy, France).

Serum insulin, cystatin C, GLP-1, and GPCR were measured using sandwich ELISA kits according to the manufacturers' instructions. The insulin and GLP-1 kits were obtained from Elabscience Biotechnology Co., Ltd. (China), the cystatin C kit from Elabscience Biotechnology Co., Ltd. (Wuhan, China), and the GPCR kit from BlueGene Biotechnology Co., Ltd. (China). Concentrations were calculated from standard curves.

A spot urine sample was collected on the same day. Urinary albumin-to-creatinine ratio was assessed using ACR reagent strips (Siemens Healthineers, Erlangen, Germany) and reported as mg/g.

The glomerular filtration rate (GFR) was calculated using the 2021 CKD-EPI creatinine equation and reported as mL/min/1.73 m^2.

Statistical analysis. IBM SPSS Statistics for Windows, version 26.0 (IBM Corp., Armonk, NY, USA) was used for statistical analysis. The Shapiro-Wilk test was used to determine whether continuous variables were normally distributed. The median and interquar-

tile range [Me (Q25–Q75)] were used to display continuous data that were not regularly distributed. Numbers and percentages were used to display categorical variables.

The Kruskal–Wallis test was utilized for continuous variables in order to compare the three study groups. Pairwise comparisons using Dunn's post-hoc test with Bonferroni correction were carried out if the overall test was significant. Diabetes duration was compared only between the two diabetic groups using the Mann–Whitney U test. The chi-square test was used to compare categorical variables. Spearman's rank correlation coefficient was used to evaluate relationships between continuous variables.

Multiple linear regression was performed separately for each biomarker and each kidney outcome. Because uACR was right-skewed, it was log-transformed before regression. GLP-1 and GPCR were entered in separate models. Age, BMI, duration of diabetes, and HbA1c were entered in every model. Outputs include standardized β with 95% confidence intervals, p values, model F statistics, and adjusted R^2. All tests were two-sided, and $p < 0.05$ was the significance threshold.

Results. The total sample size was 150 people and consisted of 50 subjects per group. Age and sex distributions were not different among the Control and T2DM groups, as shown in Table1.

Table 1

Clinical, metabolic, kidney-related, and biomarker profile of the study cohort

Variable	Control Group (n = 50)	T2DM-A1 (n = 50)	T2DM-A2/A3 (n = 50)	p-value
Age, years	45.0 (43.2–47.0)	45.0 (43.0–47.8)	44.5 (43.0–45.0)	0.203
Male/female, n	25/25	24/26	26/24	0.923
BMI, kg/m^2	24.8 (22.9–29.4)	26.6 (26.4–27.2)	24.2 (23.6–24.5)	<0.0001
Diabetes duration, years	–	2.00 (1.7–2.3)	9.00 (8.0–12.0)	<0.0001
Fasting blood glucose, mg/dL	89.5 (88.0–99.0)	191.5 (118.0–240.0)	279.0 (245.0–290.0)	<0.0001
HbA1c, %	4.9 (4.6–5.0)	9.1 (8.2–9.9)	10.2 (9.8–10.7)	<0.0001
Insulin, μU/mL	5.6 (4.9–5.9)	15.1 (14.7–15.6)	17.5 (14.1–19.8)	<0.0001
Urea, mg/dL	22.0 (19.2–24.0)	28.0 (26.0–29.8)	31.0 (28.0–32.0)	<0.0001
Creatinine, mg/dL	0.76 (0.60–0.98)	1.20 (1.00–1.30)	1.10 (1.00–1.40)	<0.0001
eGFR, mL/min/1.73 m^2	100.0 (97.0–105.0)	84.0 (77.0–86.8)	68.0 (66.0–70.0)	<0.0001
uACR, mg/g	10.0 (7.2–13.0)	17.0 (14.0–21.0)	134.0 (84.5–194.2)	<0.0001
Cystatin C, mg/L	0.58 (0.55–0.63)	1.35 (1.10–1.60)	1.85 (1.60–2.27)	<0.0001
GLP-1, ng/mL	0.54 (0.51–0.61)	1.71 (1.67–1.73)	2.23 (2.11–2.30)	<0.0001
GPCR, ng/mL	0.76 (0.75–0.79)	1.95 (1.77–2.18)	3.50 (3.20–3.75)	<0.0001

