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Irisin Levels Related to Glycosylated Hemoglobin in Type 2 Diabetic Obese Women

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Abstract

The aim of the preset study is to explain the role of irisin hormone levels in type-2 obese diabetic women and compare these levels with those in obese nondiabetic women. In addition, we investigated the relation of irisin levels with those of glycosylated hemoglobin (HbA_{1c}) and body mass index (BMI) in the patients. Eighty eight subjects were included in this study, including 44 type-2 Iraqi obese diabetic women as a patients group, and 44 obese nondiabetic women as a control group. Serum irisin was measured by Enzyme-linked Immune-Sorbent assay (ELISA), while determination of glycosylated Hemoglobin was carried out by The SD A1c Care™ system. Diabetic type-2 obese women showed a highly significant decrease in the levels of serum irisin when compared to levels in obese non-diabetic women, while no significant changes were observed in the mean±SD values when comparing age and duration of DM. In the patients, a negative correlation was found between serum irisin and HbA_{1c} while no significant correlation was recorded between the hormone levels and BMI.

Keywords: Irisin, T2DM, HbA_{1c}, Obesity.

مستويات الايرسين وعلاقتها بالسكر التراكمي HbA1c عند النساء المصابات بالسمنة وداء السكري من النوع الثاني

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الخلاصة:

هدفت الدراسة إلى تقييم دور هرمون الايرسين (Irisin) عند النساء العراقيات المصابات بالسمنة و داء السكري النوع 2 ، ومقارنتها مع النساء البدنيات الغير المصابات بداء السكري. بالإضافة إلى ذلك ، للبحث في علاقة الايرسين مع السكر التراكمي HbA1c و مؤشر كتلة الجسم (BMI) في النساء المصابات بداء السكري النوع 2. شملت الدراسة (88) امرأة: (44) من النساء المصابات بالسمنة و داء السكري النوع 2 (كمجموعة مرضية) ، و (44) من النساء البدنيات الغير المصابات بداء السكري (كمجموعة سيطرة). تم قياس الايرسين بواسطة طريقة مقايسة المناعة الماصة (ELISA) المرتبطة بالإنزيم.

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أظهرت مجموعة النساء المصابات بالسمنة وداء السكري من النوع 2 ، انخفاضاً بشكل ملحوظ في مستويات هرمون الأيرسين عند مقارنتها مع مستويات النساء البدينات الغير المصابات بداء السكري وليس هناك تغيير معنوي في مستويات الأيرسين عند مقارنتها وفقاً للفئات العمرية ومدة الإصابة بالمرض. في مجموعة النساء المصابات بالسمنة وداء السكري من النوع 2: تم العثور على علاقة سلبية معنوية بين الأيرسين و السكر التراكمي ، ولكن لم يكن هناك ارتباط معنوي بين الأيرسين و مؤشر كتلة الجسم.

Introduction

Type-2 diabetic mellitus (T2DM) is typically a progressive metabolic disease caused by both environmental and genetic factors. The pathogenesis of T2DM includes functional defects in all main organs governing metabolic control, involving liver, pancreatic beta-cells (β -cells), adipose tissue, and skeletal muscles. These defects cause an impairment in the capacity of insulin for regulating whole-body glucose homeostasis; a condition generally referred to as “insulin resistance” (IR) [1]. Obesity is generally characterized by an excess accumulation of adipose tissue and associated with different disorders, such as T2DM and IR [2]. Obesity is principally an independent risk factor for developing type-2 DM, leading to the term “diabesity”, or obesity associated with type-2 DM [3].

Irisin is a hormone discovered by Boström *et al.* in 2012 [4], as a muscle-derived myokine which promotes formation of the brown-adipocyte-like cells in mice. Irisin is secreted into the bloodstream by the cleavage of fibronectin type III domain containing protein 5 (FNDC5). Irisin is a peroxisome proliferator-activated receptor coactivator 1- α (PGC-1 alpha) - dependent myosin. The hormone acts as a messenger between skeletal muscles and other different parts of the body. The name Irisin originates from the Greek Goddess "Iris" who was the messenger among the Gods [4]. Depending on the current knowledge, irisin is not only a myokine, but also an adipokine, with paracrine as well as autocrine functions [5].

