Effect of Leptin and Oxidative Stress in the Blood of Obese Individuals

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Abstract

Background: Obesity is a multifaceted condition and represents a pandemic that needs urgent attention. Obesity, both directly and indirectly, increases the risk for a variety of disease conditions including diabetes, hypertension, liver disease, and certain cancers, which in turn, decreases the overall lifespan in both men and women. Leptin most likely indicates satiety and fullness of energy stores under physiological conditions, but obesity is characterized by hyperleptinemia and hypothalamic leptin resistance. Many studies have found association between obesity leading to oxidative stress and diabetes mellitus type 2, and many others have shown that the level of ROS increase in obesity.

Methods: In this study conducted on 176 individuals in the age group from (20-55) years, from Tikrit and Kirkuk Governorates. Blood samples were divided into three groups according to BMI: Group One: Control group (Normal Weight): 66 individual (32 male, 34 female), BMI (18.5–24.9 kg/m²). Group Two: Over Weight group: 50 individual (16 male, 34 female), BMI (25.0–29.9 kg/m²). Group Three: Obese group: 60 individual (28 male, 32 female), BMI (≥ 30 kg/m²).

Results: The results showed a high significant increase (p=0.000088) in the BMI levels in obese and overweight groups comparison with normal weight group. The results showed a high significant increase (p=0.000008) in the Leptin hormone levels in obese and overweight groups comparison with normal weight group. There is a high significant increase in the (cholesterol, TG, VLDL and LDL) levels in obese and overweight groups comparison with normal weight group (p=0.00002)and (p=0.000041) respectively, while the results showed a high significant decrease (p=0.000034) in the HDL concentration in obese and overweight groups comparison with normal weight group, the results showed a high significant decrease (p=0.000005) in the GSH concentration in obese and overweight groups comparison with normal weight group, the results showed a high significant increase (p=0.00003) in the MDA levels in obese and overweight groups comparison with normal weight group. The results showed that there was a positive correlation between leptin with Cholesterol (r=0.526), Triglyceride (r=0.594), LDL (r=0.645), VLDL (r=0.594) and MDA (r=0.692), but there was a negative correlation between leptin with HDL (r=-0.642), GSH (r=-0.734).

Conclusion: The results of (leptin and lipid profile) indicated highly associated with oxidative stress (MDA, GSH) levels and these correlations caused obesity.

Keywords: Leptin; Oxidative stress; Glutathione; Malondialdehyde; BMI; Lipid profile; Obese individuals

Introduction

Obesity is a multifaceted condition and represents a pandemic that needs urgent attention. Obesity, both directly and indirectly, increases the risk for a variety of disease conditions including diabetes, hypertension, liver disease, and certain cancers, which in turn, decreases the overall lifespan in both men and women [1]. Leptin most likely indicates satiety and fullness of energy stores under physiological conditions, but obesity is characterized by hyperleptinemia and hypothalamic leptin resistance [2]. Many studies have found association between obesity leading to oxidative stress and diabetes mellitus type 2 [3], and many others have shown that the level of ROS increase in obesity [4,5]. Glutathione is a master antioxidant cellular defense, prevent damage to the important components caused by ROS such as free radicals and peroxide [6,7]. Oxidative stress is an imbalance between oxidant and antioxidant pathways that result in the accumulation of lipid oxidation products such as lipid hydro peroxides and malondialdehyde. These materials are toxic and cause increased risk of arteriosclerosis in the blood by other lipoproteins. In addition, increased oxidative stress in adults after exercise increases. It has been shown that aerobic exercise reduces oxidative stress in obese men [8,9].

The aim of this study was to determine how the leptin hormone disturbance may leads to lipid level disorders which considered a risk factor of obesity and study the relationship of leptine with oxidative stress (GSH, MDA) and lipid profile.

Methods

This study was conducted on 176 individuals in the age group of (20-55) years. All individuals were randomly taken from Tikrit and Kirkuk Governorates. Blood samples were divided into three groups
Al-Hamodi et al. [19] and probably several studies addressed leptin and its association with diseases like obesity [23], hypertension [24,25], and metabolic syndrome [26,27]. Variations in total body fat content and fat distribution explain approximately 50% of circulating leptin level variance [28].

The results showed a high significant decrease (p=0.00005) in the GSH concentration in obese and overweight groups comparison with normal weight group, and the Mean ± SD of serum GSH level was (1.7932 ± 0.5960), (3.1272 ± 0.7709), and (4.3664 ± 1.0720) µmol/l, respectively (Table 1). This study was agreement with Louise et al. [29]. GSH plays multiple roles in the cell, including being a free radical scavenger as a primary antioxidant defense [30]. The glutathione concentration may be affected by many factors related to the life style such as non-healthy food and psychological stress, leading to decrease antioxidants level [31]. It dysregulation represents one of the main factors responsible for overproduction of ROS in diabetes mellitus and many other obesity associated diseases [7]. The results showed a high significant increase (p=0.00003) in the MDA levels in obese and overweight groups comparison with normal weight group, and the Mean ± SD of serum MDA (13.735 ± 2.311), (11.775 ± 1.498), and (8.883 ± 1.569) µmol/l, respectively (Table 1). These results are agreement with Selvakumar et al. [32]. Increased production of reactive oxygen species as well as reduced antioxidant defense mechanisms have been suggested to play a role in both humans and animal models of obesity [33,34]. Lipid peroxidation is thought to be a component of obesity-induced pathology [35]. There is a high significant increase in the (cholesterol, TG, VLDL and LDL) levels in obese and overweight groups comparison with normal weight group (p=0.00002) and (p=0.000041) respectively (Table 1), while the results showed a high significant decrease (p=0.000034) in the HDL concentration in obese and overweight groups comparison with normal weight group (Table 1). These results are agreement with Garcia et al. [21], Louise et al. [29], and Eda Beccer et al. [36]. Obesity is associated with derangements in the lipid profile, which further increases the risk of coronary heart disease, diabetes mellitus, stroke and certain cancers. In some studies, higher total cholesterol (TC), Triacylglycerol (TAG), low density lipoprotein cholesterol (LDL-C) and very low density lipoprotein cholesterol (VLDL-C) levels were observed in obese subjects as compared to controls except high density lipoprotein cholesterol (HDLC-C), which was significantly lower in obese subjects [37].

