Research article

Levels of leptin, irisin, oxytocin and insulin in obese and normal weight Iraqi young men

Alaa Subhi Hammoud, Maryam I. Salman

Department of Biology, University of Anbar, College of Science, Anbar, Iraq

(Received: June 2023 Revised: July 2023 Accepted: August 2023)

Corresponding author: **Alaa Subhi Hammoud**. Email: alaasubhihammoud@gmail.com

ABSTRACT

Introduction and Aim: Obesity is a serious, life-threatening health condition that is prevalent in Iraq and the world as a whole. Since Leptin, irisin, oxytocin and insulin are proposed to play main roles in energy expenditure, glucose homeostasis, regulating body weight, reducing obesity and improving life expectancy so the aim of this study was to evaluate the concentrations of these anti-obesity hormones plus insulin resistance

Materials and Methods: The study was conducted on 100 obese young men with a mean age of 29.95 years and fifty normal weight young men with a mean age of 28.44.

Results: In obese men, the mean leptin concentration was 24.08±9.91 ng/ml which was significantly higher than in normal weight men 5.48 ng/ml. Serum irisin levels in obese men and normal weight were 8.9 ng/ml, 2.4 ng/ml respectively, and it was significantly higher in obese group in comparison to the normal weight group. The mean serum oxytocin concentration was significantly lower in obese group 6.41pg/ml in comparison to normal weight 29.55 pg/ml. Serum insulin levels in obese and normal weight were 19.55±5.56 and 3.64 micro lU/ml respectively and it was significantly higher in obese men. The mean fasting blood glucose concentration in obese men was 98.67mg/dl and it was significantly higher than in normal weight 84±9.85 mg/ml. Insulin resistance (HOMA IR) was significantly higher in obese men 6.6 than in normal weight 0.68.

Conclusion: Serum levels of leptin, irisin, insulin, and insulin resistance are higher in obese young men, while oxytocin levels were noticeably low. Our study also shows that obesity increases the likelihood of insulin resistance.

Keywords: Obesity; leptin; irisin; oxytocin; insulin resistance.

INTRODUCTION

Obesity is a multifaceted condition that exhibits strong associations with several significant diseases, including hypertension, type 2 diabetes mellitus, dyslipidemia, heart disease, fatty liver disease, and various forms of cancer (1,2). In the year 2016, the phenomenon under consideration was found to be accountable for the mortality of more than 3.4 billion individuals of mature age on a global scale. Based on data provided by the World Health Organization (WHO), it is estimated that approximately 1.9 billion individuals are classified as overweight, while approximately 650 million individuals are categorized as obese (3,4). Given the severity and potential fatality associated with obesity, it is imperative to conduct an investigation into the hormones implicated in the regulation of metabolism and energy balance among individuals who are obese. Specifically, the hormones of interest include leptin, irisin, and oxytocin. Leptin, a polypeptide hormone with a molecular weight of 16-KDa, is primarily synthesized and secreted into the bloodstream by white adipocytes and small intestinal cells (5). Leptin regulates food intake, body mass, energy balance, and body weight by its influence on hypothalamic receptors, resulting in appetite inhibition, in addition to playing a role in metabolic rate stimulation and thermogenesis (5). Irisin, a newly identified myokine which converts the white adipose tissues to brown adipose tissues, so this hormone also participates in energy expenditure, thermogenesis, and glucose homeostasis (6). Irisin a recently discovered myokine, secreted by both muscle and adipose tissues, is involved in functions such as energy expenditure, thermogenesis, and glucose homeostasis (6, 7). Myokine levels have been suggested to play a vital role in improving obesity, diabetes and life expectancy (8, 9).

The production of oxytocin, a neuropeptide hormone consisting of nine amino acids, primarily occurs in the hypothalamus. Subsequently, it is stored and released into the bloodstream through the pituitary gland (10). Oxytocin is known to control key aspects of reproduction including childbirth and lactation as well as in many neuropsychiatric activities such as social behavior, learning, memory, sexual behavior, and food intake (11). In addition to food intake, oxytocin has also been demonstrated to regulate metabolic and energy balance (12).

