CIRCULATING IRISIN LEVEL IN DIAGNOSED PATIENTS WITH METABOLIC SYNDROME

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ABSTRACT

Background: Metabolic syndrome is characterized by reversible diagnostic components such as reduced serum HDL-cholesterol, raised serum triglycerides, increase serum glucose concentration, increase blood pressure, all of which are related to large waist circumference. Irisin is an adipokine hormone that is mostly secreted by white subcutaneous adipose tissue and has a critical regulatory function in lipid metabolism. The present study aimed to evaluate serum irisin level among metabolic syndrome.

Materials and methods: A case control study was conducted among138 individuals, 69 patients with metabolic syndrome and 69 healthy individuals as a control group. The study was conducted from June 2022 to June 2023After a night of fasting, blood samples were taken the next morning. Glucose, insulin, total cholesterol, triglycerides, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and blood HbA1c% were all determined using the Cobas 6000 (Hitachi, Roche) device, with the exception of serum irisin, which was determined using an ELISA.

Results: The MS participants have higher percentage of high irisin levels compared to control participants with statistically significant differences (37 (53.6%); 24 (34.8%); p=0.039). Furthermore; there were insignificant differences between the mean ±SD levels of serum irisin of the studied groups (p=0.220).

Conclusion: Mean serum irisin level was higher among MS patients compared to healthy individuals, as well as, serum irisin levels had a positive correlation with isolated component of MS such as waist circumference, dyslipidemia and impaired glucos e metabolism.

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Keywords: Serum irisin, Metabolic syndrome, Obesity, Diabetes mellitus, Serum triglyceride.

Metabolic syndrome (insulin resistance syndrome) is defined as a biochemical and clinical condition characterized by reversible diagnostic components such as reduced serum HDL-cholesterol, raised serum triglycerides, increase serum glucose concentration, increase blood pressure, they are all related to weight gain particularly intra-abdominal with large waist circumference[1].

MS considered as a double major risk factor for cardiovascular disease and type 2 diabetes[2]. The prevalence of the metabolic syndrome was 30% to 40% and anticipated to increase significantly in tandem with the worldwide obesity epedimic[3]. Weight gain, particularly an increase in intra-abdominal fat storage (large waist circumference), causes the metabolic syndrome phenotype to emerge[4].

Irisin is an adipokine hormone that is primarily secreted by white subcutaneous adipose tissue and has a critical regulatory function in lipid metabolism (positive effect on hyperlipidemia) as well as a part in the conversion of white fat to brown fat, indicating that it may have a role in reducing fat accumulation and obesity and improving metabolic state[5]. Furthermore, irisin plays an important function in glucose metabolism by enhancing skeletal

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muscle glucose absorption and improving hepatic glucose uptake (insulin sensitizing hormone)[6]. It is accurate that irisin has a favorable influence on the metabolism of the liver and pancreatic islets, as it improves hepatic metabolism by reducing endoplasmic reticulum stress and β-islet cell mass survival and function, lowering the chance of developing type 2 diabetes[7].

Several studies showed inconsistent results of circulating irisin level and metabolic syndrome patients and its components consist of large waist circumference (increase body weight) and impaired glucose metabolism (IR, prediabetes, diabetes). Some research found a link between serum irisin levels, diabetes, waist circumference and impaired glucose metabolism. Whereas others found negative correlation between those three parameters[8,9,10].

As well as the components of MS are common all over the world including our locality,[11,12] & this issue was uncommonly done in our locality, therefore; The aim of our study was to determine the levels of serum irisin in MS patients compared to healthy control, and determine the association between serum irisin levels and metabolic syndrome components.

MATERIAL AND METHOD

A case control study was carried out at several primary health care clinics in Duhok, Kurdistan region, Iraq. The study included 138 individuals, 69 patients diagnosed with metabolic syndrome who visited the center for follow up and checking and 69 healthy individuals as a control group chosen from the staff of same centers. The study was conducted for 1 year interval from June 2022 to June 2023.

Metabolic syndrome was diagnosed according to the NCEP ATP III definition, and if three or more of the following five criteria were satisfied, the metabolic syndrome was present: waist circumference over 88 cm in female and over 102 cm in male, blood pressure over 130/85 mmHg or on anti-hypertensive treatment, serum triglyceride level over 150 mg/dl, serum HDL-cholesterol level less than 40 mg/dl in men or 50 mg/dl in women and serum glucose equal or more than 100 mg/dl.[13].

