SEBHA UNIVERSITY JOURNAL OF MEDICAL SCIENCES VOL.21 NO. 1 2026
DOI: 10.51984/18DD9796

مجلة جامعة سبها للعلوم الطبية
Sebha University Journal of Medical Sciences
Journal homepage: www.sebhau.edu.ly/journal/joms

Serum Adiponectin as a Diagnostic Marker of Early Renal Dysfunction in Patients with Hypertension and Type 2 Diabetes

*Amira Fatehi Masoud Akrio[1], Al-Bashir Mohammed Al-Bashir[2], Walied Saeed Abdo Hibat Allah[3], Basmah Jummah Jufarah[4]

[1] Clinical Biochemistry. Wadi Al-Shati University, College of Medical Technology, Department of Medical Laboratory Technology
[2]Clinical Biochemistry, Vice Dean of Scientific Affairs, Faculty of Science, Wadi Al-Shati University
[3] Clinical biochemistry, Al-Hikmah university, Department of biochemistry
[4] Physiology, Wadi Al-Shati University, College of Medical Technology, Department of Medical Laboratory Technology

Keywords:
Adiponectin
Hypertension
Renal Complications
ROC Analysis
T2DM
UACR

ABSTRACT

Background: The coexistence of type 2 diabetes mellitus (T2DM) and hypertension markedly increases the risk of renal complications. This study evaluated the relationship between adiponectin and the urinary albumin-to-creatinine ratio (UACR) and examined the diagnostic value of the UACR/adiponectin ratio for early detection of kidney dysfunction. **Methods**: In this cross-sectional study, 90 participants (40 to 80 years) were divided into four groups: hypertension (n=24), T2DM (n=24), combined T2DM with hypertension (n=24), and healthy controls (n=18). Key metabolic and renal markers were assessed. Serum adiponectin was measured by ELISA, UACR and CRP were determined, and renal function was evaluated using eGFR (CKD-EPI equation). Data were analyzed using SPSS version 27. **Results:** Urinary albumin-to-creatinine ratio (UACR) showed a statistically significant difference among the studied groups (P=0.006), with higher levels observed in diabetic patients. Moreover, UACR was independently associated with renal dysfunction (OR=1.415, P=0.002). In contrast, adiponectin levels did not demonstrate statistically significant differences between groups or according to sex. However, ROC curve analysis indicated a moderate diagnostic performance for adiponectin (AUC=0.674), with a cutoff value >17.46 yielding a sensitivity of 58.82% and a specificity of 78.18%. Notably, the UACR/adiponectin ratio exhibited excellent diagnostic performance (AUC=0.934). At a cutoff value >1.67, it demonstrated a sensitivity of 86% and specificity of 90%, with an overall accuracy of 90.28%. **Conclusion:** The UACR/adiponectin ratio outperformed adiponectin alone and may serve as a reliable combined biomarker for early detection of renal dysfunction in patients with metabolic disorders.

الأديبونيكتين في المصل كمؤشر تشخيصي مبكر لخلل وظائف الكلى لدى مرضى ارتفاع ضغط الدم وداء السكري من النوع الثاني

*أميرة فاتحي مسعود عكربو[1]، البشير محمد البشير[2]، وليد سعيد عبدو هبة الله[3]، بسمة جمعة جوفاره[4]

[1] الكيمياء الحيوية السريرية، جامعة وادي الشاطئ، كلية التقنية الطبية، قسم تقنية المختبرات الطبية
[2] الكيمياء الحيوية السريرية، نائب عميد الشؤون العلمية، كلية العلوم، جامعة وادي الشاطئ
[3] الكيمياء الحيوية السريرية، جامعة الحكمة، قسم الكيمياء الحيوية
[4] علم وظائف الأعضاء، جامعة وادي الشاطئ، كلية التقنية الطبية، قسم تقنية المختبرات الطبية

الكلمات المفتاحية:
الأديبونيكتين
ارتفاع ضغط الدم
المضاعفات الكلوية
تحليل منحنى
ROCداء السكري من النوع الثاني
نسبة الألبومين إلى الكرياتينين في البول

الملخص

الخلفية :يؤدي التزامن بين داء السكري من النوع الثاني (T2DM) وارتفاع ضغط الدم إلى زيادة ملحوظة في خطر حدوث المضاعفات الكلوية. هدفت هذه الدراسة إلى تقييم العلاقة بين الأديبونيكتين ونسبة الألبومين إلى الكرياتينين في البول(UACR) ، بالإضافة إلى فحص القيمة التشخيصية لنسبةUACR / الأديبونيكتين في الكشف المبكر عن خلل وظائف الكلى. **المنهجية** :أُجريت هذه الدراسة المقطعية على 90 مشاركًا تتراوح أعمارهم بين 40 و80 عامًا وقُسموا إلى أربع مجموعات: مرضى ارتفاع ضغط الدم (24 مشاركًا) ومرضى السكري من النوع الثاني (24 مشاركًا) ومرضى السكري من النوع الثاني المصحوب بارتفاع ضغط الدم (24 مشاركًا) ومجموعة ضابطة من

