

## 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/m<sup>2</sup>). Group Two: Over Weight group: 50 individual (16 male, 34 female), BMI (25.0–29.9 kg/m<sup>2</sup>). Group Three: Obese group: 60 individual (28 male, 32 female), BMI (≥ 30 kg/m<sup>2</sup>).

**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 ( $p=0.00008$ ) 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 ( $p=0.00005$ ) 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 leptine 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

according to BMI: Group One: Control group (Normal Weight): 66 individual BMI (18.5-24.9 kg/m<sup>2</sup>). Group Two: Overweight group: 50 individual BMI (25.0–29.9 kg/m<sup>2</sup>). Group Three: Obese group: 60 individual BMI (≥ 30 kg/m<sup>2</sup>). 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 [10] was measured by ELISA. Serum GSH [11,12], serum MDA [13] and serum lipid profile [14-18] 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.

## 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/m<sup>2</sup>, 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 Al-Hamodi et al. [19] and 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].

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 Becer 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 (HDL-C), which was significantly lower in obese subjects [37].

Parameters (N)	Normal weight Mean ± SD	Overweight Mean ± SD	Obese Mean ± SD	T-Test	P-value
BMI (kg/m <sup>2</sup> )	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

\*\*( $P < 0.0001$ )

**Table 1:** Mean  $\pm$  SD of serum parameters of the study groups.

### Correlations study

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 ( $r=-0.734$ ). As shown in (Table 2).

Hyperglycemia, hypertension, and hyperleptinemia are also possible sources of increased oxidant stress in the obese state [38]. It is not known whether obesity-associated oxidant stress is related to excess adipose tissue accumulation or is a consequence of obesity-related diseases i.e., hypertension, hyperlipidemia, hyperleptinemia, and hyperglycemia [39].

Parameters	(r) value
GSH ( $\mu\text{mol/l}$ )	-0.734
MDA ( $\mu\text{mol/l}$ )	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.

### References

- Chandra A, Biersmith M, Tolouian R (2014) Obesity and kidney protection. *J Nephropathol* 3: 91-97.
- DePaoli A (2014) 20 years of leptin: Leptin in common obesity and associated disorders of metabolism. *J Endocrinol* 223: 71-81.
- Bhatia S, Shukla R, Venkata MS, Kaur GJ, Madhava PK (2003) Antioxidant status lipid peroxidation and nitric oxide end products in patients of type 2 diabetes mellitus with nephropathy. *Clin Biochem* 36: 557-562.
- Mokdad AH, Ford ES, Bowman BA, Dietz WH, Vinicor F, et al. (2003) Prevalence of obesity diabetes and obesity-related health risk factors 2001. *JAMA* 289: 76-79.
- Kawakita S, Kitahata H, Oshita S (2009) Glutathione level estimation in obese individuals. *World J Gastroenterol* 15: 4137-4142.
- Pastore A, Ciampalini P, Tozzi G, Pecorelli L, Passarelli C, et al. (2010) All glutathione forms are depleted in blood of obese and type 1 diabetic children *All Diabetes* 13: 272-277.
- Goyal R, Singhai M, Faizy AF (2011) Glutathione peroxidase activity in obese and non-obese diabetic patients and role of hyperglycemia in oxidative stress. *J Midlife health* 2: 72-76.
- Vincent HK, Bourguignon C, Vincent K (2006) Resistance training lowers exercise-induced oxidative stress and homocysteine levels in overweight and obese older adults. *obesity* 14: 1921-1930.
- Khalesi M, Gaeini AA, Shabkhiz F, Samadi A, Tork F (2011) The effect of a period of discontinuous endurance exercise on ICAM-1 and lipid profile of non-athletic male students. *Quarterly Journal of Sabzevar University of Medical Sciences* 18: 198-205.
- Check JH, Ubelacker L, Lauer CC (1995) Falsely elevated steroidal assay levels related to heterophile antibodies against various animal species. *Gynecol Obstet Invest* 40: 139-140.
- Tietz NW (1999) Text book of clinical chemistry (3rd edn) CA Burtis ER, Ashwood WB (eds.) Saunders 826-835.
- Sedlak J, Lindsay RH (1968) Estimation of total protein-bound and non-protein sulfhydryl groups in tissue with Ellman's reagent. *Anal Biochem* 25: 192-205.
- Guidet B, Shah SV (1989) Enhanced in vivo H<sub>2</sub>O<sub>2</sub> generation by rat kidney in glycerol-induced renal failure. *Am J. Physiol* 257: 440-445.
- Allian CC (1974) Estimation of serum cholesterol. *Clin Chemistry* 25: 470-475.
- Trinder P (1969) Estimation of serum triglyceride. *Clin Biochem* 6: 27-29.
- Burnstein M (1970) Estimation of serum HDL-C. *Journal of Lipid Research* 11: 583-595.
- Friedwald WT (1972) Estimation of serum LDL-C. *Clin Chem* 18: 499.
- Andreoli TE, Carpenter J, Griggs RC (2001) Cecil essentials of medicine: Disorder of lipid metabolism (5th edn) Herbert P. N. (ed) Philadelphia W. B. Saunders company, Toronto, London 16: 526-532.
- Zaid Al-Hamodi Molham A, Ali A, Riyadh SA (2014) Association of adipokines leptin/adiponectin ratio and C-reactive protein with obesity and type 2 diabetes mellitus. *Diabetol Metab Syndr* 6: 99.
- Afiy M, Samy N, Hashim M, El-Maksoud A, Saleh O (2012) Assessment of biochemical changes among Egyptian women with increased body weight. *J Obes Wt Loss Ther* 2: 127.
- García OP, Ronquillo D, Caamaño Mdel C, Camacho M, Long KZ, et al. (2012) Zinc vitamin A and vitamin C status are associated with leptin concentrations and obesity in Mexican women: Results from a cross sectional study. *Nutr Metab* 9: 59.
- Martin SS, Qasim A, Reilly MP (2008) Leptin resistance: a possible interface of inflammation and metabolism in obesity-related cardiovascular disease. *J Am Coll Cardiol* 52: 1201-1210.
- Schinzari F, Tesauro M, Rovella V, Di Daniele N, Mores N, et al. (2013) Leptin stimulates both endothelin-1 and nitric oxide activity in lean subjects but not in patients with obesity-related metabolic syndrome. *J Clin Endocrinol Metab* 98: 1235-1241.
- Galletti F, Delia L, De Palma D, Russo O, Barba G, et al. (2012) Hyperleptinemia is associated with hypertension systemic inflammation and insulin resistance in overweight but not in normal weight men. *Nutrition Metabolism and Cardiovascular Diseases* 22: 300-306.
- De Haro MC, Figueiredo VN, De Faria AP, Barbaro NR, Sabbatini AR (2013) High-circulating leptin levels are associated with increased blood