**Results and Discussion**

This study included 3 groups: Obese, Overweight and Normal weight (Control). The results showed a high significant increase (p=0.000088) in the BMI levels in obese and overweight groups comparison with normal weight group, and the Mean ± SD of BMI was (34.867 ± 3.538), (27.684 ± 1.473), and (22.440 ± 1.478) kg/m², respectively (Table 1). The results showed a high significant increase (p=0.00008) in the Leptin hormone levels in obese and overweight groups comparison with normal weight group, and the Mean ± SD of serum leptin level was (34.792 ± 6.249), (26.837 ± 5.679), and (11.318 ± 2.954) ng/ml, respectively (Table 1). This study was agreement with Afifi et al. [20] and Garcia et al. [21]. In humans, obesity is associated with high circulating leptin levels probably reflecting a state of leptin resistance, i.e. impaired leptin signalling and action. This state could interfere with the physiological relationship between leptin and β-cell function and promote the development of IR and Type 2 DM [22]. Over the few recent years, several studies addressed leptin and its association with diseases like obesity [23], hypertension [24,25], and metabolic syndrome [26,27].

| Parameters (N) | Normal weight Mean ± SD | Overweight Mean ± SD | Obese Mean ± SD | T-Test | P-value |
|---------------|--------------------------|----------------------|----------------|--------|---------|
| BMI (kg/m²)   | 22.440 ± 1.478           | 27.684 ± 1.473       | 34.867 ± 3.538 | 426.81** | 0.000088 |
| Leptin (ng/ml)| 11.318 ± 2.954           | 26.837 ± 5.679       | 34.792 ± 6.249 | 349.63** | 0.00008 |
| GSH (µmol/l)  | 4.3664 ± 1.0720          | 3.1272 ± 0.7709      | 1.7932 ± 0.5960 | 144.26** | 0.00005 |
| MDA (µmol/l)  | 8.883 ± 1.569            | 11.775 ± 1.498       | 13.735 ± 2.311 | 111.16** | 0.00003 |
| Cholesterol (mmol/l) | 4.1671 ± 0.7946 | 5.2258 ± 0.8281 | 5.9153 ± 1.1027 | 57.84** | 0.00002 |
| Triglyceride (mmol/l) | 1.6839 ± 0.5763 | 2.2348 ± 0.6279 | 2.9202 ± 0.7261 | 57.76** | 0.00002 |
| HDL (mmol/l)  | 2.1476 ± 0.7186          | 1.5468 ± 0.5548      | 1.0712 ± 0.2482 | 60.71** | 0.000034 |
| LDL (mmol/l)  | 1.2586 ± 0.6922          | 2.6686 ± 0.9170      | 3.5211 ± 1.1815 | 92.17** | 0.000041 |
| VLDL (mmol/l) | 0.7609 ± 0.2614          | 1.0104 ± 0.2857      | 1.3230 ± 0.3305 | 57.77** | 0.00002 |

According to BMI: Group One: Control group (Normal Weight): 66 individual BMI (18.5-24.9 kg/m²), Group Two: Overweight group: 50 individual BMI (25.0–29.9 kg/m²), Group Three: Obese group: 60 individual BMI (≥ 30 kg/m²). About 5 ml of venous blood were withdrawn from (obese individuals, over weight individuals and controls) using a disposable syringe after 12-hour fasting. The collected blood was then allowed to clot in a plain tube at room temperature, after which the serum was separated by centrifugation at 3000 rpm for 10 min, and kept frozen at -20°C to be analyzed later on. Serum Leptin was measured by ELISA. Serum GSH, serum MDA and serum lipid profile were measured by spectrophotometer. Statistical analysis was performed by statisticians with the SPSS 15.01 Statistical Package for Social Sciences and also Excel 2003. Data analysis was done using chi- square test for tables with frequencies, while independent sample t-test was used for tables with means and standard Deviation. P value of ≤ 0.05 was used as the level of significance. Correlation coefficient used to find the correlation between studied markers by using Pearson correlation.
**Table 1**: Mean ± SD of serum parameters of the study groups.

| Parameters       | (r) value |
|------------------|-----------|
| GSH (µmol/l)     | -0.734    |
| MDA (µmol/l)     | 0.692     |
| Cholesterol (mmol/l) | 0.526    |
| Triglyceride (mmol/l) | 0.594    |
| HDL (mmol/l)     | -0.642    |
| LDL (mmol/l)     | 0.645     |
| VLDL (mmol/l)    | 0.594     |

**Table 2**: Correlations between leptin and other parameters.

**Conclusion**

There was a significant increase in the levels of leptin. There was a significant increase in the levels of BMI, MDA, TC, triglycerides, LDL-C and VLDL-C and decrease in the level of GSH and HDL-C in overweight and obese individuals. From the relationship between leptin with lipid profile, leptin a positively associated with TC, triglycerides, LDL-C and VLDL-C, and a negatively correlated with GSH and HDL-C. This relationship showed a strong link between hyperleptinemia and hyperlipidemia, and that consider a risk factor. The results of this study suggested a high correlation of leptin level with lipid profile and oxidative stress (MDA, GSH) levels, and these correlations caused obesity.

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