Values are presented as Me (Q25-Q75). BMI, body mass index; eGFR, estimated glomerular filtration rate; GLP-1, glucagon-like peptide-1; GPCR, G-protein-coupled receptor; HbA1c, glycated hemoglobin; uACR, urinary albumin to creatinine ratio.

BMI was highest in the T2DM-A1 group, while diabetes duration was longer in the T2DM-A2/A3 group than in the T2DM-A1 group. Fasting blood glucose, HbA1c, and insulin were higher in both diabetic groups than in controls. These values were highest in the T2DM-A2/A3 group.

Kidney-related variables also differed across the T2DM groups. The T2DM-A2/A3 group had higher uACR, lower eGFR, and higher cystatin C compared with the T2DM-A1 group. GLP-1 and GPCR followed the same graded pattern. Their levels were lowest in controls, higher in T2DM-A1, and highest in T2DM-A2/A3.

Spearman correlation analysis was performed in the diabetic cohort only. GLP-1 showed a positive correlation with uACR ($\rho = 0.770$, $p < 0.0001$) and cystatin C ($\rho = 0.491$, $p < 0.0001$) and a negative correlation with eGFR ($\rho = -0.634$, $p < 0.0001$). GPCR showed a similar pattern (Fig. 1).

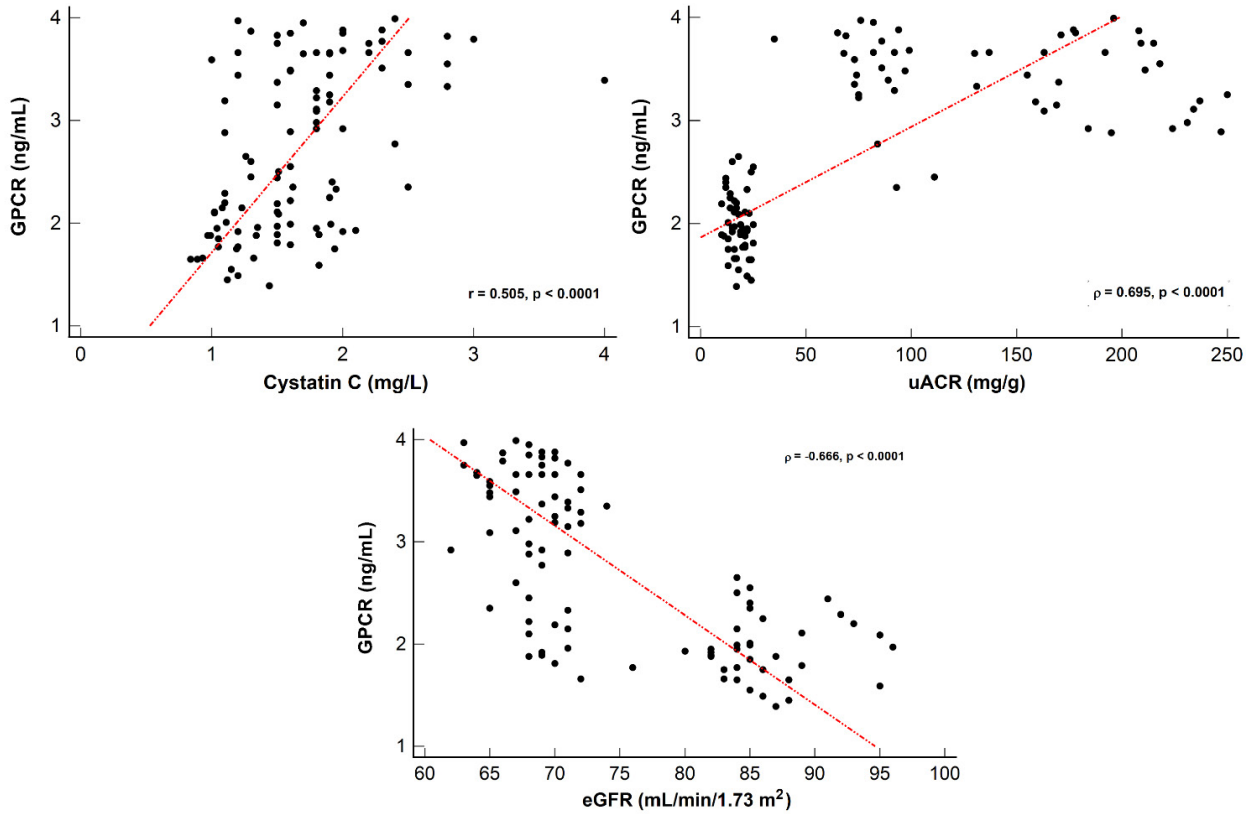

Fig. 1. Correlations between serum GPCR and kidney-related variables in the diabetic cohort.

Both markers, GLP-1 and GPCR, were also correlated with diabetes duration (ρ=0.732, $p < 0.0001$ and ρ=0.731, $p < 0.0001$, respectively) and HbA1c duration (ρ=0.379, $p = 0.0001$ and $\rho = 0.416$, $p < 0.0001$, respectively). Creatinine was not significantly correlated with GLP-1 ($\rho = 0.023$, $p = 0.818$) or GPCR ($\rho = 0.129$, $p = 0.201$).

To examine whether GLP-1 and GPCR were associated with kidney-related outcomes independently of available clinical covariates, adjusted linear regression models were performed in the diabetic cohort. GLP-1 and GPCR were tested in separate models to avoid multicollinearity. Models were age- and BMI-, diabetes duration- and HbA1c-adjusted. All albuminuria outcome models contained log-transformed uACR as the outcome variable.

