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Evaluation of Oxidative Stress and Leptin Level in Samples of Iraqi Obese Women

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Abstract

The aim of this study is to investigate oxidative stress and leptin level in obese women. Fifty obese women with BMI value of ≥ 30.0 kg/m² and thirty healthy women with BMI < 24.9 kg/m² were involved in the study during their attendance at Gastroenterology and Liver Hospital/ Medical city in Baghdad province from October 2018 to February 2019. The age range for all women was 30-50 years. Blood samples were collected from each participant for the evaluation of the levels of leptin hormone, Super Oxide Dismutase (SOD), and Malondialdehyde (MDA). The results of BMI, leptin hormone, MDA and SOD showed highly significant increase (P<0.01) in obese women in comparison with the control group.

Results: The results show that BMI value were significantly higher (P<0.01) in obese women (41.90 ± 0.87 kg/m²) in comparison with the control (23.58 ± 0.28 kg/m²). The level of leptin hormone was significantly higher (P<0.01) in obese women (1444.00 ± 10.67 pg/ml) in comparison with the control (932.26 ± 25.92 pg/ml). Also, MDA level was significantly higher (P<0.01) in obese women (6.81 ± 0.29 mg/dl) in comparison with the control (4.53 ± 0.44) mg/dl. The level of SOD was significantly higher (P<0.01) in obese women (15.67 ± 1.42 mg/dl) in comparison with the control group (3.75 ± 0.60 mg/dl).

Conclusions: Obesity is detected by the level of leptin Hormone; leptin is regarded as a good parameter for monitoring obesity, showing a high increase with increasing BMI. The increase in obesity causes oxidant stress and formation of MDA that is considered as a major risk factor in obesity, where a decrease in antioxidants was also recorded.

Keywords: Obesity, BMI, Leptin, MDA, SOD.

تقييم جهد الاكسدة و مستوى هرمون اللبتين في عينة من النساء العراقيات البدنيات

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الخلاصة

هدفت الدراسة الى التحري عن جهد الاكسدة ومستوى هورمون اللبتين في النساء البدنيات. خمسون امراه بدنيه بمؤشر كتلة جسم اكثر من 30كغم/م² وثلاثون امرأة بمؤشر كتلة جسم اقل من 24.9 كغم/م² تم شمولهن في هذه الدراسة خلال حضورهن الى مستشفى الكبد وامراض الجهاز الهضمي في مدينة الطب في محافظة بغداد الفترة من تشرين الاول 2018 الى شباط 2019. معدل اعمار جميع النساء كان من 30-50

عاما. جمعت عينات الدم من النساء لتقدير مستوى هورمون اللبتين وانزيم سوبر اوكسايد دسميوتيز ومستوى المالوندهايد.

النتائج: اظهرت النتائج حصول ارتفاع معنوي عالي ($P < 0.01$) في مؤشر كتلة الجسم ومستويات كل من اللبتينو اوكسايد دسميوتيز ومستوى المالوندهايد. في النساء البدنيات مقارنة مع الاصحاء. ارتفعت قيمة مؤشر كتلة الجسم ($BMI(kg/m^2)$) ارتفاعاً معنوياً ($P < 0.01$) في النساء البدنيات (41.90 ± 0.87) مقارنة مع مجموعة السيطرة (23.58 ± 0.28)، اظهر مستوى هرمون اللبتين (pg/ml) ارتفاع عالي المعنوية ($P < 0.01$) في النساء البدنيات (1444.00 ± 10.67) مقارنة مع مجموعة السيطرة (932.26 ± 25.92) بينما اظهر مستوى MDA(mg/dl) اظهر ارتفاع معنوي عالي ($P < 0.01$) في النساء البدنيات (6.81 ± 0.29) مقارنة مع مجموعة السيطرة (4.53 ± 0.44). اظهر SOD (mg/dl) ارتفاع معنوي عالي ($P < 0.01$) في النساء البدنيات (15.67 ± 1.42) مقارنة مع مجموعة السيطرة (3.75 ± 0.60). الاستنتاج: تُكشف البدانة عن طريق هرمون اللبتين، يعتبر هرمون اللبتين كعيار جيد للتحكم بالبدانة التي تين زيادة كبيرة في مؤشر كتلة الجسم و زيادة في جهد الاكسدة و تكوين مالوندهايد الذي يعتبر عامل اساسي خطر عند البدناء بالإضافة الى نقص في مضادات الاكسدة.