Insulin, a hormone, is accountable for regulating the levels of glucose in the bloodstream. Insulin resistance is a pathological state characterized by the diminished capacity of body cells to uptake glucose from the bloodstream, consequently leading to elevated levels of blood glucose. This condition is associated with various disorders, including diabetes and obesity (13). The aim of this study was to assess and compare the

levels of leptin, irisin, oxytocin, and insulin resistance in a cohort of young obese and non-obese men from Iraq, as these hormones are recognized for their potential anti-obesity effects.

MATERIALS AND METHODS

The study was done on 100 obese young men aged 29.95±5.18 who visit outpatient clinic owing to their extreme weight and 50 normal weight men aged 28.44±5.75 willing to join in this study. The study protocol was approved by the Clinical Research Committee, University of Anbar, Ramadi, Iraq in September 2020. Participants in the study who were male and had been excluded were those who had been diagnosed with chronic and genetic diseases, endocrinologic disorders, individuals who were taking lipid-lowering pharmaceuticals, individuals who had a history of drug use, and individuals who were now taking these medications.

Clinical parameters

To obtain anthropometric measurements, we adhered to established protocols and methodologies that are widely accepted in the field. We recorded the height and weight of each participant. The calculation of the body mass index (BMI), a metric used to assess obesity, involves dividing an individual's weight in kilograms by the square of their height in meters.

Biochemical parameters

Five ml of intravenous blood was drawn from each participant in this study. The blood collected was transferred to the test tube, allowed to clot and centrifuged. The serum obtained was stored at -40°C until use. The levels of leptin, irisin, oxytocin, and insulin were assessed through the utilization of enzyme-linked immunosorbent assay (ELISA). The determination of leptin concentration was conducted utilizing an ELISA kit obtained from LDN Labour Diagnostica Nord GmbH and Co.KG, a company based in Germany. The levels of irisin and oxytocin were measured utilizing an enzyme-linked immunosorbent assay (ELISA) kit obtained from Wuhan Fine Biotech Co., Ltd., located in Wuhan, China. The insulin level was quantified utilizing an enzyme-linked immunosorbent assay (ELISA) kit (Monobind Inc., Lake Forest, USA). The measurement of insulin resistance was conducted using the formula fasting glucose (mg/dl) × fasting insulin (μIU/L)/405, as described in the homeostasis model assessment of insulin resistance (HOMA-IR) (14).

Statistical analysis

The data was subjected to statistical analysis using SPSS version 20. The mean ± standard deviation (SD) was used to express all the studied parameters. A t-test was conducted to determine the statistical significance of differences between the two sets. A significance level of $P < 0.05$ was used to determine statistical significance.

RESULTS

The study included a sample of 100 young men who were classified as obese, with a mean age of 29.95±5.18 years. Additionally, 50 young men with normal weight and with a mean age of 28.44±5.71 years, were included in the study, The body mass index (BMI) level exhibited a statistically significant increase ($p< 0.001$) among obese men (37.22±3.049) compared to those with normal weight (23.09±1.268) as depicted in Fig.1.

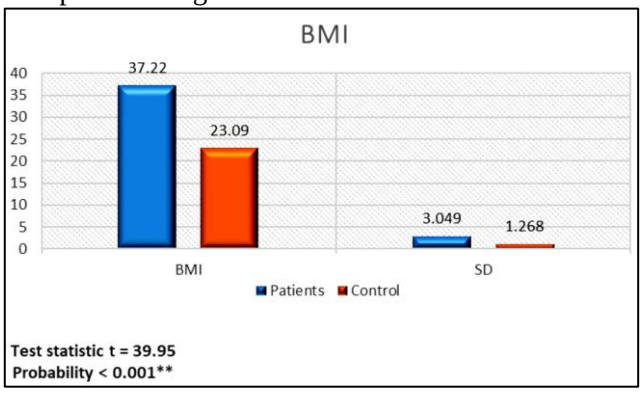

Fig. 1: The average body mass index of obese and normal weight control group individuals