Both models had statistical significance. In Model 1, GLP-1 was positively associated with log-transformed uACR (standardized $\beta = 0.529$, $p < 0.001$). In Model 2, GPCR was also positively associated with log-transformed uACR (standardized $\beta = 0.319$, $p = 0.002$). Diabetes duration was positively associated with uACR in both models (Table 2).

Table 2

Adjusted linear regression models for uACR in the diabetic cohort

Variable	Model 1: GLP-1 model, standardized β (95% CI)	p-value	Model 2: GPCR model, standardized β (95% CI)	p-value
GLP-1, ng/mL	0.529 (0.350 to 0.707)	<0.001	–	–
GPCR, ng/mL	–	–	0.319 (0.118 to 0.520)	0.002
Age, years	0.007 (-0.088 to 0.101)	0.888	0.009 (-0.093 to 0.111)	0.859
BMI, kg/m^2	-0.104 (-0.344 to 0.136)	0.396	-0.198 (-0.459 to 0.063)	0.138
Diabetes duration, years	0.297 (0.131 to 0.463)	<0.001	0.410 (0.186 to 0.634)	<0.001
HbA1c, %	0.075 (-0.033 to 0.183)	0.174	0.045 (-0.074 to 0.165)	0.456
Model F-statistic	F(5,94) = 90.59	<0.001	F(5,94) = 67.29	<0.001
Adjusted R^2	0.819	–	0.770	–

The dependent variable was log-transformed uACR. Original uACR values were expressed as mg/g. Values are standardized regression coefficients with 95% confidence intervals. Each model was adjusted for age, BMI, diabetes duration, and HbA1c. BMI, body mass index; CI, confidence interval; GLP-1, glucagon-like peptide-1; GPCR, G-protein-coupled receptor; HbA1c, glycated hemoglobin; uACR, urinary albumin-to-creatinine ratio.

For kidney function, eGFR was used as a dependent factor. Both models had statistical significance. In Model 1, GLP-1 was negatively linked to eGFR (standardized β = -0.415, p < 0.001). In Model 2, GPCR was also negatively associated with eGFR (standardized β = -0.365, p = 0.002). BMI was positively associated with eGFR in both models (Table 3).

