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RESEARCH ARTICLE - MEDICAL TECHNIQUES

Determination of Irisin, Body Mass Index, and Other Biochemical Parameters in a Sample of Iraqi Type II Diabetic Patients

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Abstract

Evidence suggests that Irisin, a peptide hormone, may play a role in lipid metabolism, insulin resistance, and obesity. On the other hand, its role in type 2 diabetic Mellitus [T2DM] in humans is uncertain. As a result, we investigated if irisin levels in T2DM patients were dysregulated and whether there was a link between serum irisin levels and anthropometric obesity indices and biochemical parameters. [T2DM patients] group [n = 90] and control groups [n = 90], males [n=81], females [n=99] were selected among 180 people. [43.17 ±11.13] years was the average age. ELISA was used to measure serum irisin levels. The mean serum Irisin level in the control group was considerably higher [P<0.01] than in the case group [6.9±1.3 vs. 5.8±1.2], respectively. The results showed that body mass index and irisin [P-value<0.001]. Irisin seems to have a significant negative connection [P-value<0.001] with body mass index, fasting blood sugar, glycated hemoglobin, insulin, and homeostasis model assessment of insulin resistance. There was also a substantial negative association between irisin, low-density lipoprotein, and triglyceride, but none with cholesterol or high-density lipoprotein. In conclusion, irisin appears to be involved in regulating glucose metabolism. In this investigation, circulating irisin concentrations were considerably lower in T2DM patients. These findings imply that higher plasma irisin levels in T2DM are linked to adiposity indices. As a result, irisin has the potential to be a novel therapeutic option in the field of obesity.

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1. Introduction

The second most prevalent kind of diabetes is Type 2 Diabetes Mellitus [T2DM]; Hyperglycemia and a failure of the body to respond to insulin adequately are the hallmarks of this condition. It is known as insulin resistance [IR] [1]. T2DM accounts for almost 90% of all diabetes cases. T2DM is caused by obesity, sedentary lifestyles, high-calorie meals, and population ageing [2].T2DM patients are more likely to be obese or have a higher body fat percentage, typically in the abdominal area [3]. Obesity is defined as a low-grade inflammatory condition leading to insulin resistance, metabolic abnormalities, and T2DM [4].

Signs of inflammation and new myokines, such as irisin, have been studied in the recent decade as circulating variables implicated in metabolic and inflammatory disorders found in both obesity and T2DM [5]. Irisin is a 112-amino-acid cleavage product of fibronectin type III domain-containing protein 5 [FNDC5], activated by peroxisome proliferator-activated receptor-α (PPAR-α) - and its coactivator peroxisome proliferator-activated receptor-coactivator 1 [PGC1] [6]. Muscles release Irisin during exercise to upregulate genes involved in thermogenesis and browning in white adipose tissue [WAT], such as uncoupling protein 1 [UCP-1], leading to higher energy expenditure and weight loss [7]. As a result, it has also been shown to reduce insulin resistance in the bloodstream [8]. Irisin is classified as an adipocytokine since it can be secreted by subcutaneous adipose tissue. Irisin may play a role in the pathophysiology of obesity and the metabolic problems that accompany it [9]. According to the vast majority of research, there is an association between irisin levels and adiposity, as well as other biochemical indicators of obesity in humans, even though others have discovered the contrary [10, 11]. As a result, the goal of this study was to compare patients with T2DM to healthy controls in terms of Irisin levels and their relation with BMI, as well as metabolic and anthropometric data.

2. Materials and Methods

2.1. Chemicals

An automated ELISA reader is used to quantify blood insulin and irisin hormones using the sandwich enzyme-linked immunosorbent assay [ELISA] method [PKL PPC 230]. The COBAS INTEGRA® 400 plus automatic biochemistry analyzer [Roche/Hetachi Diagnostics Ltd Company, Japan] was used to measure FBS, HbA1c, CHO., TG, HDL, LDL, and VLDL in this study.