The average leptin concentration in obese men was 24.08±9.91 ng/ml, which was found to be significantly higher ($p< 0.001$) compared to the average concentration of 5.48±2.5ng/ml in individuals of normal weight (Fig. 2). The serum irisin levels in individuals classified as obese and those with normal weight were measured to be 8.9±2.64 ng/ml and 2.4±0.72 ng/ml, respectively. It was observed that the irisin levels were significantly higher in the obese group compared to the normal weight group ($p< 0.001$), as depicted in Fig. 3. The average serum oxytocin concentration was found to be significantly lower ($p< 0.001$) in the obese group (6.41±3.28 pg/ml) compared to the normal weight group (29.55±14.51 pg/ml) (Fig. 4). Serum insulin levels in obese and normal weight were 19.55±5.56 μIU/ml and 3.64±1.92 μIU/ml respectively and it was significantly higher ($p< 0.001$) in obese men (Fig.5). The mean Fasting blood glucose concentration in obese men was 98.67±24.77 mg/dl and it was significantly higher ($p< 0.001$) than in normal weight 84±9.85 mg/ml (Fig.6). Insulin resistance (HOMA-IR) was significantly higher ($p< 0.001$) in obese men 6.6±2.3 than in normal weight 0.68±0.36 (Fig.7).

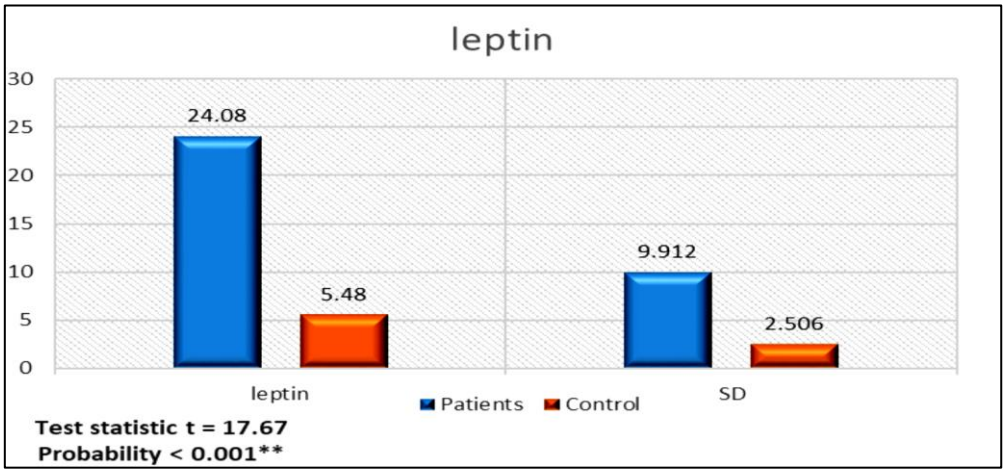

Fig. 2: The average concentration of leptin (measured in ng/ml) in obese patients and a control group of individuals with normal weight.

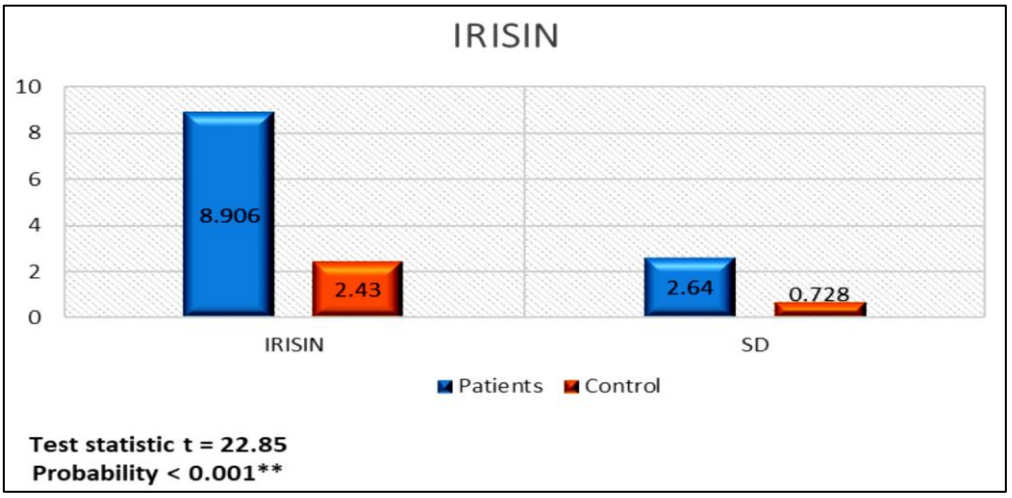

Fig. 3: The average concentration of irisin (measured in ng/ml) in obese patients compared to a control group of individuals with normal weight.