Table 3

Adjusted linear regression models for eGFR in the diabetic cohort

Variable	Model 1: GLP-1 model, standardized β (95% CI)	p-value	Model 2: GPCR model, standardized β (95% CI)	p-value
GLP-1, ng/mL	-0.415 (-0.614 to -0.216)	<0.001	–	–
GPCR, ng/mL	–	–	-0.365 (-0.593 to -0.138)	0.002
Age, years	0.066 (-0.127 to 0.258)	0.503	0.063 (-0.122 to 0.248)	0.505
BMI, kg/m^2	0.297 (0.042 to 0.551)	0.022	0.309 (0.052 to 0.566)	0.018
Diabetes duration, years	-0.058 (-0.250 to 0.135)	0.559	-0.111 (-0.280 to 0.058)	0.200
HbA1c, %	-0.017 (-0.157 to 0.123)	0.812	0.014 (-0.132 to 0.160)	0.851
Model F-statistic	F(5,94) = 24.72	<0.001	F(5,94) = 23.87	<0.001
Adjusted R^2	0.545	–	0.536	–

The dependent variable was eGFR, expressed as mL/min/1.73 m . Values are standardized regression coefficients with 95% confidence intervals. Each model was adjusted for age, BMI, diabetes duration, and HbA1c. BMI, body mass index; CI, confidence interval; eGFR, estimated glomerular filtration rate; GLP-1, glucagon-like peptide-1; GPCR, G-protein-coupled receptor; HbA1c, glycated hemoglobin.

Overall, higher GLP-1 and GPCR levels were associated with higher albuminuria and lower eGFR after adjustment for available clinical covariates.

Discussion. The current study examined the relationship between circulating GLP-1 and GPCR and kidney-related outcomes in patients with T2DM. Both markers were found to be higher in diabetic patients with more advanced albuminuria. Compared to the T2DM-A1 group, the T2DM-A2/A3 group presented with higher GLP-1 and GPCR levels. In the adjusted regression models, both GLP-1 and GPCR were found to be associated with higher uACR and lower eGFR, adjusting for age, BMI, diabetes duration, and HbA1c. These findings provide a novel analysis of the combined relationships between GLP-1, GPCR, cystatin C, uACR, and eGFR in a diabetic cohort across KDIGO albuminuria categories and allow us to describe a potential GLP-1-GPCR-kidney marker profile associated with increased albuminuria in T2DM.

Cystatin C was higher in the T2DM-A2/A3 group and was positively correlated with albuminuria. This finding is expected and is consistent with previous studies showing that cystatin C increases with diabetic nephropathy progression as well as detects kidney dysfunction in T2DM better than creatinine alone [**5, 6**]. In our cohort, creatinine was not strongly correlated with GLP-1 or GPCR, while cystatin C showed stronger associations with the biomarker profile. This supports the value of cystatin C as an additional kidney-related marker in diabetic patients.

The association between GLP-1 and kidney variables should be interpreted carefully. GLP-1 receptor agonists have demonstrated improved renal outcomes in T2DM CKD trials [**12**]. For example, the FLOW trial showed Semaglutide's impact on reducing the rate of clinically relevant renal events in T2DM and CKD [13]. However, these trials examined pharmacologic agonists rather than endogenous GLP-1. As such, the increased GLP-1 in the T2DM-A2/A3 group can not be considered equivalent to the therapeutic benefit of a GLP-1 agonist drug.

Possible explanations include the possibility of an elevated endogenous GLP-1 as an adaptive response to poor metabolic and kidney status as reflected by longer diabetes duration, increased HbA1c, higher albuminuria, and reduced eGFR in the T2DM-A2/A3 group [**14, 15**]. Alternatively, reduced renal handling of circulating peptides might play a role in patients with impaired kidney function [**16**]. Given that our study design was cross-sectional, it remains difficult to distinguish between the cause and consequence of this association. Furthermore, the results contrast with those from a Korean cohort study, which found that albuminuria and fasting GLP-1 were negatively correlated in T2DM patients [**17**]. This could be explained by variations in study populations, disease duration, glycemic control, kidney phenotyping, medication status, or assay procedures; hence, the findings should be described as cohort-specific rather than proof of a causal relationship between GLP-1 and albuminuria.