Irisin is secreted, activated and after that transported to targets on numerous organs/tissues in order to execute its corresponding physiological body functions, such as regulating white adipose tissue (WAT), browning, improving the energy consumption, as well as utilization of glucose, reducing IR, and treating metabolic disorders, such as T2DM and obesity [6]. A study on mice predicted that irisin is an insulin-regenerating hormone which can specially accelerate generation of β -cells and increase their number [7]. Another study on humans predicted that the regeneration of β -cells will put forward a new pathway for DM treatment [8].

The aim of this study was to evaluate the role of serum irisin hormone levels in type-2 obese diabetic women and compare these levels with those in obese non-diabetic women. In addition, we investigated the relation of irisin with HbA_{1c} and BMI in type 2 obese diabetic women.

Materials and Methods

This study was conducted at the Chemistry and Biochemistry Department/College of Medicine and National Diabetes Center (NDC) /Mustansyriah University in December 2017 to April 2018. A total of 88 subjects were examined in this study, which included 44 obese Iraqi women with type 2 DM as patients group, and 44 obese nondiabetic women who were regarded as controls. The two groups were comparable in BMI and age. Patients with T2DM were diagnosed by the physicians according to WHO [9] and ADA [10] criteria. The Body Mass Index (BMI) was determined by dividing weight (Kg) with height (m²) [11]. Subjects with BMI ≥ 30 kg/m² were considered as obese according to the WHO criteria [12].

Peripheral venous blood (10 ml) was aspirated from each subject after an overnight fasting. Two ml was transferred into EDTA tube for the estimation of Hemoglobin A_{1c}. The remaining sample was transferred into tubes, allowed to clot, and then centrifuged and stored at -20 °C until the time of measurements. Serum levels of human irisin were measured by Enzyme-linked Immune-Sorbent assay (ELISA) method. Determination of glycosylated Hemoglobin was carried out by The SD A1c Care™ system. Statistical analysis was performed by using SPSS- version 24. Results in this study were indicated as mean \pm SD.

Results

Mean \pm SD values of age and duration of diabetes (years) of study subjects are presented in Table-1. The age range of type 2 obese diabetic women and obese controls was 36-59 years, and the mean value of age in type 2 obese diabetic women was higher than that in the obese non-diabetic control, but with no statistically significant difference.

The results in Table-1 show that the age range of all subjects is classified as: <40 years (6.8%), 40-44 years (27.3%), 45-49 years (20.5%), 50-54 years (20.5%) and =>55 years (25%) for type 2 obese diabetic women. While the age ranges of obese non-diabetic controls were 15.9%, 36.4%, 18.2%, 15.9%, and 13.6%, respectively. In addition, it can be noticed from Table-1 that the mean duration of disease was 6.6±4.6 years. The duration of disease in obese diabetic women was less than 5 years in 40.9 %, 5-9 years in 29.5 %, and 10 years and more in 29.5 %.

Table 1-Mean ± SD of age and disease duration (years) in type 2 obese diabetic and obese non-diabetic control women

Studied Parameters	T2DM N=44		Controls N=44		P value
	No	%	No	%	
Age (years) <40	3	6.8	7	15.9	0.413[NS]
40---44	12	27.3	16	36.4	
45---49	9	20.5	8	18.2	
50---54	9	20.5	7	15.9	
=>55	11	25.0	6	13.6	
Mean±SD	48.7±6.6		45.8±7.1		
Age (years) <50	24	54.5	31	70.5	0.123[NS]
=>50	20	45.5	13	29.5	
Duration (years) <5	18	40.9	-	-	-
5---9	13	29.5	-	-	
=>10	13	29.5	-	-	
Mean±SD	6.6±4.6		-		

[NS] =no significant differences by using the Pearson Chi-square test between proportions.

Data in Table-2 demonstrate that no statistically significant difference was found in the mean±SD values between type 2 obese diabetic women and obese control regarding BMI. The mean±SD HbA_{1c} (%) value (8.07±1.27 %) for type 2 obese diabetic women was significantly higher (P<0.0001) compared with that in obese non-diabetic controls (5.44±0.41 %). It can also be noticed from Table-2 that the mean value of serum irisin in type 2 obese diabetic women (62.72±26.12 ng/ml) was significant lower (P<0.0001) compared with that in obese non-diabetic controls (105.41±46.89 ng/ml).

