OBAT: Jurnal Riset Ilmu Farmasi dan Kesehatan
Volume. 4 Nomor. 1 Januari 2026
e-ISSN : 3031-0148; p-ISSN : 3031-013X, Hal. 01-16
DOI: https://doi.org/10.61132/obat.v4i1.1960
Tersedia: https://journal.arikesi.or.id/index.php/OBAT

Serum Irisin and Asprosin Levels as Potential Biomarkers an Type 2 Diabetes Mellitus and its Renal Complications: A Biochemical Investigation of Hormonal and Metabolic Profiles

Aqeel M. Rasool [1,*], Alaa Hussein J. Al-Qaisi[2]
[1] Ministry of Education, Directorate of Education Al-Muthanna, Al-Samawah, Al-Muthanna, Iraq.
[2] Department of Chemistry, College of Science, Al-Nahrain University, Jadriya, Baghdad, Iraq.
*Korespondensi Penulis: aqeelchem122@gmail.com

Abstract. *This study investigates the levels of asprosin and irisin in patients with type 2 diabetes mellitus (T2DM) and diabetic nephropathy (DN), and evaluates their relationships with insulin resistance, glycemic control, and renal function. Additionally, it explores their diagnostic performance as potential non-invasive biomarkers for the early detection of DN using ROC curve analysis. A controlled prospective study was conducted involving 130 participants, categorized into healthy controls, T2DM patients, and T2DM with DN. Serum asprosin, irisin, and insulin levels were measured using ELISA, while biochemical and renal parameters such as fasting blood glucose, HbA1c, creatinine, urea, and eGFR were assessed using standard spectrophotometric techniques. ROC analysis was employed to assess the diagnostic accuracy of asprosin and irisin. Asprosin levels were significantly elevated, while irisin levels were markedly reduced in DN patients compared to T2DM and control groups ($p < 0.001$). Moreover, DN patients exhibited higher levels of fasting glucose, HbA1c, HOMA-IR, creatinine, and urea, with lower eGFR, indicating substantial renal dysfunction. ROC analysis revealed that asprosin had an AUC of 0.910 (95% CI: 0.839–0.981), with 90.0% sensitivity and 88.9% specificity at a cutoff value of 11.27 ng/mL. Irisin showed an AUC of 0.886 (95% CI: 0.812–0.960), with 95.0% sensitivity and 71.1% specificity at a 158.25 ng/mL cutoff. Asprosin and irisin are strongly associated with insulin resistance and renal impairment in patients with T2DM and DN. Their high diagnostic performance supports their utility as promising non-invasive biomarkers for the early detection and monitoring of diabetic nephropathy progression.*

Keywords: *Adipocytokine, Asprosin, Diabetic nephropathy, Insulin resistance, Irisin*.

1. INTRODUCTION

Diabetes Mellitus (DM) is an endocrine disorder characterized by hyperglycemia. Diabetes mellitus is a prevalent and rapidly increasing condition globally, resulting from insufficient insulin synthesis by the pancreas or the body's ineffective utilization of the generated insulin (1) . Type 2 diabetes mellitus (T2D) is the predominant kind of diabetes mellitus (2) . T2D is a multifaceted disorder influenced by several genetic and environmental variables. Genetic variations now linked to susceptibility to Type 2 Diabetes account for just 10% of the hypothesized "primary" contribution to the risk of T2D (3). The World Health Organization (WHO) estimates that approximately 426 million people worldwide live with diabetes. It further reports that between 91% and 94% of these cases are classified as type 2 diabetes, underscoring its predominance among diagnosed forms of the disease (4). The illness predominantly impacts adipose tissue and skeletal muscles, as well as the liver, affecting insulin receptors, the signal transduction pathway, and/or effector enzymes or genes (5). Numerous issues associated with T1DM or T2D impact essential organs, such as the kidneys

Naskah Masuk: 10 November 2025; Revisi: 30 November 2025; Diterima: 20 Desember 2025; Terbit: 30 Desember 2025

(nephropathy). Diabetic nephropathy (DNP) is a significant medical problem associated with diabetes mellitus (DM), since it has emerged as the primary cause of end-stage kidney damage in recent years (6). The diagnosis requires urine and blood examinations, while care generally includes enhancing diabetes regulation by blood glucose monitoring, blood pressure management, dietary adjustments, and cessation of smoking (7)(8).

Insulin resistance (IR) and modified adipocytokine functions are becoming acknowledged as critical factors in the pathogenesis of diabetic nephropathy (DN). Studies demonstrate that adipose tissue dysfunction, marked by the secretion of pro-inflammatory adipocytokine, is crucial in advancing diabetic nephropathy (DN) (9). This overview will examine the correlation among insulin resistance, adipocytokines, and diabetic nephropathy**.**

Numerous secretory proteins and peptides (adipokines) originating from adipose tissue, including as irisin, adropin, and chemerin, have been found; Dysregulation in their synthesis and activity is linked to metabolic disorders. Brown adipose tissue and white adipose tissue are two varieties of adipose tissue that release different categories of adipokines (10)**.**

The FBN1 gene encodes asprosin as part of the profibrillin protein, and Specialized proteases cleave profibrillin at the C-terminus to release asprosin. This hormone stimulates glucose release from the liver via a cyclic adenosine monophosphate (cAMP) dependent mechanism (11). White adipose tissue primarily synthesizes asprosin, while its target cells are widely distributed throughout the human body. Researchers have identified asprosin receptors predominantly within the paraventricular nucleus of the hypothalamus, located in the brain's cerebral cortex. In addition, significant expression of asprosin receptors has been observed in peripheral metabolic tissues, including the pancreas, liver, myocardium, and skeletal muscle (12). Asprosin has a diurnal rhythm, with its secretion quantities affected by dietary intake and physical activity. It employs the olfactory receptor OLFR724 to modulate hepatic glucose production and sustain glucose homeostasis (13).