Introduction

Obesity is defined as a chronic disease that arises from the interaction of social, metabolic, behavioural, psychological, cellular, and molecular factors [1]. A previous study [2] reported that obesity can also be describing the accumulation of body fat. However, the location of the adipose tissue is determined by regional fat distribution in specific regions, being very different across the life cycle and between the sexes and ethnic groups. World Health Organization (WHO) defines obesity in terms of a body mass index (BMI) value of $>30 \text{ kg/m}^2$, with overweight is considered to occur at a BMI of 25 kg/m^2 [3]. Obesity increases the danger of various diseases, such as cardiovascular diseases (CVD), osteoarthritis, musculoskeletal disorders, gall stones, psychological disorders, psychosocial problems, sleep apnoea, diabetes, hypertension, liver disease, and certain cancers, which commonly reduce the lifespan in individuals [4,5].

Leptin was discovered in 1994 and its name is derived from the Greek word "leptos" that means "thin" [6]. It is a 16 kDa peptide encoded by the obesity gene (ob gene) [7] and consists of 167-amino acid with a four-helix bundle structure similar to that of cytokines [8]. The obesity gene is located in the 7th chromosome in humans [9]. Leptin is present in the plasma as a free form, or it is bound to leptin binding protein. Plasma binding proteins are possible to have a soluble structure of leptin receptor. An earlier study [10] showed that leptin circulates in the bound form in normal individuals, while it is present in a free form in obese patients. Thus, level of leptin circulating in the body changes according to the period of food intake and fasting. For example, leptin will decrease during starvation, while high food intake will increase its blood level. Leptin concentration is different according to sex, being higher in women than in men [6].

Oxidative stress is commonly associated with reactive oxygen species (ROS) and takes place under physiological conditions where it causes damages in different organs. It is related to various pathological processes such as obesity, diabetes, cardiovascular disease, and atherogenic processes [1]. ROS list includes the hydroxyl radical (OH^\cdot), nitric oxide, hydrogen peroxide (H_2O_2), lipid peroxides and superoxide. Most of these agents have beneficial roles, but when they are present in excess the cell becomes under oxidative stress [11]. The difference between the oxidant and antioxidant pathways can cause an increase in the accumulation of lipid oxidation products, such as lipid hydro peroxides and MDA. These materials are toxic and cause an increased risk of arteriosclerosis in the blood by other lipoproteins. In addition, oxidative stress increases after workout. However, aerobic exercises were reported to decrease the level of oxidative stress in obese men [12,13].

Malondialdehyde MDA is another product of lipid peroxidation, which was studied as a marker of oxidative stress. MDA is the result of polyunsaturated fatty acids (PUFA) oxidation [14] and serves as a suitable index for determining the peroxidation reactions [15].

Antioxidants are substances that have the ability to dispose free radicals and prevent them from causing more cell damage. Free radicals are responsible for causing many health problems, including cancer, ageing, heart diseases, and gastric problems [16]. Antioxidants act as a scavenger to prevent tissue and cell damage. Cells produce defences against high levels of free radicals by preventing

reform mechanisms, physical defences, and antioxidant defences [17]. The major antioxidant enzymes involved in the neutralization of ROS and RNS are SOD, CAT, GPx, and GRx[18]. They can prevent oxidation by dropping the rate of chain initiation, either by scavenging the free radicals or by stabilizing the transition of metal radicals such as copper and iron [19].

Materials and Methods

This study was conducted at the Gastroenterology and Liver Hospital in the Medical City during the period from October 2018 to February 2019. Eighty Iraqi women were included, 50 of whom were obese with a BMI of $> 30 \text{ kg/m}^2$ and 30 were non-obese with a BMI of $< 24.9 \text{ kg/m}^2$ as a control group, with an age range of 30-50 years.

Information was collected from both obese and control women before blood collection. Patients with thyroid disorder, diabetes, high blood pressure, alcohol intake and smoking were excluded from this study. Six ml of blood were collected from each woman via vein puncture using 10 ml disposable syringes. The blood was dispensed in a Gel tube and left to clot for 10 minute at room temperature, after which the serum was separated by a centrifuge at 3000 rpm for ten minute and preserved at deep freezer (-20C) before analysis. The ELISA kits that was used for leptin determination was designed for the accurate quantitative measurement, while the kit used for MDA and SOD measurement was prepared manually. The Statistical Analysis System- SAS (2012) program was used to analyse the different effects of the study parameters.