*Corresponding author:
E-mail addresses: a.kerbo@wau.edu.ly
Article History : Received 04 May 2026 - Received in revised form 25 June 2026 - Accepted 30 June 2026

الأصحاء (18 مشاركًا). تم تقييم المؤشرات الأيضية والكلوية الرئيسة وقياس تركيز الأديبونكتين في المصل باستخدام تقنية المقايسة المناعية المرتبطة بالإنزيم(ELISA) ، كما تم تحديد نسبة الألبومين إلى الكرياتينين في البول (UACR) ومستويات البروتين المتفاعل(CRP) C وتقييم وظائف الكلى باستخدام معدل الترشيح الكبيبي المقدر (eGFR) وفق معادلة CKD-EPI وقد أُجري التحليل الإحصائي باستخدام برنامج SPSS الإصدار 27. **النتائج** :أظهرت نسبة الألبومين إلى الكرياتينين في البول (UACR) اختلافًا ذا دلالة إحصائية بين المجموعات المدروسة(P=0.006) ، حيث سُجلت مستويات أعلى لدى مرضى السكري. كما ارتبطت UACR بصورة مستقلة بوجود اختلال في وظائف الكلى (OR=1.415, P=0.002) ، في المقابل، لم تُظهر مستويات الأديبونكتين فروقًا ذات دلالة إحصائية بين المجموعات أو وفقًا للجنس. ومع ذلك، أظهر تحليل منحنى خصائص تشغيل المستقبل (ROC)أداءً تشخيصيًا متوسطًا للأديبونكتين(AUC=0.674) وكانت قيمة القطع (17.46>) تحقق حساسية بلغت 58.82% ونوعية بلغت 78.18%. ومن اللافت أن نسبةUACR/ الأديبونكتين أظهرت أداءً تشخيصيًا ممتازًا (AUC=0.934)، إذ حققت عند قيمة قطع (1.67>) حساسية قدرها 86% ونوعية قدرها 90%، مع دقة تشخيصية كلية بلغت 90.28%. **الاستنتاج:** تفوقت نسبةUACR/ الأديبونيكتين على استخدام الأديبونيكتين بمفرده، وقد تمثل مؤشرًا حيويًا مركبًا وموثوقًا للكشف المبكر عن خلل وظائف الكلى لدى المرضى المصابين باضطرابات أيضية.

1. Introduction

Adiponectin is a multifunctional protein hormone predominantly secreted by white adipose tissue and is recognized as one of the key biological mediators linking obesity with hypertension and diabetes mellitus [1,2]. It was first identified in 1995, adiponectin circulates in relatively high concentrations (3–30 μg/mL), making it the most abundant adipokine in human plasma [3,4]. The hormone consists of 244 amino acids and is encoded by the ADIPOQ gene located on chromosome 3q27[5]. Structurally, adiponectin comprises an N-terminal collagen-like domain and a C-terminal globular domain homologous to complement protein C1q [2,5]. It undergoes several essential post-translational modifications, including hydroxylation, glycosylation, and disulfide bond formation, which are critical for its multimerization, secretion, and biological activity [4,5]. Compared with most hormones and cytokines, adiponectin exhibits a relatively rapid turnover rate [6]. Interestingly, despite being synthesized primarily by adipocytes, its circulating concentrations are inversely correlated with total body fat mass [1,3,6].

Circulating adiponectin exists in three major oligomeric isoforms based on molecular weight: low-molecular-weight (LMW), medium-molecular-weight (MMW), and high-molecular-weight (HMW) complexes. Among these, the HMW isoform is considered the most biologically active because of its strong association with enhanced insulin sensitivity and the regulation of glucose and lipid metabolism [7]. Adiponectin plays a pivotal role in maintaining metabolic homeostasis by improving insulin sensitivity, regulating glucose and lipid metabolism, suppressing inflammatory responses, and promoting cardiovascular health [1,2,8,9]. Furthermore, circulating adiponectin levels are inversely associated with obesity, insulin resistance, and the risk of developing type 2 diabetes mellitus [1,8].

The Middle East and North Africa (MENA) region has experienced a significant rise in the prevalence of non-communicable diseases, particularly T2DM and hypertension, which are often comorbid and substantially increase the risk of renal, cardiovascular, ocular, and neurological complications [10,11]. Diabetes mellitus is a metabolic disorder characterized by impaired glucose regulation, with T2DM being the most prevalent form due to insulin resistance or beta-cell dysfunction, leading to chronic hyperglycemia and progressive organ damage [12,13]. Hypertension, defined as persistent blood pressure exceeding 140/90 mmHg, is a major risk factor for cardiovascular disease, stroke, and chronic kidney disease, often presenting asymptomatically [11,14,15].

Both diabetes and hypertension are among the leading contributors to chronic kidney disease (CKD), as they induce metabolic and hemodynamic disturbances that cause glomerular injury and gradual deterioration of renal function [16]. The risk is further exacerbated when both conditions coexist, increasing the likelihood of diabetic nephropathy and progression to end-stage renal disease [17]. Evidence indicates that early control of blood glucose and blood pressure represents a critical strategy for mitigating renal complications and slowing disease progression [18].