Nomenclature			
BMI	Body Mass Index	mg/dL	Milligrams per deciliter
CHO	Cholesterol	NS	Non–Significant
DM2	Diabetes Mellitus Type 2	S	Significant
FBS	Fasting Blood Sugar	VLDL	Very Low-Density Lipoprotein
HbA1c	Glycation Hemoglobin	ELISA	enzyme-linked immune-sorbent assay
FFA	Free Fatty Acid	SD	Standard Deviation
HDL	Lipoproteins of High Density	HOMA-IR	Homeostatic Model Assessment for Insulin Resistance
IR	insulin resistant	SN	Sensitivity
SP	specificity	UCP-1	uncoupling protein 1
LDL	Lipoproteins of Low Density	SPSS	A statistical package for social sciences research
(PPAR-α)	peroxisome proliferator-activated receptor-α	HS	Highly Significant
TG	Triglyceride		

2.2. Study design

From December 2021 to February 2022, 90 Iraqi T2DM patients (48 females and 42 males) were chosen from those attending Dr. Ali Muneeb Al- Rubaie's lab in [Baghdad- Iraq]. The WHO-recommended criteria for diagnosing T2DM were used to make the diagnosis[12].90 Iraqi control subjects [51 females and 39 males] who were equivalent to the diabetes mellitus patients in terms of gender [51 females and 39 males] were included in the comparisons. Both groups had a mean age of [43.17±11.13] years.

2.3. Statistical analysis

The data was analyzed using the available SPSS-24 [Statistical Packages for Social Sciences-version 24] statistical package. The data will be presented with simple frequency, percentage, mean, and standard deviation measurements. Student's t-test for difference between two independent means or Paired t-test for difference of paired observations, ROC, and Tukey test was used to determine the significance between the difference of various means [quantitative data]. When the p-value was less than 0.05, the statistical significance was evaluated.

3. Results

A total of 90 patients diagnosed with T2DM participated in the current study, with a mean age of [43.17 ±11.13] years and a substantial difference in mean age across the study groups, as shown in Fig. 1.
According to the findings, no significant difference in gender distribution between the study groups [P-value=0.765], as indicated in Table 1.
The BMI distribution results revealed a significant difference between the research groups [p-value < 0.001]. As indicated in Table 2, 23.3% of the participants in the control group were obese, and 6.7% had marked obesity, while 38.9%of the individuals in the case group were obese, and 30% had marked obesity. As shown in Table 3, the case group had significantly higher [P-value <0.05] levels of FBS, HbA1c, LDL, CH, TG, and IR than the control group, while there was no significant difference [P-value <0.442] between the study groups in HDL. Additionally, the means of irisin were significantly lower [P-value <0.05] among the participants in the case group compared to those in the control group. Furthermore, as indicated in Table 4 and Fig. 2, there was a strong negative connection [P-value <0.001] between irisin and BMI. Based on the findings, there was a substantial negative connection [P-value 0.000] between irisin and FBS, HbA1C, fasting insulin, and HOMA-IR. Table 5 and Fig. 3 demonstrate this.
The cut-off point of irisin for optimal sensitivity [SN] and specificity [SP] in detecting T2DM was [76.95] ng/ml, according to the receiver operating characteristic [ROC] curve, as shown in Fig. 4. Finally, as indicated in table 6, there was a strong negative connection between irisin and triglyceride, LDL, and VLDL.

