Kufa Medical Journal | Vol.22, No.1, 2026

Original article | DOI: https://doi.org/10.36330/kmj.v22i1.23039 | p-ISSN: 1993-517X e-ISSN: 2709-4464

Association of Serum Irisin Level with BMI, Glycemic Control and Inflammatory Marker in Iraqi Patients with Type 2 Diabetes Mellitus

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ABSTRACT

Background: *Type 2 diabetes mellitus is a significant global health concern, with dramatically increased cases over all region. Irisin, a secreted novel myokine, is produced by skeletal muscles and promote energy expenditure. This hormone may play an important role in the metabolism of glucose and lipids and improve insulin resistance. Furthermore, it could be effective in treating disease such as inflammation, apoptosis, oxidative stress and atherosclerosis by inhibiting the expression and release of proinflammatory cytokines.* ***Objectives****: assess level of irisin in type 2 diabetes mellitus. Also, assess the association between irisin and glycemic control, Body Mass Index and C-Reactive Protein.* ***Methods****: this case-control study involves 62 participants, 41 diabetic cases and 21 control subjects. Patient are diagnosed according to American Diabetes Association criteria. Irisin hormone assay was measured by using Human Irisin ELISA. C-Reactive Protein analysis was measured by C-Reactive Protein Rapid Quantitative Test; the result is considered as high or normal C-Reactive Protein.* ***Results****: irisin level in diabetic group is higher than control group with highly significant difference (171.03 vs 107.9, p= .008). The correlation between irisin hormone in diabetic group show negative correlation with Body Mass Index but without significant difference (r= - .341, p= .29), also Glycated Hemoglobin shows negative correlation (but weak) without significant difference (r= - .28, p= .07). irisin hormone level in patients with high and normal C-Reactive Protein level show no significant differences (p= .4).* **Conclusion:** *increased irisin level in diabetic patients, no significant negative correlation between irisin with Body Mass Index and Glycated Hemoglobin, no significant difference between irisin in high and normal level of C-Reactive Protein.*

Keywords: Type 2 diabetes mellitus, Irisin hormone, BMI, HbA1c, Glycemic control, CRP.

Article Information

Received: January 18, 2026; Revised: June 13, 2026; Online June, 2026

INTRODUCTION

Irisin hormone is a myokine derived from FNDC5 protein in proteolytic mechanism by PGC1α. It discovered in 2012 by Boström and his colleagues as an exercise-induced hormone [(1)]. The main secretion is from skeletal muscle, adipose tissue also secretes it, for that called an adipocytokine hormone [(2)]. The main induces for irisin secretion are exercise and cold exposure [(3,4)]. diet, age and diseases like metabolic disorder and obesity also affect its secretion [(2)]. The first description of its role is converting white adipose tissues to brown adipose tissues by what is called beiging. Activation of brown adipose tissues dissipates energy as a heat; this can help in wight loss in obesity and type 2 DM patients (T2DM) [(1)]. After that, it was found that irisin also regulates glucose homeostasis, helps in improving insulin

resistance and improving cell functions of pancreas [5]. Irisin hormone exhibits anti-inflammatory effects such as reducing expression of cytokines [6]. Moreover, Korta et al. show that irisin inhibits release of pro-inflammatory cytokine especially in those with obesity and T2DM patients [7].

There is controversy about the correlation between irisin hormone and diabetes mellitus (DM), also between it and disease parameters such as glycemic control, age, sex, duration of DM, Body Mass Index (BMI) and other parameters. Furthermore, irisin role in pathogenesis is yet unclear [6].

Many studies show decreased irisin hormone in T2DM patient than control [8]. Furthermore, metanalysis studies also showed lower irisin hormone in diabetes mellitus [6,9]. Conversely, some studies report higher irisin level in diabetic patients than control [10]. Also, a few studies find no link between irisin hormone and diabetic mellitus [11]. In Iraq, studies also show controversial results about irisin hormone in diabetic patients [5,12].

The aims in this study are to assess the irisin hormone in type 2 diabetes mellitus and assess the correlation between irisin hormone with glycemic control, BMI and inflammatory marker such as C-Reactive Protein (CRP).

METHODS

This research is a case-control study that involves 62 participants, 41 diabetic cases (22 male, 19 female) and 21 control subjects (12 male, 9 female). Patients are recruited from Marjan Teaching Hospital in Babil city in Endocrinology and Diabetes Center from late October 2024 until February 2025.

