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The role of Meteorin - like protein and some adipokines in menopause in obese women

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Abstract :

Obesity is a major global health challenge rather, it is a persistent, moreover Menopausal was associated with an increase in abdominal fat due to both hormones and metabolic abnormalities. The aim of study determine the involvement of the role adipokines in metabolism problems associated with obese. The cross-sectional comparative study was conducted on 240 Iraqi menopausal women in Mosul city , whose age range is 45–65 years. They were divided into three groups, each involving 80 women, according to their weight and BMI: control, overweight, and obese. Venous blood samples withdrawn from all subscribers to obtain serum, from which adipokines (Meteorin-like protein, kisspeptin, leptin and Irisin) levels were determined by (ELISA). The analytical adipokines (Meteorin-like protein and kisspeptin) levels were significantly higher in the obesity group as compared to both control group and over-weight groups, respectively ($p\leq0.01$). Nevertheless, The concentration of LEP was significantly higher in the obese group when compared to both overweight and control groups ($P<0.001$). The LEP concentrations of over-weight were significantly higher ($P<0.001$) than those of the control group. Moreover, a significant increase in the level of Irisin in serum of both over weight and obese groups compared with control group ($P\leq0.001$).

Keywords: Menopause, Meteorin-like protein, kisspeptin, Obesity .

دور بروتين شبيه بالميتيورين وبعض الأديبوكينات في فترة انقطاع الطمث عند النساء البدينات.

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مستخلص:

السمنة هي أحد التحديات الصحية العالمية الكبرى، بل هي مشكلة مستمرة، علاوة على ذلك، ارتبط انقطاع الطمث بزيادة الدهون في البطن بسبب كل من الهرمونات والاضطرابات الأيضية. يهدف البحث إلى تحديد دور الأديبوكينات في مشاكل التمثيل الغذائي المرتبطة بالسمنة. أجريت الدراسة المقارنة المقطعية على 240 امرأة عراقية في سن اليأس في مدينة الموصل، تتراوح أعمارهن بين 45 و65 عامًا. تم تقسيمهن إلى ثلاث مجموعات، تضم كل منها 80 امرأة، وفقًا لوزنهن ومؤشر كتلة الجسم: المجموعة الضابطة، والوزن الزائد، والسمنة. تم سحب عينات الدم الوريدي من جميع المشتركين للحصول على مصل، والتي تم تحديد مستويات الأديبوكينات (بروتين شبيه بالميتيورين، وكيسبيبتين، وليبتين، وإريسين) منها بواسطة (ELISA). كانت مستويات الأديبوكينات التحليلية (بروتين شبيه بالميتيورين وكيسبيبتين) أعلى بشكل ملحوظ في مجموعة السمنة مقارنة بكل من المجموعة الضابطة والمجموعات ذات الوزن الزائد، على التوالي ($p\leq0.01$). مع ذلك، كان تركيز LEP أعلى بشكل ملحوظ في المجموعة التي تعاني من السمنة مقارنةً بكلٍّ من مجموعتي الوزن الزائد والضبط ($P<0.001$). كما كانت تركيزات LEP لدى الأشخاص الذين يعانون من زيادة الوزن أعلى بشكل ملحوظ ($P<0.001$) من تلك الموجودة في مجموعة الضبط. علاوةً على ذلك، لوحظت زيادة ملحوظة في مستوى Irisin في مصل كلٍّ من مجموعتي الوزن الزائد والسمنة مقارنةً بمجموعة الضبط ($P\leq0.001$).

الكلمات المفتاحية: انقطاع الطمث، بروتين شبيه بالميتيورين ، الكيسبيبتين، السمنة.

Introduction

Obesity is a chronic, complex, and multifaceted metabolic disorder influenced by a combination of genetic, biochemical, environmental, behavioral, social, and economic factors. Obesity necessitates perpetual intervention. It presents multiple health-related hazards [1]. Menopause is a natural occurrence in middle-aged women resulting from reproductive aging. The menstrual cycle is terminated in a way that is both permanent and irreversible, which constitutes the end of the reproductive capacity of the individual [2], which is connected with a decline in estrogen and progesterone levels, which leads to imbalances in the homeostasis of the body. These imbalances include reduced insulin sensitivity, modulation in glucose and lipid metabolism, and other metabolic related issues. When it comes to obesity, the most common cause is an imbalance between energy intake and expenditure. Obesity induces harmful diseases in people, particularly in women, due to many biological and hormonal variables [3]. Weight gain throughout midlife is regarded as an unavoidable consequence of the menopausal transition. Women in midlife are susceptible to weight increase owing to many physiological, biochemical, endocrinological, and psychological alterations [4].