After an overnight fast and in the morning, all the participants were notified to attend the clinical biochemistry unit of laboratory department at Azadi Teaching Hospital, and the blood samples (7ml) were collected from every participant. The blood pressure was rechecked and waist circumference was measured depend on Word Health Organization protocol. At the same time, the serum was separated and used for measurement of glucose, HDL-c and TG. The remaining serum was stored for subsequent analysis of irisin. Serum glucose, HDL-c and TG was measured by Cobas 6000 (Roche, Hitachi) depending on enzymatic-colorimetric method[14]. Moreover; irisin was measured by Elisa depending on antigen antibody reaction (Bioassay technology Laboratory, Zhejiang, China).

ETHICAL APPROVE

The Research Ethics Committee of the General Directorate of Health in Duhok City gave its approval to the study (June 1 2021) and registered by reference number: 01062021-5-6.

STATISTICAL ANALYSES

The (IBM) SPSS Version 26.0 application was used to conduct the statistical analysis. The general information of study participants was shown in mean (SD) or number (%). Pearson chi-square and independent t-test were applied to evaluate the differences between characteristics of metabolic syndrome and healthy control participants. ANOVA one-way was used for evaluate the association between serum irisin levels and components of metabolic syndrome. The relationship of serum irisin levels with biochemical measurements and characteristics of metabolic syndrome participants were examined in bivariate

regression analysis. A p-value of less than 0.05 was used to assess the difference's significant level.

RESULTS

General characteristics of study participants presented in table 1. There was a significant difference between genders of the study participants as females of MS participants was more than the control participants (56.5%, 29.0%, respectively). Fifty-six (81.2%) of metabolic syndrome patients were more than 40 years old age compared to 12 (17.4%) of healthy controls with a significant difference (p<0.0001). The MS participants have higher percentage of high irisin levels compared to control participants with statistically significant differences (37 (53.6%); 24 (34.8%); p=0.039).

Table 1. General characteristics of studied participants

Characteristics			MS (n=69) N%	Controls (n=69) N%	*p* value
Gender		Male	30 (43.5%)	49 (71.0%)	**0.001**
		Female	39 (56.5%)	20 (29.0%)	
Age (year)		< 40 years	13 (18.8%)	57 (82.6%)	**< 0.0001**
		≥ 40 years	56 (81.2)	12 (17.4%)	
Waist circumferences	**Male**	<102 cm	4 (5.8%)	46 (66.8%)	**< 0.0001**
		≥102 cm	26 (37.7%)	3 (4.3%)	
	Female	<88 cm	4 (5.8%)	17 (24.6%)	**< 0.0001**
		≥ 88 cm	35 (50.7%)	3 (4.3%)	
Systolic BP		< 130 mmHg	16 (23.2%)	57 (82.6%)	**< 0.0001**
		≥130 mmHg	53 (76.8%)	12 (17.4%)	
Diastolic BP		<85 mmHg	24 (34.8%)	61 (88.4%)	**< 0.0001**
		≥85 mmHg	45 (62.5%)	8 (11.6%)	
FBS		<100 mg/dl	17 (24.6%)	59 (85.5%)	**< 0.0001**
		≥100 mg/dl	52 (75.4%)	10 (14.5%)	
TG		<150 mg/dl	3 (4.3%)	58 (84.1%)	**< 0.0001**
		≥150 mg/dl	66 (95.7%)	11 (15.9%)	
HDL	**Male**	< 40 mg/dl	29 (42.0%)	16 (23.2%)	**< 0.0001**
		≥ 40 mg/dl	1 (1.4%)	33 (47.8%)	
	Female	< 50 mg/dl	34 (49.3%)	5 (7.3%)	**< 0.0001**
		≥ 50 mg/dl	5 (7.3%)	15 (21.7%)	
Irisin		<350 g/dl	32 (46.4%)	45 (65.2%)	**0.039**
		≥350 mg/dl	37 (53.6%)	24 (34.8%)	

The Pearson chi-square test was used for statistical analysis.

The numbers in bold present the significant differences.