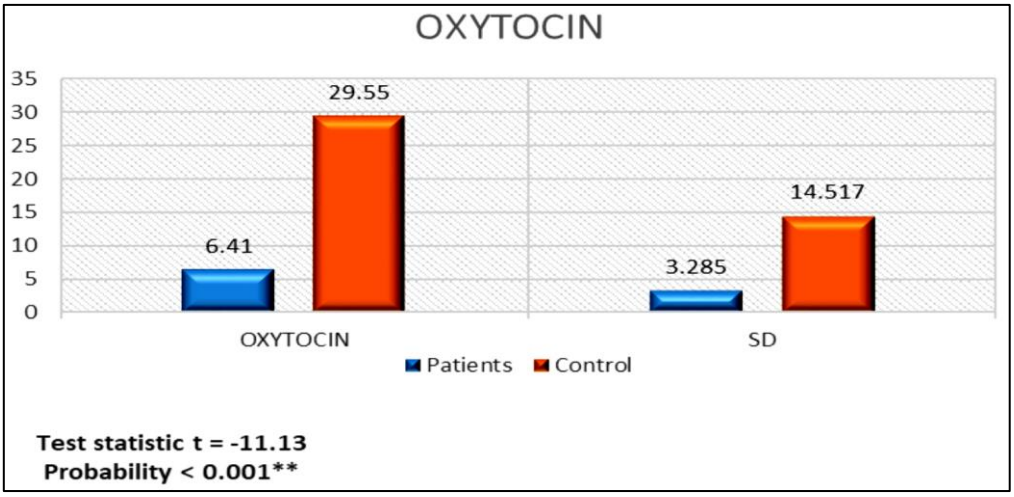

Fig. 4: The average concentration of oxytocin (pg/ml) in obese patients compared to a control group of individuals with normal weight.

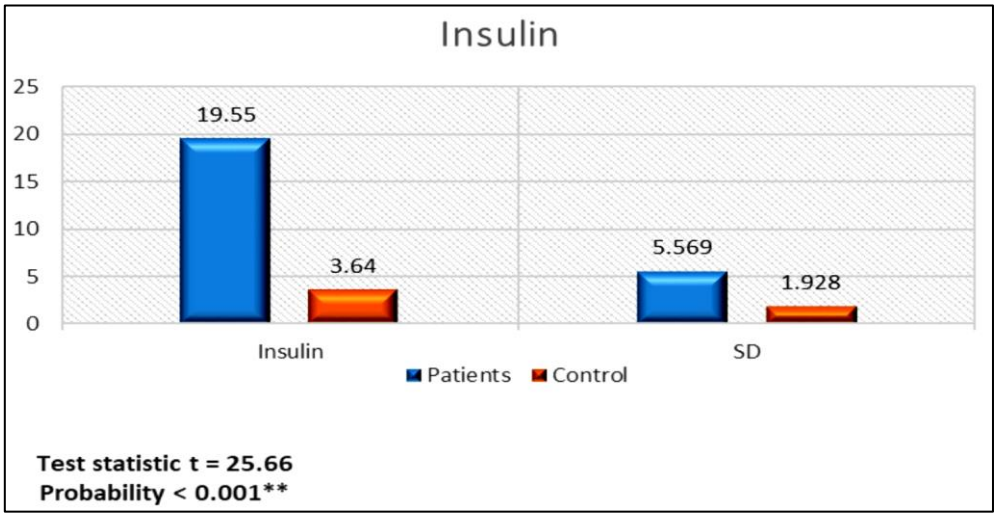

Fig. 5: The average insulin levels (µIU/ml) in obese patients and control group of individuals with normal weight.