Adiponectin contributes to maintaining renal arterial integrity, reducing proteinuria, and improving the glomerular filtration rate through the modulation of anabolic signaling pathways and attenuation of oxidative stress, highlighting its potential as a therapeutic target in various metabolic disorders [8,19]. Despite this, its value as an early biomarker for detecting renal impairment in patients with T2DM accompanied by hypertension remains insufficiently understood. Most previous studies have examined diabetes or hypertension separately, while data regarding the combined impact of these conditions on adiponectin levels and their association with renal dysfunction are still limited. Therefore, this study aims to evaluate the relationship between serum adiponectin levels and renal function in patients with T2DM and hypertension, as well as to investigate the potential diagnostic value of adiponectin and the Urinary albumin-to-creatinine ratio to adiponectin ratio (UACR-to-adiponectin ratio) as a biomarker for the early detection of renal impairment.

2. Materials and methods

An exploratory cross-sectional study was conducted at Brack General Hospital, Libya, between 22 December 2023 and 22 April 2024, following ethical approval from the Research Ethics Committee of Wadi Al-Shati University. The study included 90 participants of both sexes (45 males and 45 females), aged 40 to 80 years. Participants were recruited using a convenience sampling method according to predefined inclusion and exclusion criteria.

The study population was divided into four groups: a control group (G1) consisting of 18 apparently healthy individuals; a hypertension group (G2) comprising 24 patients; a type 2 diabetes mellitus group (G3) including 24 patients; and a combined type 2 diabetes mellitus with hypertension group (G4) also including 24 patients.

Participants with cardiovascular diseases, renal failure, type 1 diabetes mellitus, malignancies, previous stroke, or hepatic and thyroid disorders were excluded, as well as those receiving insulin therapy.

Demographic and clinical data were collected using a structured questionnaire that included age, sex, medical history (hypertension, diabetes mellitus, or both), disease duration, current treatment, dietary habits (dietary adherence), and level of physical activity (walking exercise). These variables were subsequently used in the statistical analysis to examine their associations with the biochemical and clinical parameters under investigation.

Anthropometric measurements were performed for all participants. Body weight and height were measured, and Body Mass Index (BMI) was calculated according to the World Health Organization (WHO, 2010) formula. Systolic and diastolic blood pressure (SBP and DBP) were measured using a mercury sphygmomanometer after an adequate rest period under standardized conditions.

Venous blood samples were collected under aseptic conditions. Serum was separated and subjected to biochemical and hormonal analyses. Fasting blood glucose (FBS) was measured using the i-STAT 1 Analyzer (Abbott, USA), while glycated hemoglobin (HbA1c) was determined using the ichroma™ II analyzer (Boditech Med Inc., Korea) based on fluorescence immunoassay technology. Estimated average glucose (eAG) was calculated using the following equation: eAG (mg/dL) = (28.7 × HbA1c) − 46.7 (Nathan et al., 2008). In addition, serum albumin was determined using a colorimetric method on the Roche Cobas Integra 400 Plus Chemistry Analyzer.

Lipid profile parameters, including total cholesterol, triglycerides, high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C), were analyzed using the Afinion 2 Analyzer. Serum adiponectin levels were measured using a Human Adiponectin ELISA Kit (China), and absorbance was read using a microplate reader (BioTek ELx800, USA) according to the manufacturer's instructions.

Blood urea nitrogen (BUN), creatinine, sodium (Na^+), and potassium (K^+) levels were measured using the i-STAT 1 Analyzer (Abbott, USA). Urinary albumin-to-creatinine ratio (UACR) was assessed using morning spot urine samples collected in a sterile container. Samples were analyzed using the Afinion 2 Analyzer (Abbott, USA). Estimated glomerular filtration rate (eGFR) was calculated using the CKD-EPI 2021 equation (Inker et al., 2021), and then adjusted for body surface area (BSA) using the Du Bois formula:

$$BSA = 0.007184 \times W^{0.425} \times H^{0.725} \quad (1)$$

The final adjusted eGFR was calculated as:

eGFR value x BSA / 1.73 (2)

Serum C-reactive protein (CRP) was determined using the CRP Latex Test.

Data analysis was performed using SPSS software (version 28) and Microsoft Excel 2016. The Shapiro–Wilk test was applied to assess data normality. Based on the distribution of variables, one-way analysis of variance (One-way ANOVA) with Bonferroni post hoc correction was used for parametric data, while the Kruskal–Wallis test followed by Dunn's post hoc test was applied for non-parametric data. The Mann–Whitney U test was additionally used for pairwise comparisons between two independent groups when appropriate. Receiver operating characteristic (ROC) curve analysis and logistic regression were also performed to evaluate the predictive ability of the studied variables. Effect size was calculated using eta squared (η^2) according to Cohen's (1988) guidelines. A p-value of ≤ 0.05 was considered statistically significant.