Demographic and biochemical parameter were expressed in table 2. All the five components of metabolic syndrome were statistically and significantly differed from that of healthy control (p < 0.0001). additionally; there were insignificant differences between the mean ±SD levels of serum irisin of the studied groups (p=0.220).

Table 2. Demographic and biochemical characteristics among studied groups.

Characteristics	MS (n=69)	Controls (n=69)	*p* value
	Mean± SD	Mean± SD	
Age years	47±10	33±7	**< 0.0001**
Waist circumferences cm	105.42±10.7	86.15±7.5	**< 0.0001**
Systolic BP mmHg	139.47±16.87	120.56±8.37	**< 0.0001**
Diastolic BP mmHg	88.51±10.42	79.49±7.81	**< 0.0001**
FBS mg/dl	137.55±67.66	91.48±7.68	**< 0.0001**
TG mg/dl	248.52±86.99	108.12±44..24	**< 0.0001**
HDL mg/dl	35.75±7.58	48.21±11.81	**< 0.0001**
Irisin mg/dl	399.32±221.96	359.73±148.67	0.220

For statistical analysis, an independent t-test was used.
The numbers in bold indicate the significant differences.

Association between mean serum irisin and components of metabolic syndrome was shown in Table 3. There were insignificant differences between the number of components of MS and mean serum irisin as there was a higher mean levels of serum irisin level with raising the number of components of MS (p=0.707).

Table 3. association of serum Irisin levels with the number of components of metabolic syndrome.

Character	Metabolic syndrome participants (N=69)			
	3 components	4 components	5 components	*p* value
No (%)	15 (21.8%)	25 (36.2%)	29 (42.0%)	0.016
Irisin mg/dl	392.27±272.84	412.89±234.09	447.80±226.84	0.707

For statistical analysis, a one-way ANOVA was applied.
The red numbers show the significant differences

There was a statistically insignificant correlation between serum irisin levels and WC, glucose, BP, TG and HDL as shown in table 4.

Table 4. Correlation between serum Irisin level, general characteristics and biochemical parameters of metabolic syndrome participants

Characteristics	Metabolic syndrome participants Mean irisin (n=69)	
	Pearson Correlation (r)	Sig. (2-tailed) (*p* value)
Waist circumferences cm	0.084	0.327
Systolic BP mmHg	0.069	0.422
Diastolic BP mmHg	0.131	0.125
Glucose mg/dl	-0.005	0.953
Triglyceride mg/dl	0.017	0.843
HDL mg/dl	-0.035	0.686

Bivariate correlation was performed for statistical analyses.

DISCUSSION

This case control study observed that the MS was highly prevalent among females with age of equal or more than 40 years. This was similar with the findings of a research conducted by Beigh SH et al and Njelekela MA et al that showed a threefold increase of MS in Female than Male 15,16. In contrast by other study done by Jahan et al found in his study predominate high MS in male than Female[17]. In the current study, the majority of MS patients had abdominal obesity and dyslipidemia (high TG and low HDL-c). This result was consistent with others as they showed that the Central obesity appears to precede the emergence of the other metabolic syndrome components and plays a critical

role to precede the appearance of the other metabolic syndrome components[18]. Weight gain, specifically a rise in intra-abdominal fat storage, which is matched by a greater waist circumference, causes the metabolic syndrome phenotype to develop[19].

The present study found statistically insignificant higher mean serum irisin level with statistically significant higher prevalence rate of hyperirisenemia among MS patients compared to healthy individuals. This result was consistent with studies done in different parts of the world, and in contrast, other studies found lower serum irisin levels in MS patients. It is reasonable to believe that various variables, including as body fat, muscle, and exercise hype, influence circulating irisin levels[20]. These results can be explained by either raised releasing of irisin by muscle tissue or adipose tissues, or a compensatory rise in irisin to overcome underlying irisin resistance in metabolically sick people. Increased irisin production from muscles and adipose tissue in obese individuals is intended to enhance energy utilization and glucose homeostasis in order to establish metabolic balance[21]. The hyperirisenemia exhibited in metabolic obese persons may be interpreted as a compensatory strategy to compensate for the observed irisin resistance and to enhance the hormone's anti-obesity and anti-hyperglycemic effects[22].