Irisin is a hormone that was identified in 2012 within mouse skeletal muscle (14). It pertains to adipocytokines due to its effects on adipose and muscle tissues (adipokine and myokine). Irisin consists of 112 amino acid residues (12 kDa), and its chemical structure exhibits no species diversity; specifically, the chemical structures of irisin in humans, rats, and mice are similar (15). Irisin increases energy expenditure, decreases weight, improves diet-induced insulin resistance, and extends life. Thus, irisin reduces fat and insulin resistance. This process explains why exercise is important for reducing the impact on health policy/practice/research /medical education. Dysregulated energy expenditure in chronic renal

failure causes protein-energy waste and higher mortality. The mechanisms of energy expenditure dysregulation in chronic renal failure remain unknown (16).

Currently, little research examines the relationship between irisin and asprosin levels in patients with diabetic nephropathy. Therefore, this study aims to evaluate the circulating levels of asprosin and irisin in patients with type 2 diabetes mellitus (T2DM) and those with diabetic nephropathy (DN), and to explore their relationships with glycemic control, insulin resistance, and renal function markers. We hypothesize that elevated serum asprosin and reduced irisin levels are independently associated with the progression of diabetic nephropathy and may serve as sensitive, non-invasive biomarkers for its early detection. Furthermore, we assess their diagnostic performance using ROC curve analysis to determine their utility in clinical risk stratification for diabetic kidney disease.

2. MATERIALS AND METHODS

Data and Study Participants

This study employed a cross-sectional, case-control design conducted between April and November 2024 in Muthanna Province, Iraq. Participants were recruited from the Specialized Center for Endocrinology and Diabetes and Al-Hussein Teaching Hospital. Sample size estimation was based on previous studies examining serum asprosin and irisin levels in diabetic populations, aiming for a power of 80% and $\alpha = 0.05$ to detect a medium effect size. A total of 130 participants were included, stratified into three groups: healthy controls (n=40), T2DM without nephropathy (n=45), and T2DM with nephropathy (n=45). Diabetic nephropathy (DN) was diagnosed when at least two of the following three clinical criteria were met : elevated levels of creatinine in the blood (> 1.1 in males or > 0.9 in females), a weakened estimated glomerular filtration rate (eGFR <90 min/mL/1.73 m^2), and distinctive findings indicative of diabetic nephropathy on renal imaging or biopsy, offered there is no other primary kidney disease present. This work was approved by Al-Nahrain University, College of Science, Department of Chemistry, Baghdad, and by the Iraqi Ministry of Health's Research Ethics Committee, Iraq. Ethical number: (2/3/735 at 5/2/2024)

Exclusion criteria

The study excluded individuals with type 1 diabetes, kidney diseases unrelated to diabetes, any current or previous history of cancer, severe cardiovascular conditions, gestational diabetes, autoimmune disorders, thyroid-related diseases, or those taking medications known to be nephrotoxic, such as naproxen, aminoglycosides, and methotrexate (17)(18).

Sample Collection Procedures

Blood samples were collected from all participants using standard venipuncture protocols. Samples were promptly transferred under controlled conditions to the laboratory for processing. From each participant, 10 milliliters of venous blood were drawn—8 mL were placed in gel tubes for general biochemical analyses, and 2 mL was drawn in EDTA tubes for A1c testing. Following standardized procedures, gel tubes were centrifuged at 3500 rpm for 12 minutes to isolate the serum. The resulting serum samples were then stored at −20°C until analysis. All procedures were conducted in compliance with accepted ethical guidelines and relevant legal regulations. Verbal informed consent was obtained and documented for each participant within the questionnaire prior to sample collection.

Hormone and Analytical Assessment

Asprosin, irisin, and insulin levels in serum were quantified using ELISA kits from MyBioSource (USA). Biochemical parameters, including urea, creatinine, HbA1c, lipid profile, and glucose, were assessed spectrophotometrically using commercial kits from Biosystem Company (Spain). Medical history was obtained from all participants, covering symptoms, treatment history, family history, age, and BMI. Insulin resistance was evaluated using the Homeostasis Model Assessment of Insulin Resistance (HOMA-IR), calculated by the formula: HOMA-IR = ([glucose] × [insulin] / 405). a HOMA-IR of ≥2.5 indicates insulin resistance (19)**.**

Statistical Analysis

The information collected was analyzed using the statistical program SPSS Software, edition 27.1.1 (Armonk, NY, USA). A one-way analysis of variance (ANOVA) was utilized for comparing the mean values through at least three different groups. A post hoc test, specifically Tukey's test, was performed after ANOVA to evaluate the statistical significance of the difference between the two categories. Results are presented as mean ± standard deviation (SD), with statistical significance at $P < 0.05$. Pearson's correlation coefficient was calculated to assess the association between asprosin, irisin, and other measured variables.