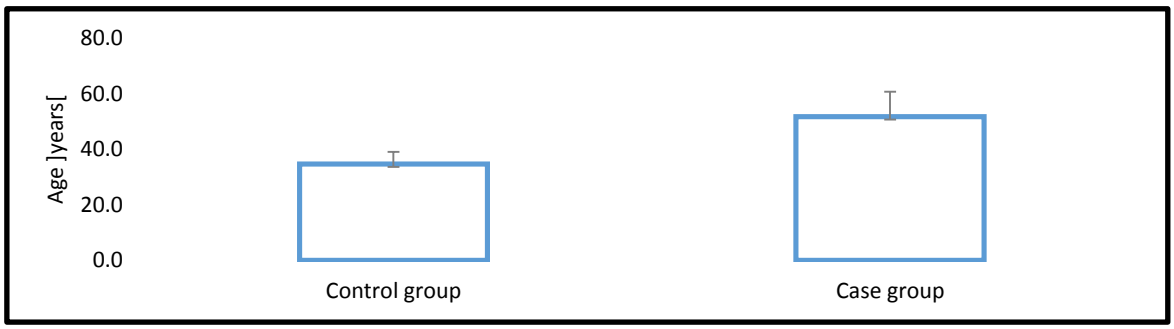

Fig 1. Age distribution of the participant

Table 1: Gender distribution in the research groups

Gender	Groups		Total	P-value
	Control group N [%]	Case group N [%]		
Female	51 [56.7]	48 [53.3]	99 [55.0]	0.765
Male	39 [43.3]	42 [46.7]	81 [45.0]	
Total	90 [50.0]	90 [50.0]	180 [100.0]	

A Chi-square test was used

Table 2 The BMI distribution according to the research groups

BMI	Groups		Total	P-value
	Control group N [%]	Case group N [%]		
Normal	42 [46.7]	12 [13.3]	54 [30.0]	<0.001
Overweight	21 [23.3]	16 [17.8]	37 [20.6]	<0.001
Obesity	21 [23.3]	35 [38.9]	56 [31.1]	<0.001
Markedobesity	6 [6.7]	27 [30.0]	33 [18.3]	<0.001

A Chi-square test was used

Table 3 The study markers were distributed according to the study groups

Variables	Groups		P-value
	Control group Mean [±SD]	Case group Mean [±SD]	
Fasting blood sugar [mmol/L]	5.4 [±0.4]	9.8 [±2.9]	<0.001
HbA1C	4.3 [±0.6]	8.3 [±2.5]	<0.001
Cholesterol [mg/dl]	163.2 [±21.1]	208.5 [±54.0]	<0.001
Triglycerides [mg/dl]	78.1 [±19.7]	216.5 [±85.9]	<0.001
LDL [mg/d]	100.8 [±21.3]	132.4 [±33.2]	<0.001
HDL [mg/dl]	48.1 [±6.6]	50.5 [±28.6]	0.442
VLDL [mg/dl]	18.1 [±8.3]	36.9 [±20.7]	<0.001
Fasting Insulin [mIU/L]	9.0 [±0.8]	10.7 [±4.4]	<0.001
Insulin resistance	2.1 [±0.3]	4.5 [±1.5]	<0.001
Irisin [ng/ml]	6.9 [±1.3]	5.8 [±1.2]	<0.001

t-test was used

Table 4 Correlation between irisin and BMI

	Irisin[ng/ml]	
	Pearson Correlation	P-value
BMI [kg/m2]	-0.687	<0.001

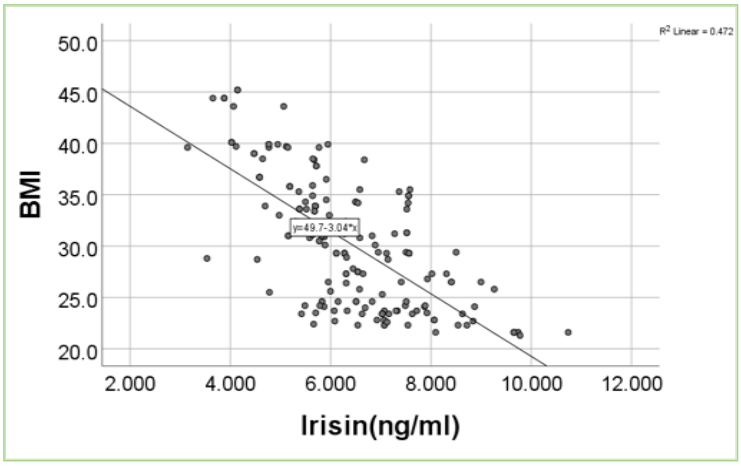

Fig 2 Correlation between irisin and BMI

Table 5 Correlation between irisin and other diabetic variables

	Irisin[ng/ml]	
	Pearson Correlation	P-value
FBS [mmol/L]	-0.361	<0.001
HbA1C	-0.386	<0.001
Insulin[mIU/L]	-0.155	<0.001
HOMA-IR	-0.377	<0.001