The finding of the present study that GPCR was associated with higher uACR and lower eGFR is biologically plausible because signaling pathways of GPCR are involved in metabolic, inflammation, vasculature and renal regulation [**18, 10**]. In experimental settings, GPR120 activation has been shown to protect podo-

cytes from inflammation and fibrosis during diabetic nephropathy [11]. The recently reported findings on abnormal serum GPR120 levels in diabetic nephropathy also provided human evidence of the relationship between this specific receptor and renal function [19]. However, GPCR measurements in this study represent a sum value of various receptor subtypes rather than a specific receptor. Our findings thus suggest an association between a serum GPCR biomarker and the kidney-related phenotype.

The adjusted models also showed that GLP-1 and GPCR were not identical in their associations with kidney-related outcomes. GLP-1 showed a stronger association with uACR, suggesting a closer link with albuminuria. In contrast, GPCR showed a negative association with eGFR of similar direction and magnitude to GLP-1. This pattern suggests that GLP-1 may be more closely related to the albuminuric component of the diabetic kidney phenotype, whereas GPCR may reflect a broader kidney-function-related signal. Therefore, the two markers appear to represent related but not fully overlapping aspects of kidney involvement in T2DM.

The study has certain limitations that need to be discussed. Firstly, the cross-sectional design limits the capacity to ascertain causal relationships or directional changes in CKD progression. Therefore, GLP-1 and GPCR should be treated as associational markers, not prognosticators of incident CKD. Secondly, data collected at a single center with a relatively limited sample size should be interpreted cautiously. Thirdly, a comprehensive list of medications used by patients was unavailable. Since GLP-1 receptor agonists, DPP-4 inhibitors, SGLT2 inhibitors, insulin, and renin-angiotensin system blockers are known to influence glycaemic control, albuminuria, kidney function, and incretin metabolism, the lack of this information limits our adjustment of this confounding variable. Fourthly, our adjustment set for multivariate analyses included only age, BMI, duration of diabetes, and HbA1c and lacked adjustment for blood pressure values. Finally, the GPCR assay failed to identify the receptor subtype, which may prevent exploration of specific pathways and potential target-specific treatments.

Conclusions. The present study showed that GLP-1 and GPCR levels increased with albuminuria severity in patients with T2DM. Both markers were linked to higher uACR, lower eGFR, and higher cystatin C. After adjustment for age, BMI, diabetes duration, and HbA1c, GLP-1 and GPCR remained associated with higher uACR and lower eGFR. GLP-1 was more closely related to albuminuria, whereas GPCR showed a similar negative association with kidney function. The findings of this work suggest that GLP-1 and GPCR reflect related but not identical parts of the diabetic kidney phenotype. Further longitudinal studies with medication data, blood pressure data, and receptor-specific GPCR assays are needed to confirm their clinical value.

Ethics approval. The study was approved by the Ethics Committee of Middle Technical University, Baghdad, Iraq (approval No. MEC No.233 on 3/1/2026). The study was performed under the Declaration of Helsinki principles. All subjects had given signed informed consent before enrollment in the study.

Consent for publication. Not applicable. The manuscript does not contain any individually identifiable human data.

Availability of data and materials. Reasonable requests for the analyzed dataset may be directed to the corresponding author.

Competing interests. The authors affirm that they have no conflicting interests.

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Use of artificial intelligence tools. Grammarly word extension was employed to help with editing in English, grammar correction, and improvement of text clarity. No artificial intelligence tool was employed to produce original data, perform our statistical analysis, or make scientific conclusions. The authors, who bear full responsibility for the final manuscript, examined and approved all content.

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