3. RESULTS

Table 1 summarizes the descriptive statistics for the control, type 2 diabetes (T2D), and diabetic nephropathy with T2D (NP+T2D) groups. The groups were comparable in body mass index (BMI), with no statistically significant differences. Patients with T2D and NP+T2D exhibited significantly elevated markers of glucose metabolism, including FBS, HbA1c, insulin, and HOMA_IR, in relation to healthy controls. In addition, participants in the T2D and

NP+T2D groups showed significantly higher values for age, total cholesterol (TC), triglycerides (TG), and (LDL-C), along with significantly lower levels of (HDL-C), relative to the control group. Renal function parameters also varied significantly between the groups. Serum creatinine was elevated in both T2D and NP+T2D patients compared to controls, while urea levels were specifically higher in the NP+T2D group than in both the T2D and control groups. Furthermore, the (eGFR) was markedly reduced in NP+T2D patients relative to the other study groups.

Table 1. Descriptive statistics and biochemical study of T2D patients in comparison to healthy individuals.

Variables	Controls [40] (mean ± SD)	(T2D) [45] (mean ± SD)	(NP +T2D) [45] (mean ± SD)	P-value
Age	50.57 ± 5.55	54.02 ± 5.59	55.13 ± 5.01	<0.001
BMI	29.99 ± 2.75	29.95 ± 2.96	30.42 ± 2.83	0.694
FBG(mg/dl)	95.17 ± 9.46	230.56± 40. 13	251.37± 34.29	<0.001
Insulin(µIU\ml)	5.536 ± 0.707	10.374 ± 0.817	15.764 ± 1.187	<0.001
HOMA-IR	1.299 ± 0.207	5.877 ± 0.952	9.491 ± 1.658	<0.001
HbA1c (%)	5.018 ± 0.394	8.553 ± 0.979	9.289 ± 0.932	<0.001
Urea(mg/dl)	31.65 ± 6.94	36.13 ± 6.39	48.04 ± 10.44	<0.001
Cr (mg/dl)	0.65 ± 0.10	0.67 ± 0.08	1.55 ± 0.54	<0.001
eGFR (mL/min/1.73cm^2)	116.45 ± 12.92	108.78 ± 6.65	53.98 ± 17.98	<0.001
TC (mg/dl)	165.79 ±15.54	179.17 ± 25.59	205.95 ± 33.24	<0.001
TG (mg/dl)	125.72 ± 23.53	159.05 ± 27.99	175.96 ± 33.94	<0.001
LDL-C (mg/dl)	112.78 ± 19.05	125.69 ± 24.82	140.51 ± 29.62	<0.001
HDL-C(mg/dl)	38.97 ± 8.11	29.88 ± 6.12	29.57 ± 4.81	<0.001
Asprosin(ng\ml)	8.50 ± 1.08	14.36 ± 1.38	18.16 ± 1.77	<0.001
Irisin(ng\ml)	357.51 ± 35.07	205.38 ± 21.13	172.37 ± 17.64	<0.001

**P < 0.0010 (highly significant), P < 0.050 (significant), and P > 0.050 (not significant). FBG – fasting blood glucose; BMI – body mass index; HOMA-IR – homeostatic model assessment for insulin resistance; HbA1c – glycosylated hemoglobin; eGFR – estimated glomerular filtration rate; Cr – creatinine; TG – triglycerides; TC – total cholesterol; LDL-C – low-density lipoprotein cholesterol; HDL-C – high-density lipoprotein cholesterol; T2D – type 2 diabetes mellitus; NP – nephropathy.

Moreover, circulating levels of asprosin showed a significant elevation (P = 0.0010) in the diabetic nephropathy group (NP+T2D), with a mean concentration of 18.16 ± 1.77 ng/mL,

compared to both the T2D group (14.36 ± 1.38 ng/mL) and the apparently healthy individuals (8.50 ± 1.08 ng/mL). In contrast, circulating irisin concentrations were markedly reduced in the NP+T2D (172.37 ± 17.64 ng/mL) and T2D (205.38 ± 21.13 ng/mL) groups compared to the healthy group (357.51 ± 35.07 ng/mL), with the differences reaching statistical significance (P = 0.001). These findings are illustrated in (Figure 1,2).

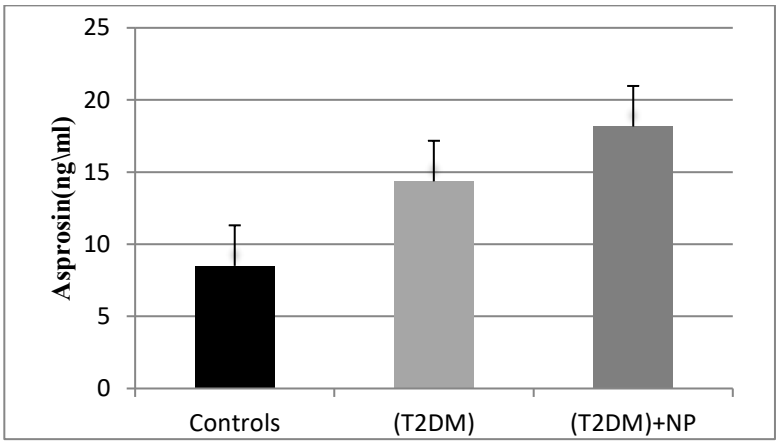

Figure 1. Comparison of asprosin levels in both T2D, NP+T2D and control groups. Data are presented as mean ± SD. Statistical significance: $p < 0.05$, $P < 0.0010$.