The patients are diagnosed with T2DM by physician according to American Diabetes Association criteria. They included if they are T2DM and aged lower than 60 years old. Patients with type 1 diabetic mellitus, chronic kidney disease or renal failure, hepatic failure, inflammatory diseases such as systemic lupus erythematosus, rheumatoid arthritis and inflammatory bowel disease, neoplasia, pregnancy and hypothyroidism or hyperthyroidism are excluded. Control group collected from relatives of patient that visit the clinical laboratory in the hospital. The consideration of choosing them is apparently healthy individuals with normal level of glucose and Glycated Hemoglobin (HbA1c).

All participants undergo a personal and medical history and physical examination, as well as obtaining BMI according to WHO by dividing weight (kilogram) on height (meters) squared. Venous blood sample has been drawn is divided into 2 tubes, 4 mL in gel tube and 1 mL in EDTA tube. Gel tube left about 10 minutes before centrifugation, then separate the serum by centrifuge for 10-15 minutes in set of 4000 round per minute. The serum aliquoted into 2 Eppendorf tubes, one for CRP analysis, one for irisin hormone assay. The Eppendorf tubes are stored in refrigerator -20 Celsius. The Eppendorf tubes of CRP and irisin hormone are thawed after all samples collection is complete to use for analysis. The EDTA tube has been used for HbA1c analysis on the same day of collection.

CRP analysis was measured by CRP (C-Reactive Protein) Rapid Quantitative Test kit (Finecare/China) by fluorescence immunochromatographic analyzing device (Finecare/China), the result is considered as high or normal CRP, considered high if more than 10 mg/L. Irisin hormone assay was measured by using Human Irisin ELISA Kit (Elabscience/China) by ELISA reader (Biotec/USA) for all participants, following the manufacture's protocol for assay these markers. The (Lifotronic/China) device and materials is used to measure the HbA1c.

Statistical analysis

All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) software, version 26 (IBM Corp., Armonk, NY, USA). Quantitative variables were presented as mean ± standard deviation (SD) and compared across groups using one-way analysis of variance (ANOVA). The normality of data distribution was assessed using the Shapiro–Wilk test. Categorical variables were summarized as frequencies and percentages and compared using the Chi-square test or Fisher's exact test, as appropriate. Pearson's correlation coefficient was used to determine the association between serum irisin levels and continuous variables, including age, body mass index (BMI), glycated hemoglobin (HbA1c) and duration of diabetes. A p-value of ≤ 0.05 was considered statistically significant for all analyses.

RESULTS

The results in this study show high BMI in control (33.7±6.3) in compare with diabetic patients (29.9±4.5) with significant differences (p= .009) between them. For both groups there are no significant differences for CRP, age and sex. All data are shown in table 1.

Table (1): Demographic and clinical characteristics of diabetic and control group.

		Group		Total	P-value
		Diabetic(n=41)	Control(n=21)		
Age*		52.7±5.9	50.2±5.1	51.9±5.8	0.1
BMI*		29.9±4.5	33.7±6.3	31.2±5.4	0.009
Duration of DM (years)*		10.5±5.4	----	10.5±5.4	
HbA1C (%) *		9.2±1.7	5.5±0.4	7.9±2.3	0.0001
Sex**	**Male**	22(53.7%)	12(57.1%)	34(54.8%)	0.8
	Female	19(46.3%)	9(42.9%)	28(45.2%)	
	No	34(82.9%)	13(61.9%)	47(75.8%)	
C-RP (mg/l) **	**High**	3(7.3%)	3(14.3%)	6(9.7%)	0.4
	Normal	38(92.7%)	18(85.7%)	56(90.3%)	