Table 2-Measurements of the study related biomarkers

Studied Bio-Markers	mean±SD		P value
	Obese Type2 DM Women	Obese Non Diabetic Women	
No.	44	44	-
BMI (Kg/m ²)	33.97±3.70	33.81±2.22	0.810[NS]
HbA _{1c} (%)	8.07±1.27	5.44±0.41	0.0001*
Irisin (ng/ml)	62.72±26.12	105.41±46.89	0.0001*

*Significant difference at (0.05 level) by using the Students-t-test between 2 independent means.
[NS]=no significance.

Data in Table-3 suggest that type 2 obese diabetic women show a negative correlation between serum irisin and HbA1c ($r = -0.643$, $P < 0.001$), with no significant correlation between serum irisin levels and the mean value of BMI.

Table 3-Correlation between serum irisin levels with HbA1c and BMI in type-2 obese diabetic patients.

Studies Bio-Markers	r	p
BMI (Kg/m ²)	-0.106	0.492[NS]
HbA1c (%)	-0.643**	<0.001
** significant at the (0.01 level). [NS]=no significance.		

Data in Table-4 show the statistical analysis of the relationship between serum irisin levels and the related clinical characteristics in type 2 obese diabetic women. The results revealed that no significant change was detected in the mean \pm SD levels of serum irisin when compared according to the age groups and duration of diabetes.

Table 4-Relationship between serum irisin levels and grading of the related clinical characteristics in type 2 obese diabetic women

Characteristics	Irisin (ng/ml)		P value
	No.	Mean \pm SD	
Age (years) <50	24	66.76 \pm 27.19	0.265[NS]
=>50 years	20	57.86 \pm 24.56	
Duration (years) <5	18	71.24 \pm 31.49	0.051[NS]
5---9	13	65.03 \pm 18.67	
=>10	13	48.60 \pm 18.96	
[NS] =no significant differences by using ANOVA test among 3 independent means.			

Discussion

Irisin, a circulating hormone-like myokine, is known to regulate energy homeostasis and mediate the health benefits of physical-exercise [13].

Irisin levels in this study were significantly lower in type 2 obese diabetic women in comparison to obese non-diabetic controls, as shown in Table- 2. This finding agrees with the results previously reported by Assyov *et al.* [14] who found that irisin circulating concentrations were progressively reduced with the worsening of glucose tolerance; they were the highest in normal glucose tolerance (NGT) subjects, but lower in pre-diabetes, and the lowest in type-2 DM. In addition, they suggested that with the progression of IR, irisin circulating levels diminish.

Another study showed results that were consistent with the present findings and found that serum irisin circulating levels were significantly lower in type-2 DM patients in comparison to non-diabetic controls [15]. Several previous studies implicated PGC-1 α in the pathogenesis of type-2 DM. Especially, the expression and activity of PGC-1 α were significantly lower in the skeletal muscles of human diabetic type-2 subjects [16]. As irisin, which is a muscle-derived myokine, is induced by the expression of PGC-1 α [4], it is hence reasonable to speculate that the low-levels of plasma irisin in type-2 DM subjects were as a result of impaired PGC-1 α expression and mitochondrial functions in their muscles.

A recent study by Khidr *et al.* [17] also demonstrated that a sample of Egyptian population who were suffering from T2DM exhibit lower circulating levels of irisin than non-diabetic persons. In addition, it was shown that the FNDC5 gene rs16835198 G \rightarrow T polymorphism was a protective factor against T2DM, being accompanied by improved irisin glycosylation, a process which favorably influences irisin function [18].

Importantly, there are inconsistencies regarding the relationship between IR, T2DM, and irisin [19]. High serum irisin concentrations were also observed in patients suffering from T2DM [20,21], even though the bulk of research studies reported opposite results [22-24].

Table-3 reveals that type 2 obese diabetic women show a negative correlation between serum irisin and HbA1c. Glycosylated haemoglobin has been reported to be significantly negatively correlated with circulating levels of irisin in people with type-2 DM [23,25,26]. These previous experimental studies suggest that decreased circulating levels of irisin can be associated with development of IR and type-2 DM. These results are in agreement with the present study. In the present study, no correlation between irisin levels and BMI was observed.

It is concluded that diabetic type-2 obese women show a highly significant decrease in the levels of serum irisin when compared to obese non-diabetic women. There was no significant change in the mean level of serum irisin when compared according to age groups and duration of DM.

Future studies are needed in order to investigate the potential of irisin hormone to serve as a therapeutic target in type-2 DM and obesity.

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