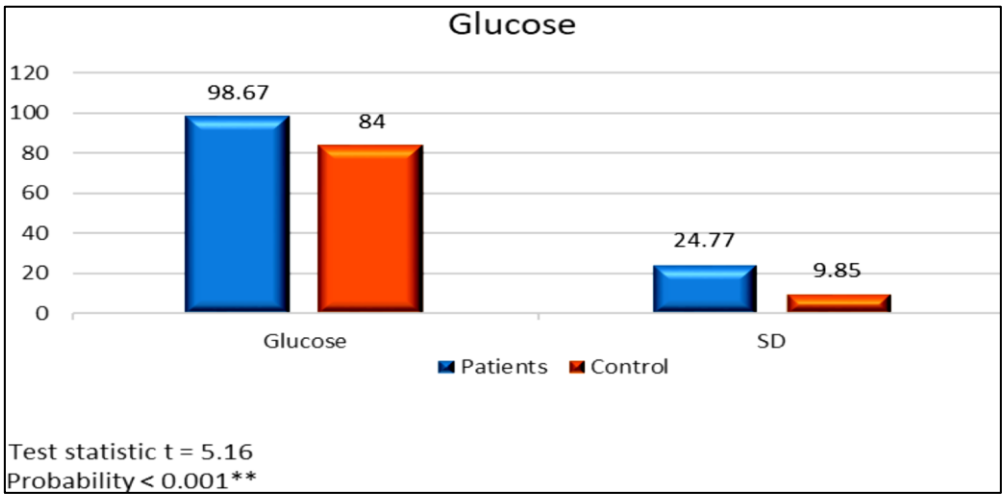

Fig. 6: The average fasting blood glucose levels (measured in mg/dl) in obese patients and the control group consisting of individuals with normal weight.

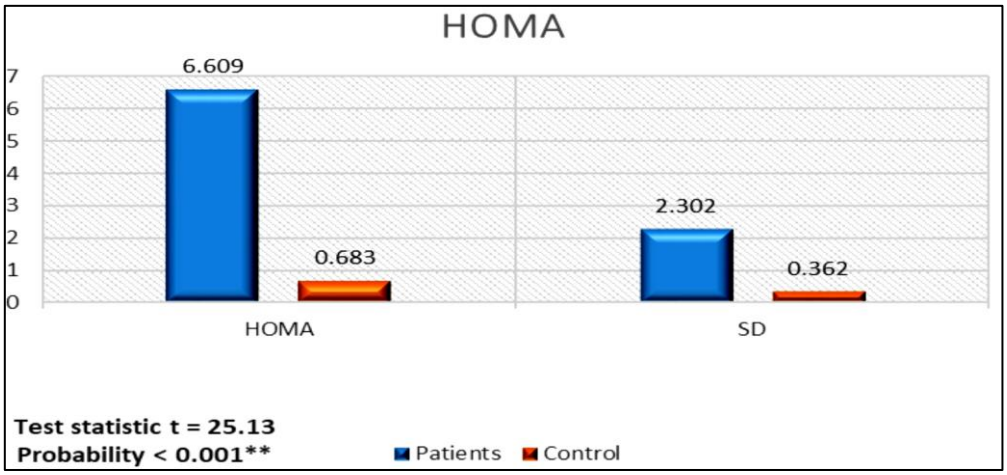

Fig.7: The average value of the Homeostatic Model Assessment (HOMA) in a group of obese patients

DISCUSSION

Several hormones that are known to influence hunger, metabolism, body fat distribution and accumulation have been linked to increase in body weight and obesity. In this study we compared the hormonal levels of leptin, irisin, oxytocin and insulin in obese as well as non-obese men. The findings of our study indicate a significant elevation in leptin concentrations among obese individuals in comparison to men with normal weight. This observation holds importance as research has demonstrated a significant association between blood leptin concentrations and the deposition of adipose tissue. Research has shown that there is an increase in leptin levels during the process of refeeding, overeating, and stressful surgical procedures, while a decrease in leptin levels occurs during fasting and energy restriction (15). Previous