3. Results

Comparisons were performed among the four study groups (G1, G2, G3, and G4). Normally distributed variables were expressed as mean ± standard deviation (Mean ± SD) and analyzed using one-way analysis of variance (One-way ANOVA), followed by Bonferroni post hoc test for multiple pairwise comparisons. Non-normally distributed variables were presented as median and interquartile range [Median (IQR)] and compared using the Kruskal–Wallis test, followed by Dunn's post hoc test for multiple comparisons.

The comparison of results across anthropometric and blood pressure variables revealed no statistically significant differences in age among the four groups ($P = 0.573$, $\eta^2 = 0.024$). Significant differences were observed in BMI ($P = 0.036$, $\eta^2 = 0.09$), with the highest mean value recorded in group G4, which was significantly higher than group G1 ($P = 0.028$). SBP showed highly significant differences between the groups ($P < 0.001$, $\eta^2 = 0.18$), with significantly higher values in group G2 compared with group G1 ($P = 0.010$) and group G3 ($P = 0.021$), as well as in group G4 compared with group G1 ($P = 0.016$) and group G3 ($P = 0.034$). DBP also showed statistically significant differences ($P = 0.012$, $\eta^2 = 0.12$), with group G2 exhibiting significantly higher values compared with group G3 ($P = 0.033$), as shown in (Table 1).

The comparison of glycemic parameters revealed statistically significant differences in FBS ($P < 0.001$, $\eta^2 = 0.24$), eAG ($P < 0.001$, $\eta^2 = 0.37$), and HbA1c ($P < 0.001$, $\eta^2 = 0.37$). The highest values were observed in groups G3 and G4 compared with groups G1 and G2, with the largest effect sizes observed across glycemic control parameters (FBS: $\eta^2 = 0.24$, eAG: $\eta^2 = 0.37$, HbA1c: $\eta^2 = 0.37$), as shown in (Table 1).

Table 1: Comparison of demographic, anthropometric, blood pressure, and glycemic variables among study groups.

Variables	Mean ± SD				P value	Eta Squared	Significant pairwise comparisons
	G1(18)	G2(24)	G3 (24)	G4 (24)			
Age (years)	52.56 ± 11.11	52.63 ± 10.02	54.75 ± 9.98	56.33 ± 11.28	0.573	0.024	
BMI (kg/m²)	27.49 ± 4.06	30.11 ± 4.89	29.22 ± 4.27	31.63 ± 4.89	0.036*	0.09	P3: 0.028
SBP (mmHg)	118.06 ± 12.26	133.08 ± 16.39	120.21 ± 11.47	132.38 ± 17.76	<0.001*	0.18	P1:0.010, P3:0.016, P4:0.021, P6:0.034
DBP (mmHg)	74.44 ± 8.56	81.04 ± 10.32	73.13 ± 8.32	80.00 ± 10.84	0.012*	0.12	P4:0.033
	Median (IQR)						
FBS (mg/dL)	94.00(20.3)	100.50(12.5)	127.50(72.3)	126.50(81.0)	<0.001*	0.24	P2,P3,P4,P5:<0.001
eAG (mg/dL)	102.40(28.70)	105.41(24.39)	152.77(53.96)	159.51(94.42)	<0.001*	0.37	P2,P3,P4,P5:<0.001
HbA1C (%)	5.20(1.00)	5.30(0.85)	6.95(1.88)	7.19(3.29)	<0.001*	0.37	P2,P3,P4,P5:<0.001

No statistically significant differences were observed in albumin, LDL-C, or HDL-C levels among females across the four study groups ($P > 0.05$). HDL-C in males showed a statistically significant difference among the groups ($P = 0.012$, $\eta^2 = 0.23$), with a significantly higher level in G4 compared with G2 ($P = 0.008$). Triglycerides (TG) also showed statistically significant differences among the groups ($P = 0.015$, $\eta^2 = 0.09$), with post hoc analysis indicating significantly higher levels in G2, G3, and G4 compared with G1 ($P = 0.030$, $P = 0.008$, and $P = 0.003$, respectively). No statistically significant differences were observed in adiponectin levels among the study groups ($P = 0.855$, $\eta^2 = 0.02$), as shown in (Table 2).

Table 2: Serum albumin, lipid profile, and adiponectin levels across study groups

Variables		Mean ± SD				P value	Eta Squared	Significant pairwise comparisons
		G1(18)	G2(24)	G3 (24)	G4 (24)			
Albumin(g/dl)		4.04 ± 0.38	4.22 ± 0.47	4.20 ± 0.25	4.14 ± 0.18	0.320	0.04	
Total cholesterol (mg/dL)		158.17 ± 32.05	165.58 ± 32.38	174.96 ± 44.37	183.46 ± 49.07	0.204	0.05	
HDL (mg/dL)	Male	38.22 ± 10.76	33.33 ± 8.76	41.25 ± 8.79	47 ± 10.47	0.012*	0.23	P5:0.008
	Female	49.44 ± 10.64	49.75 ± 13.59	53.50 ± 15.02	47.92 ± 11.74	0.757	0.03	
LDL (mg/dL)		94.56 ± 26.66	97.71 ± 33.77	92.50 ± 33.81	101.67 ± 39.72	0.812	0.01	

	Median (IQR)						
TG (mg/dL)	95.00(56)	121.50(53)	136.00(91)	132.50(91)	0.015*	0.09	P1:0.030, P2:0.008, P3:0.003
Adiponectin(ng/ml)	15.27(5.88)	15.81(4.72)	14.97(3.97)	15.32(5.20)	0.855	0.02	

Regarding renal function parameters, no statistically significant differences were found in eGFR, blood urea nitrogen to creatinineratio (BUN/Creatinine ratio), or serum electrolytes (sodium and potassium) ($P > 0.05$), with very small effect sizes. However, a statistically significant difference was observed in the UACR ($P = 0.006$, $\eta^2 = 0.13$), indicating a moderate effect size, as shown in (Table 3).