**Data are expressed as Mean±SD, ** data are expressed as No. (%).*

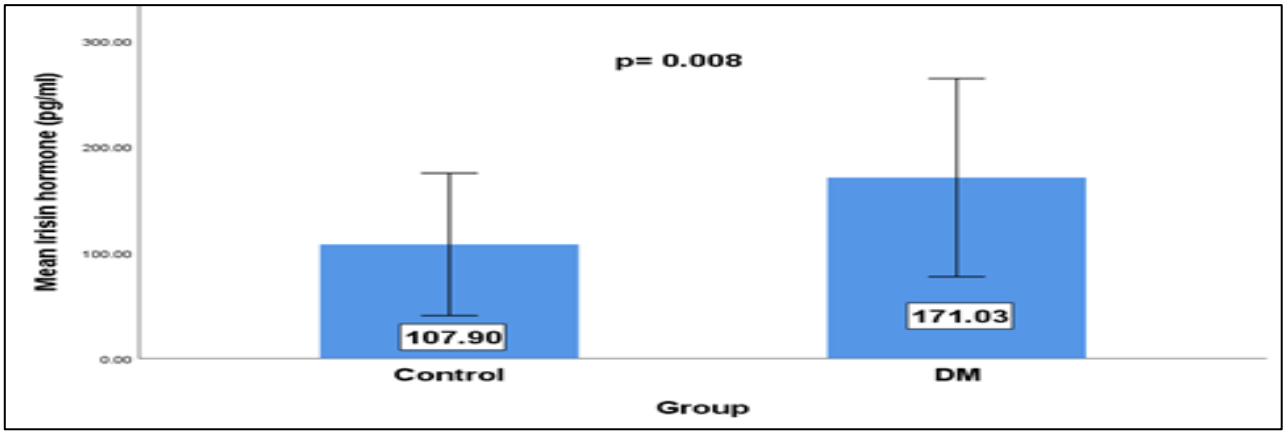

Figure (1): Comparison of mean Irisin level (pg/ml) between diabetics and control.

Irisin hormone level in this study is higher in diabetic group in comparison to control group with highly significant difference (171.03 vs 107.9, p= .008), as shown in figure 1.

The correlation between irisin hormone with different variables in diabetic group show negative correlation with BMI but without significant difference (r= - .341, p= .29), also HbA1c shows negative correlation (but weak) without significant difference (r= - .28, p= .07). The correlation between irisin with age and duration of DM shows no significant differences, as shown in table 2.

Table (2): correlation between irisin hormone and diabetic group parameters.

Parameters	Irisin Hormone (pg/ml)	
	Pearson Correlation (r)	P value
Age	-0.029	0.85
BMI	-0.341	0.29
Duration of DM	-0.127	0.43
HbA1c	-0.28	0.07

Regarding CRP, this study shows that irisin hormone level in patients with high and normal CRP level show no significant differences (p= .4), as shown in figure 2.

DISCUSSION

In this study, irisin is significantly increased in diabetic patients than control. This does not agree with many studies that show decreased irisin in diabetic patients in comparison to healthy control group [13,14]. However, this increase in irisin may be due to increase adipose tissue in obese individuals as many studies explain that [10]; but in this study, mean of BMI in control is significantly higher than diabetic group.

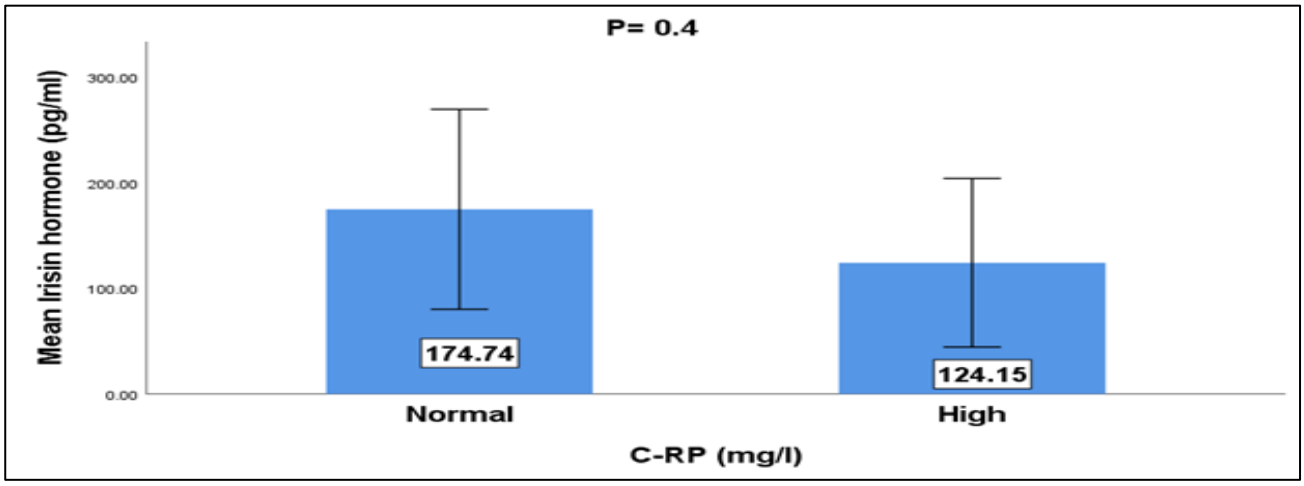

Figure (2): Comparison of mean irisin hormone in diabetic patients with normal and high CRP levels.