studies have reported an increase in serum leptin levels among individuals who are obese and also suffer from binge eating disorders (16). Leptin concentration is also seen to be elevated due to several peptide hormones such as glucagon, amylin, and pancreatic polypeptides secreted by the pancreas (17). Increased leptin concentration is linked to obesity and insulin resistance because leptin and insulin work together to regulate food intake, metabolic rate, glucose and lipid metabolism (8), this explains the results of the current research that indicate a significant rise in leptin, insulin and insulin resistance in obese people compared to those of normal weight. In case of high insulin levels, blocking glycolysis or glucose transporters prevents leptin from being produced and secreted by adipocytes (18). Hunger is linked to the decreased levels of leptin in the circulation seen following increased calorie consumption (19). The findings of the present study indicate a statistically significant elevation in irisin levels among obese males in comparison to individuals with normal weight. Physical activity in human individuals has been found to elevate the levels of irisin in the bloodstream. This increase in irisin has been associated with a rise in overall energy expenditure, a reduction in body weight, and an enhancement in insulin resistance that is often observed in cases of obesity (20). Previous research has proposed that obese individuals may exhibit an increased irisin level as a potential adaptive response to mitigate the negative effects of obesity, such as reduced insulin sensitivity and metabolic abnormalities (21).

Oxytocin has garnered a lot of attention, much like leptin and irisin, due to claims that it can treat diabetes and obesity while also lengthening life expectancy. This study observed a correlation between obesity and reduced oxytocin levels, consistent with prior research that reported significantly lower serum oxytocin levels in obese children and adults compared to control groups (22, 23). Previous research has indicated that animals maintained on a high-fat diet experience a reduction in food consumption and body weight when their oxytocin levels are elevated (24). Therefore, it is postulated that a decrease in circulating oxytocin levels may serve as a potential risk factor linked to obesity. A recent study has additionally demonstrated the potential of oxytocin administration as a therapeutic intervention for addressing leptin resistance in individuals with obesity (25). Oxytocin has been found to have various effects on body weight, primarily characterized by a reduction in food consumption, an increase in energy expenditure, and an enhancement of lipolysis (24, 26). In this study we also observed obese individuals to have significantly higher levels of insulin resistance, which agrees with previous studies (6, 8, 13). Hyperinsulinemia together with chronic low-grade systemic inflammation contribute to the progress of insulin resistance and obesity (27).

CONCLUSION

According to the findings of the study, leptin, irisin, insulin, and insulin resistance were all found in much higher levels in the serum of obese young men, although oxytocin levels were found to be significantly lower. In addition, the results of our research point to a connection between being overweight and having a greater likelihood of developing insulin resistance.

CONFLICT OF INTEREST

Authors declare no conflicts of interest.

REFERENCES

1. Jabbar, M. A., Hussain, Z. K. Study of some physiological and hematological parameters in obese women with arthritis. Biomedicine. 2023 Mar 28;43(01):423-427.
2. Al-Halaseh, L. K., Hajleh, M. N., Al-Samydai, A. M. Weight reduction in response to unauthorized treatment in a poorly controlled obese woman. Biomedicine. 2022 May 1;42(2):410-412.
3. Rekha, K., Vanitha, J., Kiran, A. Effect of respiratory muscle training with wind instrument among obese individuals. Biomedicine. 2021 Jul 7;41(2):287-293.
4. WHO. World Health Statics Overview 2019: Monitoring Health SDGs, Sustainable development goals Geneva: World Health Organization (2019) (WHO/DAD/2019).License: CC-BY-NC-SA 3.0 IGO.
5. Munzberg, H., Morrison, C.D. Structure, production and signaling of leptin. Metabolism, 2015; 64:13-23.
6. Moreno-Navarrete, J.M., Ortega, F., Serrano, M., Guerra, E., Pardo, G., Tinahones, F., *et al.*, Irisin is expressed and produced by human muscle and adipose tissue in association with obesity and insulin resistance. J Clin Endocrinol Metab. 2013; 98(4):E769-E778.
7. Boström, P., Wu, J., Jedrychowski, M.P., Korde, A., Ye, L., Lo, J.C., *et al.*, A PGC1-α-dependent myokine that drives brown-fat-like development of white fat and thermogenesis. Nature. 2012; 481(7382):463-468.
8. Crujeiras, A.B., Zulet, A.M., Lopez-Legarrea, P., Iglesia, R., Pardo, M., Carreira, M.C., *et al.*, Association between circulating irisin levels and the promotion of insulin resistance during the weight maintenance period after a dietary weight-lowering program in obese patients. 2014; 63(4): 520-531.
9. Swick, A.G., Orena, S., O'Connor, A. Irisin levels correlate with energy expenditure in a subgroup of humans with energy expenditure greater than predicted by fat free mass. Metabolism 2013; 62:1070-1073.
10. Klockars, O.A., Klockars, A., Levine, A.S., Olszewski, P.K. Oxytocin administration in the basolateral and central nuclei of amygdala moderately suppresses food intake. Neuroreport. 2018; 29(6):504-510.
11. Sarnyai, Z., Kovács, G.L. Oxytocin in learning and addiction: From early discoveries to the present. Pharmacol Biochem Behav. 2014;119:3-9.
12. Morton, G.J., Thatcher, B.S., Reidelberger, R.D., Ogimoto, K., Wolden-Hanson, T., Baskin, D.G., *et al*., Peripheral oxytocin suppresses food intake and causes weight loss in diet-induced obese rats. Am J Physiol Endocrinol Metab. 2012; 302 (1):E134-E144.
13. Ahmad, B., Sultana, R., Greene, M.W. Adipose tissue and insulin resistance in obese. Biomedicine and Pharmacotherapy. 2020;137:111315.
14. Ascaso, J.F., Pardo, S., Real, J.T., Lorente, R.I., Priego, A., Carmena, R. Diagnosing insulin resistance by simple