Adipokines are bioactive molecules secreted by adipose tissue that affect health and disease. They play important roles in regulating metabolism, inflammation, immunity, cardiovascular function, and cancer. However, adipokine dysregulation can contribute to obesity-related disorders [5]. In this line, More than 15 adipokines (such as Meteorin-like protein , Lipocalin 2 (LCN2), Kisspeptin (Kiss) adiponectin, leptin, resistin and visfatin, etc) have garnered increased attention in the prevention and treatment of obesity and its associated complications due to their involvement in the regulation of energy metabolism [6].

Metrnl, also called Meteorin-like protein, interleukin-41, and subfatin, is a recently identified hormone associated with the control of metabolism and considered a possible diagnostic marker of metabolic syndromes. It is predominantly expressed in brown ad-

ipose tissue [7]. It was first shown to be an adipokine that affects glucose homeostasis. According to [8]. it is expressed and secreted by various organs, including the brain, adipose tissue, muscle, liver, spleen, skin, heart, and activated macrophages [9]. It is consisting of 311 amino acids encoded by 936 base pairs [10]. It was considered an adipokine, garnering significant attention from researchers due to its crucial roles in regulating glucose metabolism homeostasis, enhancing insulin sensitivity, promoting browning of adipose tissue, and boosting energy expenditure in metabolic diseases [11].

Aim of study to shed light on the pivotal role of Adipokines (Meteorin-like protein, kisspeptin, leptin and Irisin,) in the pathogenesis of obesity and correlate their concentrations with metabolic markers in postmenopausal women with elevated BMI.

Methodology

Study subjects: The Committee of Research Ethics accepted the research methodology, the Department of Chemistry, College of Education for Pure Sciences, Tikrit University, Tikrit, Iraq. The participants were recruited from the National Clinic of Obesity in Al-Mosul City from December 2023 to July 2024. All participants gained permission after understanding the project aim and tests that would be performed. A questionnaire form was collected formally; it contained the (name, age, date….etc) Weights and heights of participants have been measured using an electronic balance, and the body mass index (BMI) is computed by dividing weight in kilograms by the square of height in meters [12]. All participates without any systemic disease. Two hundred forty postmenopausal females with different BMI (normal, overweight, and obese) were between the ages of 45 and 65 years.

The main group was further divided into sub-groups:

- Controls:80 Included female with a normal BMI (below 25 kg/m2)
- Overweight group: 80 Included female of BMI (25-29.9 kg/m2).
- Obese group:80 Included female with BMI ≥30 kg/m2 .

In a gel tube, collect 5 ml venous blood sample from all subscribers, put

on the bench for 15 minutes to be clotted then centrifuged at 3000 rpm till 10 minutes to get serum, after that aliquot into 4 parts in eppendorf tubes and frozen in -20 C° until collect the requested number of samples. Sera aliquots were placed in eppendorf tubes and stored at -40C° until used .

1. Biochemical Parameters

The human Meteorin-like Protein was measured in the sera for the all study groups using the (ELISA) kit according to manufactures instruction (Kit Bioassay Technology Laboratory (BT LAB)/ China), Kisspeptin 1 (KISS1)was measured using the protocol of ELISA kit ELK Biotechnology /China).while Irisin was measured using the protocol of ELISA kit , provided by (FineTest®) / China) ,with same principle of Leptin (LEP) KOMA BIOTECH INC/ Korea

2. Statistical analysis

The statistical analysis system SAS 19 program has been utilized to compare between study groups in study parameters. (Analysis of variation-ANOVA) was used to compare between means (P value of 0.05 and 0.01 has been considered to be statistically significantly.

Result and discussion

The results of current shown in Table (1) indicated that there was a significant increase in the levels of Serum meteorin-like protein (Metrnl) and kisspeptin (Kiss)in obese group compared to control and overweight groups respectively (P≤0.0001).

Table (1):Analytical parameters of adipokines profile in study groups.

Parameter	Control N=80	Over weight N=80	Obesess N=80	P value
merteroin-Like protein (ng/ml)	5.65+1.14 b	6+1.31 b	9.14+1.74 a	0.000
Kiss (pg/ml)	212.6+6.14 b	219.5+2.81 b	299.70+35.71a	0.000
LEP (ng/ml)	21.78+4.63 c	26.77+4.90 b	31.05+4.01 a	0.000
Irisin (ng/ml)	5.49+0.98 b	15.87+1.21 a	15.85+1.07 a	0.000

Horizontally different letters denote significant differences among groups at a 5%.

These findings corroborate those of a prior investigation by [13], which found that Metrnl was elevated in the blood and fat in mice who were made obese by a high-fat diet. Also, comparing with skinny children, obese children's adipocytes showed higher expression of Metrnl, according to [14] found that Metrnl is associated with obesity due to its relationship with the dynamics of adipose tissues. Nevertheless, there were conflicting connections among serum Metrnl level with obesity indices. Researchers found a negatively correlation between Metrnl levels and (BMI in obese people or those with a metabolism disorders [15,16] .