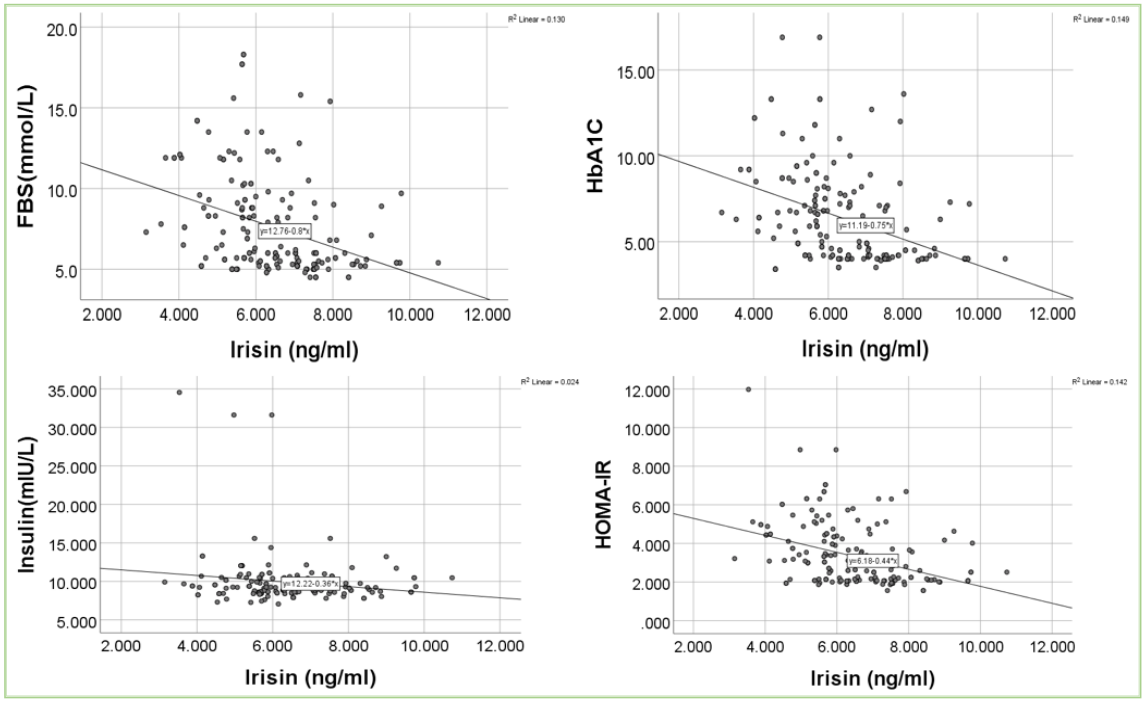

Fig 3. Correlation between irisin and diabetic variables

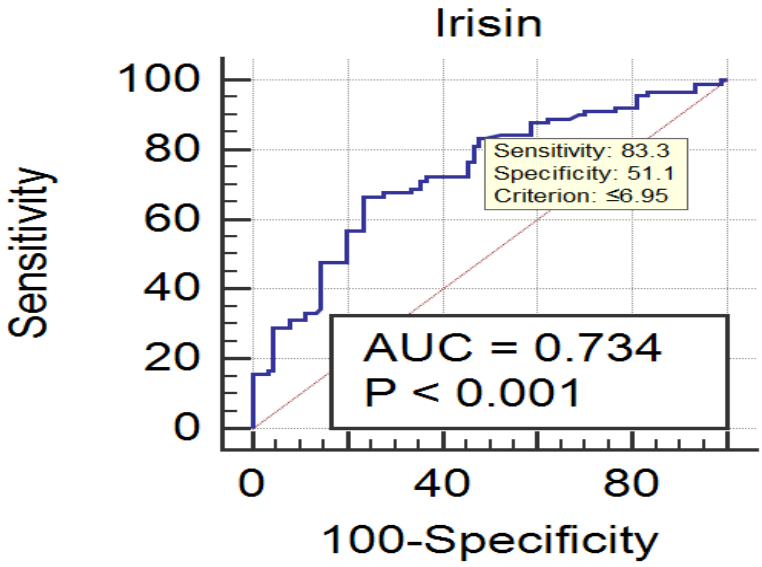

Fig 4. Receiver operating characteristic curve for irisin

Table 6 Correlation between irisin and lipids

	Irisin[ng/ml]	
	Pearson Correlation	P-value
Triglyceride [mg/dl]	-0.346	<0.001
Cholesterol [mg/dl]	-0.098	0.189
LDL [mg/d]	-0.174	0.019
HDL [mg/dl]	-0.065	0.385
VLDL [mg/dl]	-0.247	0.001

4. Discussion

Due to its role in browning white adipose tissue and, as a result, increasing energy expenditure via improved thermogenesis, irisin's potential application as a new therapeutic approach for obesity and T2DM has generated considerable interest. The study's results matched [13], which demonstrated that biochemical, hormone, and adipocytokine parameters in Iraqi T2DM patients were affected by age and gender. Furthermore, these findings were in line with Wong et al. findings. .'s According to a study, glucose intolerance prevalence [pre-diabetes and

T2DM] increased in patients aged 45 and older[14]. There are various contributing elements to consider regarding ageing and glucose intolerance. Ageing is a major contributor to age-related changes in insulin sensitivity and beta-cell function [15]. The ability of beta cells to proliferate and their sensitivity to apoptosis are lowered as people age [16].

Diabetes was shown to be more common in women than in men in Basra, Iraq [17]; although the findings contradicted those of[18], they showed that diabetes appeared to reduce the more favorable cluster of risk factors that women have as compared to men[18]. As a result, testosterone has been associated with both men and women having a bidirectional modulation of diabetes risk. Testosterone, which works as an