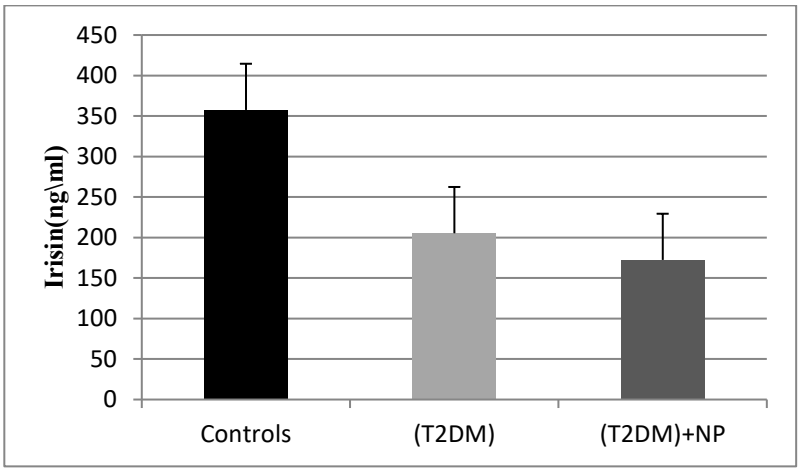

Figure 2. Comparison of irisin levels in both T2D, NP+T2D and control groups. Data are presented as mean ± SD. Statistical significance: $p < 0.05$, $P < 0.0010$.

Table 2 illustrates the correlation between asprosin and irisin circulating levels and various metabolic and renal parameters in subjects diagnosed with T2D and diabetic nephropathy (DN). In the DN group, elevated serum asprosin levels were significantly positively correlated with BMI, fasting blood glucose (FBG), creatinine, triglycerides (TG), and HOMA-IR while demonstrating strong negative associations with irisin, insulin, and

HbA1c. Additionally, irisin levels in this group were positively correlated with creatinine but inversely correlated with estimated glomerular filtration rate (eGFR) and HbA1c. In the T2D cohort, asprosin levels were positively correlated with FBG, BMI, HbA1c, total cholesterol (TC), and HOMA-IR. Conversely, significant negative correlations were observed between asprosin, irisin, and insulin. On the other hand, blood irisin levels were inversely associated with insulin, creatinine, TG, and eGFR but exhibited positive correlations with HbA1c, FBG, and HDL-C.

Table 2. Pearson correlation study of asprosin and irisin with other markers in both T2D and NP+T2D

Variable	Asprosin		Irisin	
	r	p	r	p
diabetic nephropathy (DN)				
Age	- 0.046	0.764	- 0.058	0.704
BMI	0.373*	0.012	- 0.022	-.884
FBS	0.317*	0.034	- 0.077	0.617
Insulin	- 0.213	0.160	- 0.189	0.215
HbA1c	- 0.356*	0.016	- 0.257	0.088
Urea	0.034	0.824	0.048	0.752
Creatinine	0.349*	0.019	0.157	0.302
eGFR	- 0.306*	0.041	- 0.190	0.211
HOMA-IR	0.141	0.356	0.167	0.273
TC	0.047	0.759	0.126	0.410
TG	0.202	0.183	0.107	0.484
LDL	0.123	0.421	- 0.198	0.193
HDL	- 0.057	0.710	0.097	0.527
Asprosin	1	---	- 0.412**	0.005
Irisin	- 0.412**	0.005	1	---
diabetes mellitus (T2D)				
Age	-0.023	0.879	- 0.090	0.558
BMI	0.245	0.105	- 0.091	0.554
FBG	0.285	0.058	0.174	0.254
Insulin	- 0.152	0.319	- 0.161	0.291
HbA1c	0.355*	0.017	0.167	0.272
Urea	- 0.069	0.653	0.069	0.653
Creatinine	0.048	0.756	- 0.036	0.828
eGFR	0.064	0.674	- 0.183	0.230
HOMA-IR	0.184	0.227	0.021	0.889
TC	0.263	0.081	0.047	0.758

TG	- 0.258	0.087	- 0.082	0.593
LDL-c	- 0.190	0.211	0.054	0.723
HDL-c	0.049	0.751	0.212	0.163
Asprosin	1	---	- 0.202	0.184
Irisin	- 0.202	0.184	1	---

To further assess the diagnostic accuracy of serum Asprosin and Irisin in identifying diabetic nephropathy (DN) among patients with T2DM, ROC curve analysis was conducted. Table 3 summarizes the key parameters of diagnostic accuracy for both biomarkers. For Asprosin, the area under the curve (AUC) was 0.910 (95% CI: 0.839 – 0.981; $p < 0.001$), indicating excellent discriminative power. The optimal cutoff value was 11.27 ng/mL, which provided a sensitivity of 90.3% and a specificity of 88.9%. For Irisin, the AUC reached 0.886 (95% CI: 0.812 – 0.960; $p < 0.001$), reflecting strong predictive capability. The optimal cutoff point was identified at 158.25 ng/mL, achieving 95.0% sensitivity and 71.1% specificity. The results underscore the diagnostic potential of Asprosin and Irisin as promising non-invasive biochemical markers for the early identification of diabetic nephropathy. The ROC curves are illustrated in Figures 3 and 4.