Results and Discussion

Table-1 shows that the BMI value was significant higher ($P<0.01$) in obese women (41.90 ± 0.87) kg/m^2 in comparison with the control (23.58 ± 0.28) kg/m^2 . The level of leptin hormone was highly significantly increased ($P<0.01$) in obese women (1444.00 ± 10.67) pg/ml in comparison with the control group (932.26 ± 25.92) pg/ml . Also, MDA level was highly significantly ($P<0.01$) increased in obese women (6.81 ± 0.29) mg/dl in comparison with the control group (4.53 ± 0.44) mg/dl . The level of SOD was also highly significantly increased ($P<0.01$) in obese women (15.67 ± 1.42) mg/dl in comparison with the control group (3.75 ± 0.60) mg/dl .

Table 1-Levels of leptin, MDA and SOD in obese and control groups.

Group	Mean \pm SE			
	BMI kg/m^2	Leptin (pg/ml)	MDA (mg/dl)	SOD (mg/dl)
Control	23.58 ± 0.28 b	932.26 ± 25.92 b	4.53 ± 0.44 b	3.75 ± 0.60 b
Obese	41.90 ± 0.87 a	1444.00 ± 10.67 a	6.81 ± 0.29 a	15.67 ± 1.42 a
LSD value	2.306 **	48.387 **	1.035 **	4.129 **
P-value	0.0001	0.0001	0.0001	0.0001

** ($P<0.01$).

Means having different letters in the same column are differed significantly.

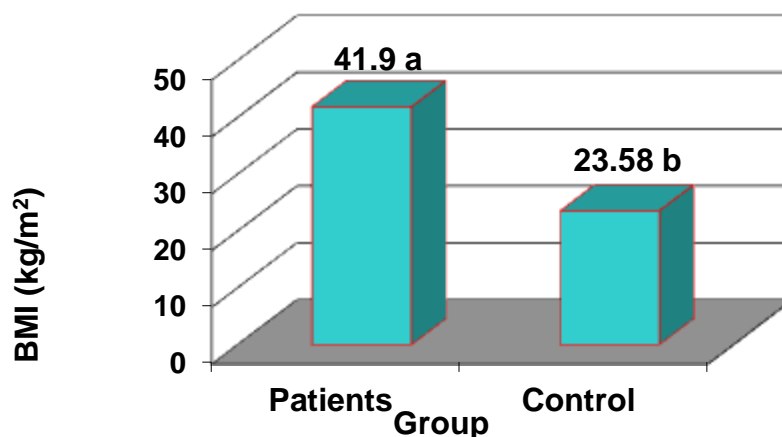


Figure 1-Values of BMI in patients and control.