antidote, can help prevent diabetes in men. The effects of testosterone on women are substantially different. In hypogonadal males, insulin sensitivity improves and cardiovascular risk decreases, whereas testosterone injection has the opposite effect. In women with high testosterone levels, initial-cell hyperfunction can lead to secondary-cell failure and T2DM [19]. Men and women have different disease risk profiles due to a range of factors, including differences between human genetics and anatomical structure. Almost all human diseases, according to some experts, are sexually dimorphic, differing in occurrence, age of onset, severity, and persistence. Because puberty occurs sooner in women, it is assumed that females are diagnosed with T2DM at a younger age. When boys approach adolescence, those ratios tend to reverse dramatically. As women become older and enter menopause, their hormones shift, impacting insulin use once more [20].

One of the risk factors for diabetes was one of the results that matched the estimated BMI [21]. These findings are from the earlier ones. According to another study, the critical causes of T2DM are personal lifestyle and eating habits that contribute to obesity and overweight [22]. In recent years, both obesity and diabetes epidemics have grown at worry levels. Insulin dysfunction is seen in obesity, insulin resistance, and pancreatic cell failure, all of which contribute to diabetes. Visceral adiposity, associated with IR and T2DM, is more common than total body fat. By activating the uncoupling protein 1 [UCP1] in adipose tissue, irisin increases the browning of white adipocytes and thermogenesis, whereas inhibiting irisin gene expression inhibits UCP1 expression and enhances adipogenesis in obesity[23, 24].