Table 3. Diagnostic performance of serum Asprosin and Irisin levels in identifying diabetic nephropathy based on ROC curve analysis.

Variable	AUC (95% CI)	Cutoff Value	Sensitivity (%)	Specificity (%)	p-value
Asprosin	0.910 (0.839–0.981)	11.27	90.0	88.9	<0.001
Irisin	0.886 (0.812–0.960)	158.25	95.0	71.1	<0.001

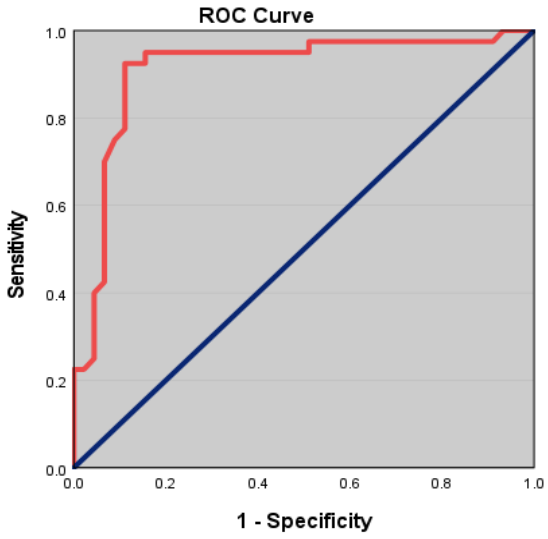

Figure 3. ROC curve of serum Asprosin for the detection of diabetic nephropathy.

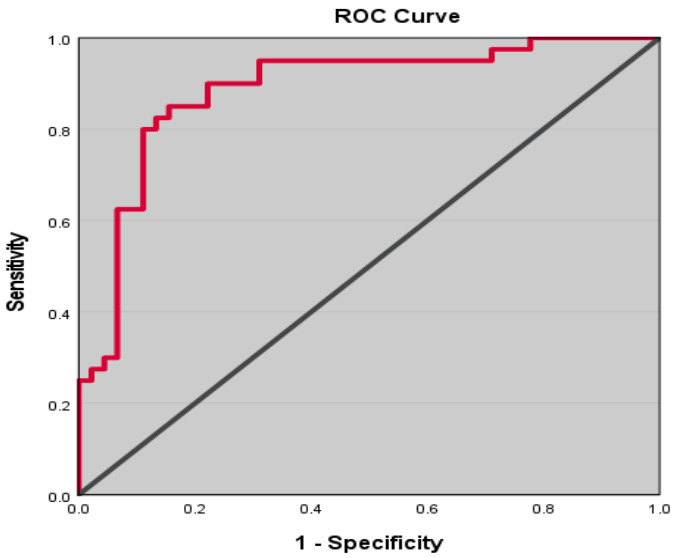

Figure 4. ROC curve of serum Irisin for the detection of diabetic nephropathy.

4. DISCUSSION

Both the T2D and NP+T2D groups compared to healthy controls, after adjustment for confounders including age, sex, and BMI. Additionally, individuals with diabetic nephropathy exhibited significantly higher asprosin levels than those with T2D alone. In contrast, circulating irisin concentrations were markedly lower in both T2D and NP+T2D patients relative apparently healthy individuals. Our results are in agreement with earlier reports (20,21) which similarly reported dysregulation of asprosin and irisin levels in diabetic and nephropathic conditions. Adipose tissue is now recognized as a dynamic endocrine organ contributing to energy homeostasis, insulin sensitivity, and overall metabolic regulation (22). Various adipokines secreted by adipose tissue influence insulin action and glucose metabolism (23). Obesity-induced insulin resistance is a well-recognized pathophysiological mechanism contributing to the development of T2D and metabolic syndrome (24). Asprosin, a novel adipokine secreted by white adipose tissue in response to fasting, stimulates hepatic glucose release and promotes insulin secretion through hypothalamic signaling across the blood-brain barrier (25). Conversely, deficiency of asprosin in humans has been associated with anorexia and fatigue. Circulating asprosin levels increase during fasting and decline significantly after food intake, supporting its role as a key regulator of glucose homeostasis (26).

The current study further supports a positive association between elevated serum asprosin levels and both T2D and diabetic nephropathy (T2D+NP), consistent with the findings reported by Romere et al. (27). These results suggest that increased circulating asprosin may act as a candidate risk marker for the development and progression of T2D. The observed elevation in

asprosin was also significantly correlated with markers of insulin resistance and impaired glucose metabolism. Although the precise mechanism underlying this elevation remains unclear, previous studies have proposed a glycogenic role for asprosin, where glucose suppresses asprosin secretion via a negative feedback loop (28). In addition to the findings discussed above, The current study revealed a significant positive association between serum asprosin levels and body mass index (BMI). This observation suggests that increased adiposity may contribute to the Dysregulation of asprosin secretion. It is plausible that excessive fat accumulation disrupts the normal functional balance of adipose tissue, alters adipokine production, and plays a role in the pathogenesis of metabolic dysfunction. These findings underscore the potential role of asprosin as a mechanistic link between obesity and insulin resistance in individuals with T2D or diabetic nephropathy (29). These results indicate that obesity could act as a critical determinant of elevated circulating asprosin levels. Furthermore, the data point to a potential link between serum asprosin and lipid metabolism. Among patients with T2D, asprosin levels were inversely and independently associated with TG and LDL-C, which may reflect asprosin involvement in hepatic lipid regulation, given its established hepatic targets. The data show a potential involvement for asprosin in the etiology of T2D and T2D+NP via mechanisms such as obesity, and insulin resistance. This study's cross-sectional methodology precludes definitive conclusions on the connection between asprosin and the aforementioned characteristics; nevertheless, more research is warranted in the future. In addition, the study identified significant correlations between serum asprosin and renal parameters, including serum creatinine and eGFR in individuals with diabetic nephropathy (T2D+NP). While previous research has reported associations between asprosin and renal biomarkers in diabetic populations, the current study highlights that such associations were not evident in T2D patients without nephropathy, suggesting a more pronounced link in the presence of renal impairment.