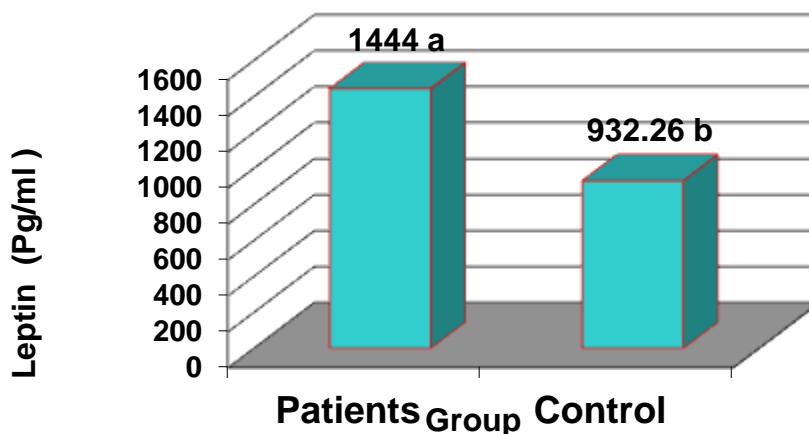


Figure 2-Levels of leptin in patients and control

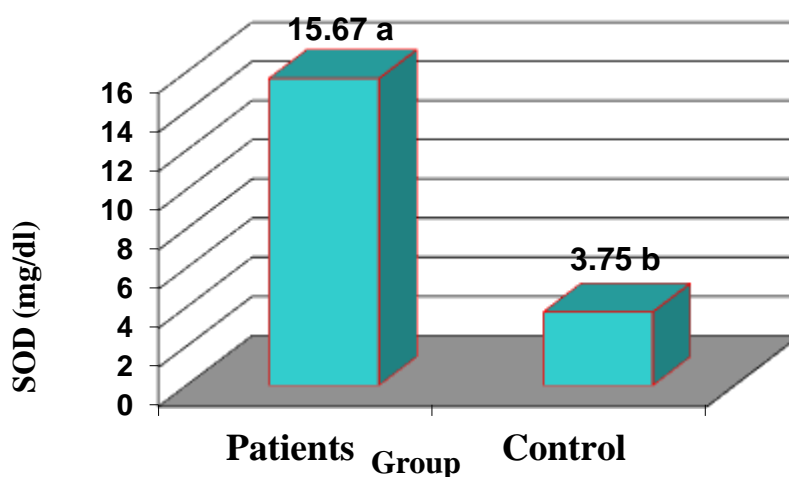


Figure 3-Levels of SOD in patients and control

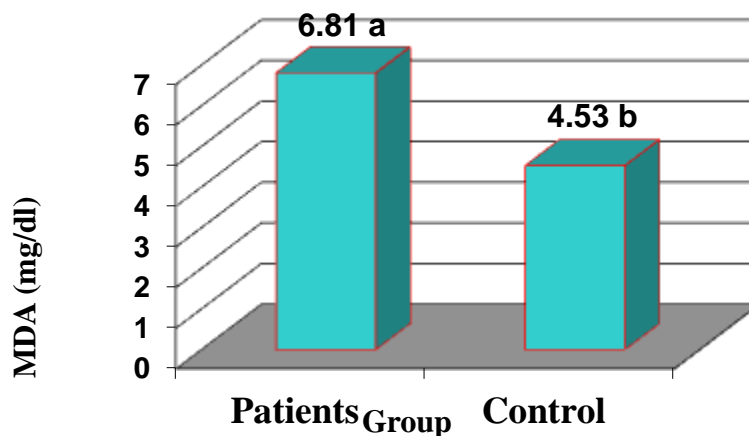


Figure 4- Levels of MDA in patients and control

The results of the present study suggest that the (BMI) significantly increased the variance which explained in abdominal subcutaneous fat, because it was described that abdominal subcutaneous fat is an independent predictor of insulin resistance. The findings provide further support for the idea that combined BMI and waist circumference (WC) are a better predictive of metabolic risk than either variable alone. Thus, the health risks that are associated with abdominal obesity are best identified by the combination of BMI and WC, but not WC alone [20].

Serum leptin level in this study showed a highly significant increase in obese women in comparison

with the control, which is in agreement with previous results [21]. Leptin is secreted by the adipocytes, and it is present in serum in a direct ratio to the amount of adipose tissue. In humans, obesity is associated with high leptin levels, probably reflecting a state of leptin resistance and impaired leptin signalling and action. Leptin inhibits lipogenesis and stimulates lipolysis, which decreases lipid levels in the skeletal muscles, liver, and pancreatic beta cells, and improves insulin sensitivity [22].

In this study, leptin secretion was increased with the increase of visceral fats. Leptin gives a signal to the brain to bind with leptin receptors to decrease food intake. In obese patients, there is a problem that occurs which makes leptin secretion increase, but it cannot bind to its receptor. Therefore, the brain won't be able to recognize that the body has an excessive amount of fat, which will cause accumulation of fats and eventually causes obesity. This case is called leptin resistance and represents a major biological abnormality in obesity. This result is consistent with previously published data [23]. Leptin resistance may result in inappropriate leptin production, lack of leptin receptors, or insensitivity of leptin receptors in the brain. These factors contribute to obesity [24].

MDA is an end-product created by decomposition of arachidonic acid and larger PUFAs. In this study, the results showed that MDA levels were increased in obese women in comparison with the control, which is in agreement with previously reported data [25]. MDA occurs naturally and it acts as an important marker for oxidative stress [26]. ROS cause degradation of PUFA which leads to the formation of MDA [27]. In obesity, the oxidative stress (OS) is increased because of increasing oxygen intake, which results in the production of ROS that cause an increased free radical production. This increase is due to the increase in lipid peroxidation of PUFA. Increased production of ROS causes an increase in MDA production [28].

SOD is an enzyme which is important to organize free radicals which may cause many problems and damages in organs. In this study, SOD levels increased in obese patients in comparison with the control group. In obesity, oxidative stress increases oxygen consumption, leading to increased production of free radicals and fat [29]. An increase of fat in obese patients will produce the ROS which induce OS. ROS is harmful for tissues and health. SOD is increased with the increase of free radicals to give an electron to reduce the free radicals which may cause many damages in the tissues [30].

Conclusions

1. Obesity can be detected by the level of leptin Hormone.
2. The increase in obesity causes oxidative stress and the formation of MDA which is considered as a major risk factor in obesity, whereas the level of antioxidants is decreased.

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