Table 3: Comparison of kidney function parameters, electrolytes, and urinary albumin-to-creatinine ratio across study groups.

Variables		Mean ± SD				P value	Eta Squared	Significant pairwise comparisons
		G1(18)	G2(24)	G3 (24)	G4 (24)			
BUN: Creatinine Ratio (mg/dL)		13.61 ± 5.24	13.90 ± 4.80	14.88 ± 5.12	15.82 ± 6.30	0.518	0.03	
Electrolyte (mmol/l)	K	4.58 ± 0.91	4.48 ± 1.02	4.83 ± 1.01	4.47 ± 0.61	0.475	0.03	
	Na	140.56 ± 4.73	143.75 ± 8.30	143.63 ± 11.66	140.75 ± 6.39	0.409	0.03	
eGFR (mL/min)		105.30± 17.53	96.93 ± 23.75	100.63 ± 20.49	104.84 ± 20.72	0.501	0.02	
		Median (IQR)						
UACR (mg/g)		8.06(5.98)	16.58(21.94)	23.17(41.56)	10.70(23.55)	0.006*	0.13	P1:0.011, P2:<0.001

P1: G1 vs G2
P2: G1 vs G3
P3: G1 vs G4
P4: G2 vs G3
P5: G2 vs G4
P6: G3 vs G4

To further characterize renal status across the study groups, participants were classified according to kidney function (normal versus reduced) based on eGFR and UACR. Overall, normal kidney function was observed in 69.4% of participants (n = 50), whereas reduced kidney function was identified in 30.6% (n = 22). In the G3 group, 58.3% of participants (n = 14) exhibited normal kidney function, while 41.7% (n = 10) showed reduced kidney function. In the G2 group, normal kidney function was present in 75.0% of participants (n = 18), compared with 25.0% (n = 6) who demonstrated reduced kidney function. Similar proportions were observed in the G4 group, where 75.0% of participants (n = 18) had normal kidney function and 25.0% (n = 6) had reduced kidney function. Despite these observed differences in proportions, no statistically significant differences in kidney function status were detected among the study groups ($P = 0.351$), as illustrated in Figure 1.

To identify factors associated with renal dysfunction, logistic regression analysis was subsequently performed. The overall model was statistically significant ($\chi^2 = 52.788$, $P < 0.001$), with a Nagelkerke R^2 value of 0.734, indicating that the model explained approximately 73.4% of the variance in renal dysfunction. Furthermore, UACR was significantly associated with renal dysfunction (OR = 1.415, P = 0.002).

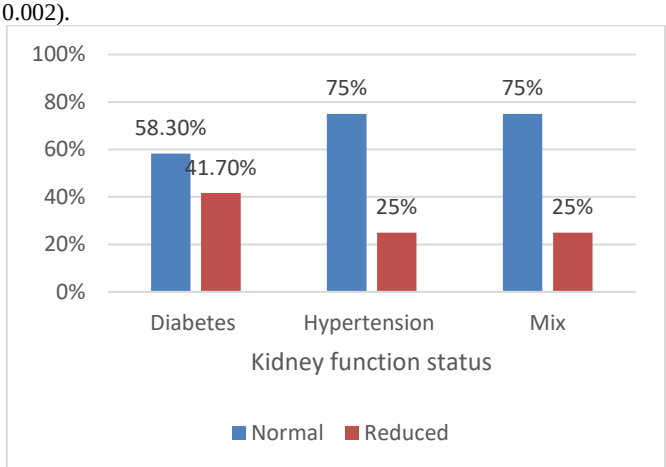

Figure 1: Distribution of Participants by Kidney Function Status (Normal vs. Reduced) Based on eGFR and UACR Across Study Groups**.**

Physical activity, defined in this study as regular walking, was assessed among treatment-adherent participants across the disease groups. Despite high levels of treatment adherence, the majority of participants were physically inactive across all groups in the study. Among individuals with G3, 55.6% (n = 10) were physically inactive, compared with 44.4% (n = 8) who reported engagement in physical activity. In the G2 group, physical inactivity was more pronounced, affecting 77.8% (n = 14) of participants, while only 22.2% (n = 4) were physically active. The G4 group exhibited the highest prevalence of physical inactivity, with 85.7% (n = 18) inactive versus 14.3% (n = 3) active. Nevertheless, no statistically significant differences were observed in physical activity levels among the studied groups ($P = 0.092$), as illustrated in Figure 2.