The data from different studies showed a conflict results regarding the correlation between mean serum irisin levels and metabolic syndrome parameters (isolated or collected). Mean serum irisin was positively and insignificantly associated with number of components of MS as the mean level of irisin was higher as the number of components was higher. Wu GZ et al discovered that circulating irisin levels were positively associated with MS components[23]. Moreover, Stengel A et al 2012 shown that Obese patients have higher circulating irisin levels compared to normal weight[24]. This rise is thought to be a physiological purpose to enhance glucose tolerance and improve insulin sensitivity among obese subjects. Other studies showed that Baseline irisin levels were significantly higher in individuals who developed prediabetes and DM, indicating an increased releasing of irisin from mature adipocytes, which enhanced activation of glycolysis, thus, uncoupling in the mitochondria reduces oxidative respiration[25,26]. A little research was conducted to examine the relationship between serum irisin and lipid profile that considered as components of MS such as serum triglyceride and HDL-c level. Liu et al. reported that serum irisin level was significant correlated with serum TG and HDL-c level in healthy non- diabetic subjects, showing that circulating irisin may play a preventive function in cardiovascular disease[27]. Moreover, Mehrabian Set al. shown that here is no significant association between serum irisin levels, serum TG levels, or serum HDL-c levels[28].

CONCLUSSION

The present study conclude insignificant higher mean serum irisin level and significant higher prevalence rate of hyperirisenemia among MS patients compared to healthy individuals. Mean serum irisin was positively correlated with number of components of MS as the mean level of irisin was higher as the number of components was higher. Moreover; serum irisin levels had a positive correlation with isolated component of MS such as waist circumference, dyslipidemia and impaired glucose metabolism.

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پوخته

گشتاندنا ئاستێ ئیریسینێ د نەخۆشێن ب نەخۆشیا گهورینێن خۆراکی هاتینە دەستنیشانکرن

پێشەکی و ئارمانج: نەخۆشیا میتابۆلیك ب پێکهاتێن نەرێنی یێن دەستنیشانکرنێ دئێنە نیاسین، وەکی دابەزینا کۆلیسترولی HDL د خۆینێ دا. هشکبوونا دەماران، بلندبوونا رێژا شەکری دخوینێ دا، بلندبوونا فشارا خوینێ، کو هەمی ئەون یێن پەیوەندی ب دەوروبەرێن کەمەرا مەزن ڤە هەین. دەربارەی (Irisin) کو هۆرمۆنەکێ (adipokine) یە پتریا جاران ب رێیا شانێن چەوریا چۆرێن سپی دبن پیستی ڤە دەردکەڤن و ئەرکەکێ گرنگ د رێکخستنا گهورینا روونی دا هەیە.

ئارمانج ژ ڤێ ڤەکۆلینا مە، خەملاندنا ئاستێ (Irisin)ێ یە د خوینا توشبویێن گهورینێن خۆراکی هەی.

رێکێن کاری: ڤەکۆلینا مە ل سەر 138 کەسان هاتیە ئەنجام دان، کو 69 ژوان نەخوشێن توشی نەخوشیا (میتابۆلیکسیندرۆم) بووین، و 69 کەسێن ساخلەم. ئەڤ کۆما کەسان بو دەمەکێ دیارکری ل ژێر چاڤدێریێ دا بوون، کو ژ هەیڤا خزیرانا 2022ێ هەتا خزیرانا 2023ێ. رۆژا دویڤ دا نموونێن خوێنێ پشتێ رۆژیبوونا شەڤەکێ هاتینە وەرگرتن (کلوگۆز، ئەنسۆلین، کۆلیسترولێ سەرجەمێ گشتی، ترایگلیسرید، کۆلیسترولێ روونێ پرۆتینێ تیریا کێم، کۆلیسترولێ روونێ پرۆتینێ تیریا بلند) ورێژا (HbA1c) ب بکارئینانا کۆباس 6000 هاتینە دیارکرن و دەستنیشانکرن، تنێ ئیریسین د سیرۆمی دا نەبیت مو ب بکارئینانا کۆباس 6000 (Hitachi, Roche) ئەلیسا هاتیە ئەنجامدان.