On other hand, Chung et al. discovered that serum meteorin-like protein levels did not correlate with body weight, BMI, waist circumference, or fat tissue mass. In clinical research, confounding variables like age, sex, medications, and physical activity may also contribute to this disparity [17]. Also , the finding of current study align with another study demonstrating increased kisspeptin level in obese women because of increased bulk of adiposity [18]. Evidence suggests that Kisspeptin ergic neurons colocalize leptin and estradiol receptors, resulting in a connection between feeding and reproduction functions. Leptin mRNA code and blood leptin increased during the estrogen cycle. Estrogen signal, BMI, nutrition, and eating regulation throughout hormones are all affected when leptin-Rs in vagal nerves are deleted [19]. The results of the other study suggested that the kisspeptin concentration may be associated with both metabolism and obesity [20].

The concentration of LEP was significantly higher in the obese group when compared to both overweight and control groups ($P<0.001$). The LEP concentrations of over-weight were significantly higher ($P<0.001$) than those of the control group. The result of current study showed an increase leptin levels in obese and overweight women, were consistent with previous epidemiological studies in that considerable changes in peptide hormone production and release have the potential to interfere with intermediate metabolism, IR, and raise BMI. These levels were negatively correlated with the abdominal fat index and/

or WHR and directly correlated with subcutaneous fat [21,22]. Moreover, the hormone leptin, which is released by adipocytes, is higher in those who have obesity even when results are corrected for BMI [23,24] , While others think that individuals with obesity have leptin resistance, IR [25] and contradictory combination of fatness with hyperleptinemia shows that leptin resistance is a disorder because leptin affects appetite and body weight [26].

The results in Table (1) indicated that there was a significant increase in the level of Irisin in serum of both over weight and obese groups compared with control group ($P \leq 0.001$). there is a positive association between sera irisin levels and lean body weight. Similarly, irisin release and body mass index have been linked in certain research investigations to a positive correlation, while in others they have been linked to a negative correlation. [27,28].Researchers have found that increased irisin levels among obese people have been linked with a reduced likelihood of metabolism syndrome. However, that's not all: higher irisin levels in obese people also seem to regulate the metabolism of lipids (by inhibiting ATP production as well as by extension, heat production), improve prediction, and smaller the possibility of insulin resistance-related complications (by lowering glucose levels [29]. As a result of their observations [30] established a connection between elevated irisin levels with control of subparticle lipoproteins as well as lipid metabolism. But other research has linked elevated irisin levels to better health outcomes. Because irisin reduces glycated hemoglobin, which in turn prevents resistant to insulin, this decrease may serve as a biomarker for metabolic diseases . On the other hand, sera irisin levels spike right after exercise. This discovery provides more evidence that irisin levels may regulate glucose with fatty acids absorption in muscular tissues. In addition to its role in homeostasis, irisin is associated with body composition via energy expenditure; there is an inverse relationship among irisin levels with body mass index, that may be due to variations in the subjects' actual composition. According to [31]. There is still a lot of mystery about the relationship among sexual

hormones and abdominal fat. Several studies have shown that low levels of estrogen cause central fat to accumulate through various pathways, such as raised adipocyte expansion, inflammatory processes, oxidative stresses in adipose tissues, reduced expenditure of energy, and raised lipid consumption through blood circulation. Additionally, some research have shown that harmful alterations to inflammation indicators with adipokines are strongly associated with elevated visceral fat mass during menopause [32]. Present study is consistent with the study that came up with Alina Kuryłowicz which says A menopause-related decrease in the expression of genes essential for estrogen synthesis and function may predispose postmenopausal women to weight gain and metabolic abnormalities because the menopausal state may affect the activity of genes in adipose tissue [33]. .

General bivariate correlation analysis and linear regression considering BMI as a dependent variable and all parameters of the study as independent variables across the study population were conducted as shown in Table (2).

The current study found that BMI in obese group was positively significant ($P<0.01$) associated with BMI and merteroin-Like protein level. However, non-significant associations between BMI and other parameters in obese group were observed.

Table (1): Body mass index association with all parameters under study groups (overweight and obese) groups.

Parameters	Over weight N=80	Obese N=80
age /year	0.262	0.117
Kiss (pg/ml)	-0.205	-0.370
merteroin-Like proten (ng/ml)	-0.095	.753**
LEP (ng/ml)	0.169	0.179
Irisin (ng/ml)	0.099	-0.192

* Correlation is significant at the 0.05 level

**Correlation is significant at the 0.01 level (2-tailed).

Conclusions:

Obesity is related factor to high level of specific-adipokine profile (meteorin-like protein , kisspeptin , leptin and Irisin) associated with the pathogenesis of menepousal.

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