- pressure in uncontrolled resistant hypertension. *J Hum Hypertens* 27: 225-230.
26. Esteghamati A, Zandieh A, Zandieh B, Khalilzadeh O, Meysamie A, et al. (2011) Leptin cut-off values for determination of metabolic syndrome: third national surveillance of risk factors of non-communicable diseases in Iran. *Endocrine* 40: 117-123.
27. Do Carmo Martins M, Faleiro LL, Fonseca A (2012) Relationship between leptin and body mass and metabolic syndrome in an adult population. *Revista Portuguesa de Cardiologia (English edition)* 31: 711-719.
28. Nawata K, Ishida H, Uenishi K, Kudo H (2008) The relationship between serum leptin concentration and the percentage of body fat in Japanese high school students. *Asia-Pacific journal of public health/Asia-Pacific Academic Consortium for Public Health* 20: 180-188.
29. Brown LA, Kerr CJ, Whiting P, Finer N, McEneny J, et al. (2009) Oxidant stress in healthy normal-weight overweight and obese individuals. *Obesity* 17: 460-466.
30. Chen Y, Dong H, Thompson DC, Shertzer HG, Nebert DW, et al. (2013) Glutathione defense mechanism in liver injury: insights from animal models. *Food and chemical toxicology* 60: 38-44.
31. Patki G, Solanki N, Atrooz F, Allam F, Salim S, et al. (2013) Depression, anxiety-like behavior and memory impairment are associated with increased oxidative stress and inflammation in a rat model of social stress. *Brain res* 1539: 73-86.
32. Selvakumar C, Uma M (2012) Oxidant-antioxidant disturbance in men classified as obese according to the preliminary WHO guidelines for Asians. *Journal of Stress Physiology & Biochemistry* 172-181.
33. Sonta T, Inoguchi T, Tsubouchi H, Sekiguchi N, Kobayashi K, et al. (2004) Evidence for contribution of vascular NAD (P) Hoxidase to increased oxidative stress in animal models of diabetes and obesity. *Free Radic Biol Med* 37: 115-123.
34. Keaney JF, Larson MG, Vasani RS, Wilson PWF, Lipinska I, et al. (2003) Obesity and systemic oxidative stress: clinical correlates of oxidative stress in the Framingham study. *Arterioscler Thromb Vasc Biol* 23: 434-439.
35. Amirkhizi F, Siassi F, Minaie S, Djalali M, Rahimi A, et al. (2007) Is obesity associated with increased plasma lipid peroxidation and oxidative stress in women. *ARYA Atherosclerosis Journal* 2: 189-192.
36. Eda B, Meral K, Mehtap T, Nedime S (2016) Association between leptin G-2548A gene polymorphism plasma leptin levels and lipid profiles in Turkish Cypriot obese subjects. *Turkish Journal of Biochemistry* 41: 1-8.
37. Nagila A, Bhatt M, Poudel B, Mahato P, Gurung D, et al. (2008) Thyroid stimulating hormone and its correlation with lipid profile in the obese Nepalese population. *Journal of clinical and diagnostic research* 2: 932-937.
38. Vincent HK, Taylor AG (2006) Biomarkers and potential mechanisms of obesity-induced oxidant stress in humans. *Int J Obese (Lond)* 30: 400-418.
39. Facchini FS, Hua NW, Reaven GM, Stoohs RA (2000) Hyperinsulinemia: The missing link among oxidative stress and age-related diseases?. *Free Radic Biol Med* 29: 1302-1306.