ئەنجام: د ناڤ ئەنجامان دا، بو مە دیاربوو، کو ئەو پشکدارێن توشی هشکبوونا دەماران (ئیسکەمرۆسیس) بووین، ئاستێ (ئیریسینیان) بلندتر بوو هەڤبەرکرن دگەل بشکدارێن توشی گرۆپێ کۆنترولکری، دگەل جوداهیەکا ئاماری یا گرنگ(p=0.039 ;(34.8%) 24 ;(53.6%) 37)، سەرەرای ڤێ چەندێ جوداهیەکا ئاماری یا بەرچاڤ دناڤبەرا ئاستێ ناڤەندی (± SD) یێ (ئیریسین) د سیرۆمێ وی گرۆپێ ڤەکۆلینلسەرکری هەبوو (p=0.220).

دەرئەنجام: دەرئەنجام و دەستکەفتێن دڤێ ڤەکۆلینێ دا بدەست مە کەتین ئەوبوو کو سەرجەمێ ئاستێ (Irisin)ێ د (serum)ی دا ل دەڤ نەخۆشێن توشیبووی ب هشکبوونا دەماران پترە، ئەگەر بێنە هەڤبەرکرن دگەل کەسێن ساخلەم.

هەروسا ئەم گەهشتینە وێ ئەنجامێ کو ئاستێ (Irisin)ێ د(serum)ی دا، پەیوەندیەکا ئەرێنی یا دگەل پێکهاتێن ژێکڤاڤارتنێ یا هەی، ئیسکەمرۆسیس، دەوربەرێن کەمەرێ، نەرێکوپێکیا روونێ خوینێ و لاوازیا میتابۆلیزمی یا کلۆگۆزی.

الخلاصة

تعميم مستوى الإيريسين في المرضى الذين تم تشخيص إصابتهم بالمتلازمة الأيضية

الخلفية والأهداف: تتميز المتلازمة الأيضية بمكونات تشخيصية عكسية مثل انخفاض نسبة الكوليسترول الحميد في الدم، وارتفاع الدهون الثلاثية في الدم، وزيادة تركيز الجلوكوز في الدم، وزيادة ضغط الدم، وكلها مرتبطة بمحيط الخصر الكبير. اما الإيريسين (Irisin-هو هرمون) أديبوكين (adipokine) التي يفرز في الغالب عن طريق الأنسجة الدهنية البيضاء تحت الجلد وله وظيفة تنظيمية مهمة في استقلاب الدهون .

الهدف من دراستنا هذه تقييم مستوى الإيريسين في الدم لدى المصابين بمتلازمة التمثيل الغذائي.

طرق العمل: أجرينا الدراسة على 138 فردا، منهم 69 مريضا يعانون من متلازمة التمثيل الغذائي و69 شخصا سليما بحيث كانت هذه المجموعة تحت المراقبة خلال فترة زمنية محددة والتي امتدت من يونيو 2022 إلى يونيو 2023، وتم اخذ العينات من الدم في صباح اليوم التالي بعد ليلة من الصيام. فتم تحديد الجلوكوز والأنسولين والكوليسترول الكلي والدهون الثلاثية وكوليسترول البروتين الدهني منخفض الكثافة وكوليسترول البروتين الدهني عالي الكثافة ونسبة HbA1cفي الدم جميعها باستخدام جهاز Cobas 6000 (Hitachi, Roche) باستثناء إيريسين المصل الذي تم تحديده باستخدام جهاز Cobas 6000 (Hitachi, Roche) إليسا.

النتائج: تبين لنا ضمن النتائج بأن المشاركين الذين لديهم مرض التصلب العصبي المتعدد كانت نسبة مستويات الإيريسين لديهم المرتفعة مقارنة بالمشاركين في المجموعة الضابطة مع فروقات ذات دلالة إحصائية (37 (53.6%); 24 (34.8%); p=0.039)، إضافة الى هذا كانت هناك فروقات ذات دلالة إحصائية بين متوسط مستويات SD ± من ايريسين المصل في المجموعات المدروسة (ع = 0.220).

الاستنتاجات: اما الاستنتاج التي توصلنا اليه خلال بحثنا هذا كان متوسط مستوى الايريسين في المصل أعلى لدى مرضى التصلب المتعدد مقارنة بالأفراد الطبيعيين، وتوصلنا ايضاً الى ذلك بأن مستويات الايريسين في المصل لها علاقة إيجابية مع المكونات المعزولة لمرض التصلب العصبي المتعدد مثل محيط الخصر، وخلل شحوم الدم وضعف استقلاب الجلوكوز.