The studies show that irisin is important in glucose homeostasis by facilitating glucose uptake by muscle [15]. For that, the increased irisin in this study perhaps the normal physiological response to hyperglycemia to restore the normal condition in the body.

However, as type 2 diabetes mellitus results in insulin resistance that causes insulin over secretion to overcome the resistance [16],

there may be the same principle in irisin hormone that causes irisin over secretion because of irisin receptors resistance [11].

Many studies agree with results of this study [5,15], they demonstrate that irisin hormone level is higher in diabetic patients than non-diabetic group. On other hand, few studies show no association in irisin hormone between diabetic and non-diabetic group [17].

The correlation between irisin hormone and BMI in this study shows negative correlation but without significant value. However, association between irisin hormone and anthropometric parameter like BMI is controversy. Most studies report positive association between irisin and BMI [10,17], On the contrary, several findings show no association or report a negative correlation with BMI [11,18,19].

The adipose tissue is considered a source of irisin hormone, and it is known that irisin secretion increases in obese individual to browning the white adipose tissue and compensates for the decrease in energy expenditure [20]. However, in this study the control group shows significantly higher BMI than diabetic patients, but the irisin hormone is still higher in diabetic group, this can explain the effect of diabetes mellitus in the secretion of irisin.

On other hand, the low level of irisin in control group may be because of the proinflammatory substances of adipose tissues hypertrophy that inhibit irisin hormone [21]. However, BMI is considered the confounder factor in this study.

Regarding the correlation between irisin and glycemic control, HbA1c is considered one of the best tests to monitor glycemic control as it was not affected by fluctuating daily changes in glucose levels but given to us an average of about 2-3 months of glucose level [22].

In this study, there is weak negative correlation between irisin and HbA1c in diabetic patients but without significant value. However, the correlation between them is also controversy between the studies. This result consists with Ibrahim and Salih study and Montazerifar et al [12,8], other results show controversial results such as Alkhairi et al and Yang et al [15,23], and some studies show no significant correlation between them such as Balaban et al and Khajebishak et al [19,24]. These conflicts need more studies to determine the role of irisin in glycemic control, bearing in mind the confounder factors.

Irisin hormone demonstrates anti-inflammatory properties by lowering cytokine expression, diminishing hydrogen peroxide synthesis, and reducing the production of reactive oxygen species [6]. Although the role of irisin is anti-inflammatory, the studies show no correlation between irisin and CRP as it is considered a biomarker for systemic inflammation [25].

In this study the level of irisin hormone in high and normal CRP level in diabetic group shows no significant association (p= .4), this consistent with many studies [26,27]. This may indicate that irisin is not affected by inflammatory status and more affected by other factors such as physical activity and disease condition. In contrast, one study shows negative correlation between them [28].

CONCLUSION

In this study, irisin hormone level was significantly higher in diabetic group than control healthy group. The correlation between irisin and BMI shows negative correlation but without significant difference. Als, the correlation with HbA1C shows weak negative correlation but without significant value. The level of irisin hormone in high and normal CRP level in diabetic group shows no significant association.

RECOMMENDATION

• Asses irisin hormone in larger study group to increase the power of the results.
• Asses irisin hormone in newly diagnostic type 2 diabetes mellitus.
• Try to exclude obese subjects in future studies.
• Included participants from multiple center rather than from one center.

ACKNOWLEDGMENT

The authors would like to express their sincere gratitude to the Endocrinology and Diabetes Center in Marjan Teaching Hospital in Babil city for their support during data collection. Special thanks to all participants in this study, whose cooperation was essential for the completion of this study.

Ethical approval

The present study which is conducted by authors (Zaid Talib Alfahham) was approved by the local medical ethics committee in Kufa faculty of medicine.

Statement of Permission and Conflict of Interests

The others declare that they have obtained all necessary permissions to collect and analyze patients' data for research purpose. The authors also declare that there is no conflict of interest regarding the publication of this paper.

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