The existing literature presents conflicting evidence regarding circulating irisin levels in individuals with T2DM and diabetic nephropathy. In the present study, serum irisin concentrations showed a significant decrease in both T2DM and T2DM+NP groups in comparison with apparently healthy individuals. This finding aligns with previous studies that reported lower irisin levels in patients with T2DM (30)(31), in contrast to others that observed elevated levels in similar populations (32)(33). For instance, Gizaw et al. (34) reported markedly decreased irisin levels in individuals with T2DM, which is consistent with our observations. Similarly, other studies have found that recently diagnosed T2DM patients exhibit significantly lower irisin concentrations compared to individuals with normal glucose

tolerance (35). Sustained reductions in irisin levels may indicate its potential utility as a diagnostic biomarker for T2DM (36). Moreover, several studies have suggested that reduced irisin levels may reflect a diminished protective mechanism against insulin resistance and metabolic dysregulation (37). In contrast, a few reports have shown increased irisin levels associated with insulin resistance, possibly representing a compensatory response (38). These discrepancies may be attributed to differences in study populations, disease duration, BMI, physical activity levels, or comorbidities, warranting further investigation.

Shelbaya et al. (39) investigated serum irisin levels in patients with diabetic nephropathy and reported a progressive decline in irisin concentrations as the disease advanced. Their findings also revealed a positive association between irisin levels, insulin resistance, and renal function. Subsequent studies further emphasized that reduced irisin levels may contribute to the onset and progression of nephropathy in diabetic individuals (40). Our investigation revealed that irisin concentration was reduced in nephropathy patients compared to healthy individuals, corroborating the findings of this research. Notably, serum irisin levels are decreased in individuals with a GFR of 1.73 m^2 fewer than 60 mL/min compared to those with a GFR of 1.73 m^2 equal to or greater than 60 mL/min. These results indicate that serum irisin levels may correlate with creatinine and reduced GFR in patients with T2DM (41). Our investigation revealed a negative correlation between GFR and irisin.

The present ROC analysis focused on evaluating the diagnostic utility of Asprosin and Irisin in identifying diabetic nephropathy among patients already diagnosed with T2DM. Both biomarkers demonstrated strong discriminatory power, with Asprosin outperforming Irisin slightly in terms of specificity. The elevated Asprosin levels in DN cases reflect its role in hepatic gluconeogenesis and systemic metabolic stress, which are exacerbated in nephropathy. In contrast, the marked decline in Irisin levels may signal muscle-adipose endocrine dysfunction, a known feature of progressive renal disease. These findings suggest that Asprosin and Irisin could serve as adjunct non-invasive biomarkers to aid in the early detection of renal complications in diabetic individuals, potentially enabling earlier intervention and better disease management.

Additional studies are needed to elucidate the potential independent association between irisin and the progression of diabetic nephropathy (DN). In particular, carefully designed prospective research is needed to evaluate whether sustained decreases in circulating irisin levels contribute causally to the onset or worsening of DN in patients with T2DM. While it may appear early to assess the efficacy of irisin as a treatment agent for obesity or T2DM, a study has underscored its importance as a primary research focus moving forward.

This research possesses many limitations. The limited sample size and single-center design may restrict generalizability. The study's cross-sectional design limits causal inferences. Subfatin levels were evaluated utilizing a single ELISA kit devoid of inter-assay validation. Future multi-center and longterm investigations are essential to validate these findings and establish causation.

5. CONCLUSION

In conclusion, the present study highlights the significant alterations in serum asprosin and irisin levels among patients with diabetic nephropathy compared to those with type 2 diabetes without renal complications. Elevated asprosin and reduced irisin concentrations were strongly associated with impaired glycemic control, increased insulin resistance, and deteriorated renal function. The ROC curve analysis demonstrated excellent diagnostic performance for both biomarkers, particularly asprosin, in differentiating diabetic nephropathy. These findings support the potential clinical utility of asprosin and irisin as non-invasive, early diagnostic biomarkers for diabetic kidney disease. Further longitudinal and mechanistic studies are warranted to validate their prognostic value and explore their role in therapeutic monitoring.

Acknowledgment

The authors express gratitude to the College of Science, Al-Nahrain University, for endorsing this study. We extend our heartfelt appreciation to the personnel of the Specialised Centre for Endocrinology and Diabetes and Al-Hussein Teaching Hospital. This work lacks financing.

Declarations

Ethics Approval And Consent To Participate:

This work was approved by Al-Nahrain University, College of Science, Department of Chemistry, Baghdad, and by the Iraqi Ministry of Health's Research Ethics Committee, Iraq. Ethical number: (2/3/735 at 5/2/2024).