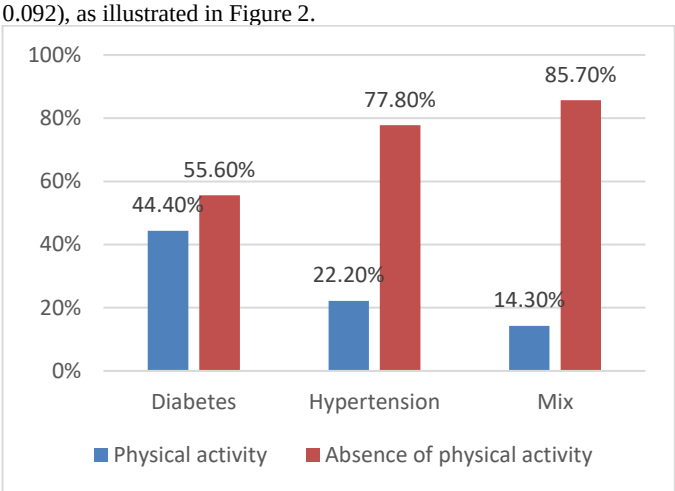

Figure 2. Physical Activity Status Among Treatment-Adherent Participants Across Disease Groups.

At the overall sample level, the majority of participants were within the normal range (93.1%, 67 cases), while 6.9% (5 cases) showed elevated CRP, indicating inflammation. In the G3 group, 79.2% (19 cases) were normal and CRP-negative, whereas 20.8% (5 cases) were CRP-positive, with females representing 60% (3 cases) and males 40% (2 cases) of the positive cases. In both the G2 and G4 groups, all cases were normal (100%, 24 cases each) with no CRP positivity. The results revealed statistically significant differences between the groups ($P = 0.005$), as illustrated in Figure 3.

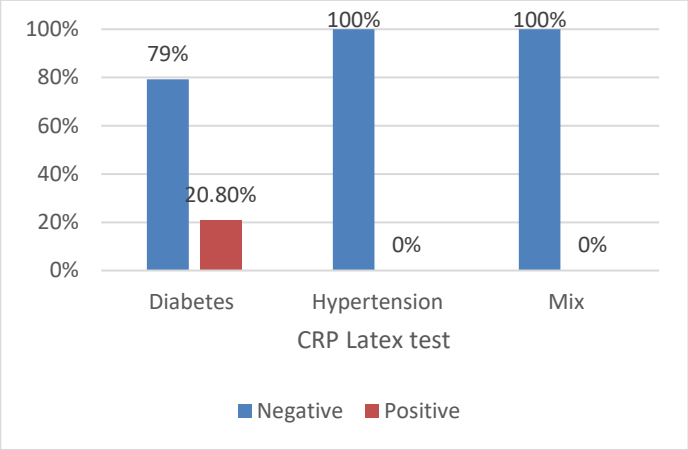

Figure 3: Percentage Distribution of Participants According to CRP Test Positivity in the Studied Disease Groups.

The results presented in Tables 4, 5, and 6 indicated that adiponectin data were not normally distributed. Therefore, the values were expressed as the median and interquartile range [Median (IQR)], and comparisons between groups were performed using the Mann–Whitney U test. The analysis revealed no statistically significant differences across most of the studied variables ($P > 0.05$), with effect sizes (η^2) ranging from small to moderate. The only exception was the dietary pattern variable in G4 group, which showed a statistically significant difference ($P = 0.014$) with a large effect size ($\eta^2 = 0.25$).

Tables 4,5,6. Median adiponectin levels across demographic and clinical subgroups in the (G2, G3, G4) groups.

Table 4: Median adiponectin levels across subgroups stratified by gender, duration of disease, diet and physical activity in G2group

Variables		Median(IQR) Adiponectin levels(ng/ml)	P value	Eta Squared
Genders	Male (12)	15.81(3.02)	>0.999	0.02
	Female (12)	15.52(6.58)		
Duration	≤5years(12)	16.53(9.19)	0.248	0.06
	>5years(12)	14.91(4.56)		
Diet	Random(13)	15.79(6.35)	0.664	0.008
	Regular(11)	15.82(4.18)		

Table 5: Median adiponectin levels across subgroups stratified by gender, duration of disease, diet and physical activity in G3 group

Variables		Adiponectin levels(ng/ml)	value	Squared
Genders	Male (12)	15.61(3.33)	0.260	0.05
	Female (12)	13.00(4.46)		
Duration	≤5years(14)	15.32(5.17)	0.838	0.002
	>5years(10)	14.47(2.86)		
Diet	Random(12)	13.99(3.33)	0.977	0.02
	Regular(12)	15.50(5.37)		

Table 6: Median adiponectin levels across subgroups stratified by gender, diet, sequential onset of diseases, and physical activity in G4 group.