It can speculate about its probable role in skeletal muscle-to-brown fat signalling because of its inhibitory effects on adipogenesis. The findings corroborated previous research [25] Obesity and overweight were on the rise among T2DM patients [26]. The majority of T2DM patients were overweight or obese. On the other hand, female participants were more likely to be overweight or obese than male ones. T2DM is associated with obesity because of a combination of pancreatic-cell insufficiency and peripheral IR [27].T2DM can only develop when IR and pancreatic-cell dysfunction occur simultaneously. Anyone who is overweight or obese has IR, but only individuals who do not make enough insulin to match their insulin resistance get diabetes even though those people's systems have a lot of insulin, which is insufficient to control their blood sugar levels [28].

Contrary to common opinion, the current finding was in keeping with earlier research that demonstrated an increase in FBG, HbA1C, CHO, Tri, LDL, and VLDL levels in T2DM patients compared to controls [29]. In contrast to the current study, several investigations have shown that HDL levels rose in T2DM patients [30]. Glycation of hemoglobin is produced by a non-enzymatic interaction between glucose and the end of the beta-N-terminal chain of hemoglobin. The Schiff base [pre-A1c] must be generated before Amador products like HbA1c can be made. Glycated hemoglobin HbA1c rises in response to increases in average plasma glucose [HbA1c]. The HbA1c blood test measures glucose control across a red blood cell's lifespan [usually 120] days [31]. Al-Naama et al. concluded that mean HDL-C levels were statistically significant in diabetic patients compared to controls [p0.05] in their HDL study, which was in keeping with the findings of [32], which revealed that T2DM patients had considerably higher blood cholesterol concentrations than controls [33]. T2DM patients had considerably lower HDL cholesterol [HDL-C] and HDL dysfunction, as well as statistically different LDL test findings [p0.05] than the control group.

In this study, the homeostasis model and fasting insulin levels were inversely associated with serum irisin levels, indicating that irisin may play a role in obesity-induced IR. A previous study backed up these conclusions [34]. Irisin improves IR via enhancing insulin receptor sensitivity in skeletal muscle, heart, and liver, improving hepatic glucose metabolism, stimulating pancreatic cell activity, and changing white fat into brown fat [35]. In the past, higher blood glucose levels are associated with plasma irisin, and there is evidence that irisin can help skeletal muscle cells absorb more glucose in an AMPK-dependent way in vitro [36]. More research is needed to understand irisin's role in glucose homeostasis and metabolic disease [37]. Irisin has been shown to improve IR by enhancing insulin receptor sensitivity in skeletal muscle, the heart, and the liver, as well as boosting hepatic glucose metabolism, promoting pancreatic cell activity, and converting white fat to brown fat [38].

The best Sensitivity (SN) and specificity (SP) in T2DM detection were attained when irisin levels were [76.95 ng/ml], according to a receiver operating characteristic [ROC] curve [39]. Even after accounting for potential confounding variables, T2DM had significantly lower irisin levels in this investigation. T2DM was shown to have an AUC of [0.734 to 1.00] about the hormone irisin. We can deduce that irisin is associated with T2DM based on these data.

Finally, the results were consistent with earlier research [40, 41]. Serum irisin levels were inversely associated with VLDL and Tri levels but adversely connected to HDL, LDL, and CHO levels. Epidemiological studies are increasingly being used to infer lipid metabolism implications. This study discovered a negative relationship between Tri levels and circulating irisin concentrations. Additional research [41]. The two variables have a negative correlation. According to experimental evidence, irisin treatment increases glycerol output while decreasing lipid accumulation by altering the expression of adipose triglyceride lipase, hormone-sensitive lipase, and fatty acid-binding protein.[42].

5. Conclusion

The study found that women had a higher percentage of T2DM than men, and the average age of T2DM patients was over 40. Furthermore, serum irisin levels in T2DM patients were lower than in healthy controls, and serum irisin levels were negatively correlated with anthropometric and metabolic markers of obesity and T2DM. Moreover, we observed a negative relationship between irisin and BMI and specific lipid profile markers. Because irisin is a novel and promising peptide hormone for insulin resistance, it can be considered a predictive marker for T2DM estimates.

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