Consent to publish:

Not applicable.

Funding:

No specific grant from a public, private, or nonprofit funding organisation was obtained for this study.

Authors' Contributions

A.M.R. and A.H.A. conceived, collected, analyzed, and interpreted data and wrote and revised the text. All authors examined and approved the final article and took responsibility for all elements of it, ensuring that any accuracy or integrity concerns were rectified.

Clinical trial number:

Not applicable.

Competing interests:

The authors declare no financial or personal conflicts of interest that could have affected the integrity or interpretation of the research findings.

Data availability:

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

References

1. Jannah M, Hidayati P, Mulyadi F, Kartika I, Irmayanti I. The Relationship between HbA1c, GDP and Disease Duration on the Occurrence of Diabetic Neuropathy at Ibnu Sina Hospital. Formosa J Sci Technol. 2024 Aug 29;3:1893–904.
2. Aly RH, Ahmed AE, Hozayen WG, Rabea AM, Ali TM, El Askary A, et al. Patterns of Toll-Like Receptor Expressions and Inflammatory Cytokine Levels and Their Implications in the Progress of Insulin Resistance and Diabetic Nephropathy in Type 2 Diabetic Patients. Front Physiol. 2020;11:609223.
3. Yang M, Chen P, Jin H, Xie X, Gao T, Yang L, et al. Circulating levels of irisin in middle-aged first-degree relatives of type 2 diabetes mellitus - correlation with pancreatic β-cell function. Diabetol Metab Syndr. 2014;6(1):133.
4. Hou Q, Song R, Zhao X, Yang C, Feng Y. Lower circulating irisin levels in type 2 diabetes mellitus patients with chronic complications: A meta-analysis. Heliyon [Internet]. 2023;9(11):e21859.
5. Poznyak A, Grechko A V., Poggio P, Myasoedova VA, Alfieri V, Orekhov AN. The diabetes mellitus–atherosclerosis connection: The role of lipid and glucose metabolism and chronic inflammation. Int J Mol Sci. 2020;21(5):1–13.
6. Aly RH, Ahmed AE, Hozayen WG, Rabea AM, Ali TM, El Askary A, et al. Patterns of toll-like receptor expressions and inflammatory cytokine levels and their implications in the progress of insulin resistance and diabetic nephropathy in type 2 diabetic patients. Front Physiol. 2020;11(December).

7. Jha R, Lopez-Trevino S, Kankanamalage HR, Jha JC. Diabetes and Renal Complications: An Overview on Pathophysiology, Biomarkers and Therapeutic Interventions. Biomedicines. 2024;12(5):1–23.
8. Swaminathan SM, Bhojaraja MV, Attur RP, Rao IR, Rangaswamy D, Shenoy SV, et al. Study of clinical and histopathological factors predicting rapid progression in biopsy-proven type 2 diabetic kidney disease. J Nephropathol. 2024;13(4).
9. Serrano E, Shenoy P, Martinez Cantarin MP. Adipose tissue metabolic changes in chronic kidney disease. Immunometabolism (United States). 2023;5(2):E00023.
10. Majeed AA, Al-Qaisi AHJ, Ahmed WA. The Comparison of Irisin, Subfatin, and Adropin in Normal-Weight and Obese Polycystic Ovary Syndrome Patients. Iran J Med Sci. 2024 Jun;49(6):350–8.
11. Romere C, Duerrschmid C, Bournat J, Constable P, Jain M, Xia F, et al. Asprosin, a Fasting-Induced Glucogenic Protein Hormone. Vol. 165, Cell. 2016. p. 566–79.
12. Zeng X, Sun X, He W, Xie J, Xin C. Relationship of asprosin and diabetes: a meta-analysis. BMC Endocr Disord. 2025;25(1):15.
13. Yuan M, Li W, Zhu Y, Yu B, Wu J. Asprosin: A Novel Player in Metabolic Diseases. Front Endocrinol (Lausanne). 2020;11:64.
14. Luo Y, Qiao X, Xu L, Huang G. Irisin: circulating levels in serum and its relation to gonadal axis. Endocrine. 2022 Mar;75(3):663–71.
15. Paoletti I, Coccurello R. Irisin: A Multifaceted Hormone Bridging Exercise and Disease Pathophysiology. Int J Mol Sci. 2024;25(24):1–28.
16. Li X, Lindholm B. The role of irisin in kidney diseases. Clin Chim Acta. 2024 Feb;554:117756.
17. Jankowski J. Diagnosis and treatment of chronic kidney diseases and Type 2 diabetes mellitus: a paradigm shift for enhancing cardiovascular prognosis. J Intern Med. 2025 Jan 20;
18. Osikov M, Efros LA, Zhuravleva Ly, Fedosov AA. Dynamic changes of inflammatory markers in the early stages of chronic kidney disease in patients with type 1 diabetes mellitus. Bull Russ State Med Univ. 2024 Dec 23;
19. Schrank Y, Fontes R, Perozo AFDF, Araújo PB, Pinheiro MFMC, Gomes DMV, et al. Proposal for fasting insulin and HOMA-IR reference intervals based on an extensive Brazilian laboratory database. Arch Endocrinol Metab . 2024;68:1–8.
20. Zhang H, Hu W, Zhang G. Circulating asprosin levels are increased in patients with type 2 diabetes and associated with early-stage diabetic kidney disease. Vol. 52, International

Urology and Nephrology. 2020. p. 1517–22.