Variables		Median(IQR) Adiponectin levels(ng/ml)	P value	Eta Squared
Genders	Male (12)	15.59(5.15)	0.773	0.003
	Female (12)	14.59(5.66)		
Diet	Random(13)	15.73(4.25)	0.014*	0.25
	Regular(11)	13.73(3.91)		
Sequential onset of diseases	Sequential onset(14)	14.54(4.14)	0.178	0.08
	Concurrent(10)	16.54(4.77)		

Table7 presents the results of the ROC analysis, which indicate that adiponectin used alone demonstrated a moderate diagnostic ability to discriminate between the studied conditions, with an AUC of 0.674, which was statistically significant ($P = 0.020$). At a cutoff value of >17.46, the sensitivity was 58.8%, while the specificity reached 78.18%. The PPV and NPV were 45.45% and 86%, respectively. In addition, the positive likelihood ratio (+LR) was 2.70, and the negative likelihood ratio (−LR) was 0.53, resulting in an overall diagnostic accuracy of 73.61%.

Conversely, the cutoff value of >1.67 demonstrated a markedly improved diagnostic performance, with an AUC of 0.934, indicating excellent discriminatory ability. At this threshold, the sensitivity reached 86% and the specificity 90%. Furthermore, the PPV was 80%, while the NPV was notably high at 95.74%. The positive likelihood ratio increased to 9.09, whereas the negative likelihood ratio decreased to 0.10, resulting in an overall diagnostic accuracy of 90.28%, as illustrated in Figure 4.

ROC analysis demonstrated that the UACR/Adiponectin ratio had excellent diagnostic performance, with an area under the curve (AUC) of 0.934 ($P < 0.001$, 95% CI: 0.872–1.000), compared with adiponectin alone, which showed moderate diagnostic ability (AUC = 0.674, $P = 0.015$, 95% CI: 0.544–0.827).

Table 7: Diagnostic Performance of Adiponectin UACR/Adiponectin ratio for the Studied Condition.

Cutoff	AUC	Sensitivity	Specificity	PPV	NPV	+LR	-LR	Accuracy
>17.46	0.674	58.82%	78.18%	45.45%	86%	2.70	0.53	73.61%
>1.67	0.934	86%	90%	80%	95.74%	9.09	0.10	90.28%

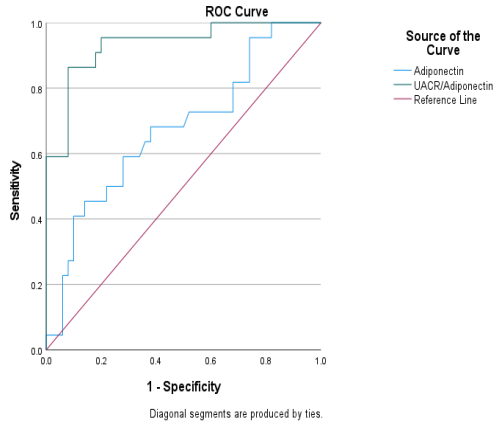

Figure 4: Analysis of the Area Under the Curve for Adiponectin Hormone and UACR/Adiponectin ratio in patients.

4. Discussion

Hypertension and diabetes are key contributors to the development of CKD, acting synergistically to induce damage in the renal microvasculature by increasing glomerular pressure, which leads to hyper filtration and a gradual decline in eGFR [27]. The study results demonstrated that FBS and HbA1c levels were significantly elevated in patients with diabetes, as well as in individuals with both diabetes and hypertension, with effect sizes ranging from $\eta^2 = 0.24$ to 0.37. This elevation reflects poor metabolic control and an increased risk of diabetes-related complications. Furthermore, this group exhibited a higher proportion of individuals with reduced renal function (41.70%) compared to those with normal renal function (58.30%), indicating a preliminary impact of metabolic disturbances on kidney function. These findings are consistent with previous literature showing that patients with diabetes, particularly those with long-standing disease or poor glycemic control, are susceptible to a wide range of metabolic complications, including blood pressure disorders and renal function decline [28], and are further supported by the American Diabetes Association guidelines linking elevated HbA1c to an increased risk of cardiovascular and renal complications [29].

Obesity, as reflected by BMI, which showed a significant difference between groups ($\eta^2 = 0.09$, $P = 0.036$), was associated with increased visceral fat accumulation, subsequently contributing to low-grade chronic inflammation and insulin resistance [30].The analysis also

indicated marked dyslipidemia among patients with diabetes, including elevated TG and reduced HDL levels, resulting from increased lipolysis in adipose tissue and impaired regulation of lipoprotein lipase, leading to the accumulation of cholesterol-rich lipoproteins and enhanced hepatic synthesis of triglycerides and cholesterol [31]. The results of the study showed gender differences in HDL levels, with higher values observed in females compared with males across most study groups. These findings are consistent with previous studies [32]. These findings suggest that obesity and diabetes-related dyslipidemia, along with decreased adiponectin levels associated with higher BMI, constitute major factors promoting metabolic and cardiovascular complications in this patient population. Blood pressure measurements indicated vascular dysfunction and increased peripheral resistance in patients with hypertension, whether alone or in combination with diabetes, with a moderate to high clinical effect ($\eta^2 = 0.12–0.18$). These findings suggest that hypertension is the primary driver of vascular impairment, while diabetes exacerbates this condition through metabolic disturbances and insulin resistance. These results are consistent with recent recommendations emphasizing the importance of strict blood pressure control (<130/80 mmHg) to reduce cardiovascular risks [33,34]. The results indicated that most renal and electrolyte parameters remained relatively stable within normal ranges, with no clear evidence of kidney dysfunction or electrolyte imbalance. This stability is likely attributable to the gradual, long-term effects of hypertension and diabetes on renal function, as well as the protective role of pharmacological management and regular clinical follow-up, suggesting preserved kidney function in this patient cohort [35].