21. Hou Q, Song R, Zhao X, Yang C, Feng Y. Lower circulating irisin levels in type 2 diabetes mellitus patients with chronic complications: A meta-analysis. Heliyon. 2023;9(11):e21859.
22. Liu Y, Qian SW, Tang Y, Tang QQ. The secretory function of adipose tissues in metabolic regulation. Life Metab. 2024;3(2).
23. Kagdi S, Lyons SA, Beaudry JL. The interplay of glucose-dependent insulinotropic polypeptide in adipose tissue. J Endocrinol. 2024;261(3).
24. Gamal S, Ibrahim S, El-deib AE raouf M, Abu- ST. Relation between Obesity , Insulin Resistance and T2DM : Review Article. 2024;3(1).
25. Shabir K, Brown JE, Afzal I, Gharanei S, Weickert MO, Barber TM, et al. Asprosin, a novel pleiotropic adipokine implicated in fasting and obesity-related cardio-metabolic disease: Comprehensive review of preclinical and clinical evidence. Cytokine Growth Factor Rev. 2021;60:120–32.
26. Mazur-Bialy AI. Asprosin-A Fasting-Induced, Glucogenic, and Orexigenic Adipokine as a New Promising Player. Will It Be a New Factor in the Treatment of Obesity, Diabetes, or Infertility? A Review of the Literature. Nutrients. 2021 Feb;13(2).
27. Romere C, Duerrschmid C, Bournat J, Petra C, Jain M, Xia F, et al. 乳鼠心肌提取 HHS Public Access. Cell. 2017;176(1):139–48.
28. Mirr M, Braszak-Cymerman A, Ludziejewska A, Kręgielska-Narożna M, Bogdański P, Bryl W, et al. Serum Asprosin Correlates with Indirect Insulin Resistance Indices. Biomedicines. 2023 May;11(6).
29. Clark M, Hoenig M. Metabolic Effects of Obesity and Its Interaction with Endocrine Diseases. Vet Clin North Am Small Anim Pract. 2016 Sep;46(5):797–815.
30. García-Fontana B, Reyes-García R, Morales-Santana S, Ávila-Rubio V, Muñoz-Garach A, Rozas-Moreno P, et al. Relationship between myostatin and irisin in type 2 diabetes mellitus: a compensatory mechanism to an unfavourable metabolic state? Endocrine. 2016;52(1):54–62.
31. Mageswari R, Sridhar MG, Nandeesha H, Parameshwaran S, Vinod K V. Irisin and Visfatin Predicts Severity of Diabetic Nephropathy. Vol. 34, Indian Journal of Clinical Biochemistry. 2019. p. 342–6.
32. Kamel SM, Ahmed NS, El Moety MAA, El Hameed NA. Fibronectin type-III domain-containing protein 5 genetic polymorphism and serum irisin-level change in relation to

type-2 diabetes mellitus with diabetic nephropathy. J Egypt Soc Nephrol Transplant. 2023;23(3).

33. Rodríguez-Carmona A, Fontán MP, Alvarellos SS, Falcón TG, Bello MLP, Muniz AL, et al. Serum levels of the adipomyokine irisin in patients with chronic kidney disease. Nefrol (English Ed. 2016;36(5):496–502.
34. Gizaw M, Anandakumar P, Debela T. A Review on the Role of Irisin in Insulin Resistance and Type 2 Diabetes Mellitus. J pharmacopuncture. 2017 Dec;20(4):235–42.
35. Wang L, Song J, Wang C, Lin P, Liang K, Sun Y, et al. Circulating Levels of Betatrophin and Irisin Are Not Associated with Pancreatic β-Cell Function in Previously Diagnosed Type 2 Diabetes Mellitus Patients. J Diabetes Res. 2016;2016.
36. Chen JQ, Huang YY, Gusdon AM, Qu S. Irisin: A new molecular marker and target in metabolic disorder. Lipids Health Dis. 2015;14(1):1–6.
37. Xuan X, Lin J, Zhang Y, Zhou L, Xu L, Jia J, et al. Serum Irisin Levels and Clinical Implication in Elderly Patients With Type 2 Diabetes Mellitus. J Clin Med Res. 2020;12(9):612–7.
38. Pedersen BK, Steensberg A, Fischer C, Keller C, Keller P, Plomgaard P, et al. Searching for the exercise factor: is IL-6 a candidate? J Muscle Res Cell Motil. 2003;24(2):113–9.
39. Shelbaya S, Abu Shady MM, Nasr MS, Bekhet MM, Mageed YAA, Abbas M. Study of irisin hormone level in type 2 diabetic patients and patients with diabetic nephropathy. Curr Diabetes Rev. 2018;14(5):481–6.
40. Wang Hongyan RL. Association Between Serum Irisin and Diabetic Nephropathy in Patients with Type 2 Diabetes Mellitus: A Meta-Analysis. Horm Metab Res [Internet]. 2021;53(05):293–300.
41. Du XL, Jiang WX, Lv ZT. Lower Circulating Irisin Level in Patients with Diabetes Mellitus: A Systematic Review and Meta-Analysis. Horm Metab Res = Horm und Stoffwechselforsch = Horm Metab. 2016 Sep;48(10):644–52.