The study identified the UACR as the only marker showing a statistically significant difference between groups, with higher values observed in diabetic patients. These modest elevations in UACR may represent an early stage of renal changes that precede more pronounced disturbances in kidney function and electrolyte balance.

Logistic regression analysis further revealed a significant association between the U ACR and renal dysfunction (OR = 1.415, p = 0.002), indicating that each one-unit increase in UACR is associated with a 1.415-fold higher likelihood of impaired kidney function. This finding reinforces the well-established role of UACR as an early marker of renal damage, reflecting increased protein leakage into the urine due to glomerular barrier dysfunction or reduced filtration efficiency. These results are consistent with previous studies demonstrating that elevated UACR is associated with a higher risk of kidney function decline and serves as a sensitive early indicator of nephropathy, particularly among patients with diabetes and hypertension [36]. Recent evidence also indicates that increased UACR is linked to a higher risk of acute kidney injury and decreased glomerular filtration rate, further supporting its utility as a predictive marker for early renal dysfunction [37].

Serum albumin, an important indicator of nutritional status and hepatic and renal function, did not differ significantly between groups, indicating preserved protein retention by the kidneys and relatively stable nutritional and liver status in this cohort [38]. These findings support the hypothesis that mild elevations in UACR may represent the earliest detectable sign of renal involvement before broader dysfunction occurs [39].

Studies suggest that the effect of physical activity on adiponectin depends on both the intensity and duration of exercise, which may explain the lack of statistical significance in samples with limited activity [40]. Additionally, 20.8% of participants were positive for CRP, which may further contribute to reduced adiponectin levels due to the well-known inverse relationship between adiponectin and low-grade inflammation [30]. Analysis of the interaction between physical activity and treatment showed that 44.40% of participants both exercised and received treatment simultaneously, whereas 55.60% received treatment without regular activity, reflecting the limited engagement in physical activity among treated individuals and partially explaining the unexpected trend of lower adiponectin levels in this cohort [41,42].

Although no statistically significant differences in adiponectin levels were observed among the studied groups or according to sex, physical activity level, disease duration, and dietary patterns, these findings suggest a relatively similar metabolic behavior of this adipokine across the different chronic conditions investigated. This observation is consistent with previous studies indicating that hormonal differences between males and females may become less pronounced in the context of chronic metabolic disorders, such as diabetes mellitus and hypertension, particularly during the stable stages of disease progression [45,47].

ROC curve analysis demonstrated that adiponectin may have limited to moderate discriminative ability for assessing renal dysfunction based on renal markers such as the UACR and eGFR. These findings indicate that adiponectin alone may not provide sufficient diagnostic accuracy to distinguish between different clinical groups; however, its diagnostic value may increase when interpreted in combination with indicators of renal injury. Therefore, adiponectin may reflect alterations associated with kidney function rather than serving as an independent predictor of disease progression, which is in agreement with previous evidence [43,44].

In the diabetes group, males exhibited a higher median adiponectin level than females ($P = 0.260$; $\eta^2 = 0.05$), which contrasts with most previous studies reporting higher adiponectin concentrations in females. Notably, 12.5% of female participants and 8.3% of males were positive for CRP, indicating the presence of low-grade inflammation. Given that adiponectin typically decreases in chronic inflammatory states, these positive cases likely contributed to lower adiponectin levels, particularly in females, thereby reversing the usual sex-related trend [46].

Importantly, the combined use of the UACR/Adiponectin ratio demonstrated markedly improved diagnostic performance, providing higher sensitivity and specificity and enabling more accurate early detection of renal dysfunction. This suggests that integrating metabolic and inflammatory markers with direct measures of renal injury can significantly enhance predictive accuracy, highlighting the clinical value of composite biomarkers for early kidney disease assessment.

5. Strengths of the Study

This study comprehensively evaluated serum adiponectin and the UACR/adiponectin ratio across four well-defined participant groups, providing evidence that this ratio may complement conventional renal biomarkers for the early identification of renal dysfunction in patients with hypertension and type 2 diabetes.

6. Clinical Implications

The UACR/adiponectin ratio could serve as a complementary marker for early detection of renal dysfunction in patients with diabetes and hypertension. Incorporating this ratio into routine clinical assessment may improve risk stratification and enable earlier preventive strategies.

7. Limitations

This study has several limitations. The sample size was relatively small and drawn from a single institution, which may limit generalizability. Data were partly self-reported, potentially introducing response bias. The study's short duration also precluded long-term follow-up, limiting the assessment of progressive renal outcomes.

8. References

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