quantitative methods in subjects with normal glucose metabolism. Diabetes Care. 2003; 26: 3320–3325.
15. Obradovic, M., Sudar-Milovanovic, E., Soskic, S., Essack, M., Arya, S., Stewart, A.J., *et al*., Leptin and obesity: Role and clinical implication. Front Endocrinol (Lausanne). 2021;12: 585887.
16. Adami, G.F., Campostano, A., Cella, F., Scopinaro, N. Serum leptin concentration in obese patients with binge eating disorder. Int J Obes Relat Metab Disord. 2002; 26(8):1125-1128.
17. Tsai, M., Asakawa, A., Amitani, H., Inui, A. Stimulation of leptin secretion by insulin. Indian J Endocrinol Metab. 2012; 16: S543- S548.
18. Casabiell, X., Piñeiro, V., De, l.a, Cruz, L.F., Gualillo, O., Folgar, L., *et al*., Dual effect of insulin on *in vitro* leptin secretion by adipose tissue. Biochem Biophys Res Commun. 2000; 276:477-482.
19. Fried, S.K., Ricci, M.R., Russell, C.D., Laferrère, B. Regulation of leptin production in humans. J Nutr. 2000;130: 3127S-3131S.
20. Elizondo-Montemayor, L., Mendoza-Lara, G., Gutierrez-DelBosque, G., Peschard-Franco, M., Nieblas, B., Garcia-Rivas, G. Relationship of circulating irisin with body composition, physical activity, and cardiovascular and metabolic disorders in the pediatric population. Int. J. Mol. Sci. 2018; 19: 3727.
21. Hojlund, K., Bostrom, P. Irisin in obesity and type 2 diabetes. J Diabetes Complications 2013; 27:303-304.
22. Binay, C., Paketçi, C., Güze, S., Samancı, N. Serum irisin and oxytocin levels as predictors of metabolic parameters in obese children. J Clin Res Pediatr Endocrinol 2017;9(2):124-131.
23. Qian, W., Zhu, T., Tang, B., Yu, S., Hu, H., Sun, W., *et al.*, Decreased circulating levels of oxytocin in obesity and newly diagnosed type 2 diabetic patients. J Clin Endocrinol Metab. 2014; 99:4683-4689.
24. Deblon, N., Veyrat-Durebex, C., Bourgoin, L., Caillon, A., Bussier, A.L., Petrosino, S., Piscitelli, F., *et al.*, Mechanisms of the anti-obesity effects of oxytocin in diet-induced obese rats. PLoS ONE, 2011; 6: e25565.
25. Altirriba, J., Poher, A.L., Rohner-Jeanrenaud, F. Chronic oxytocin administration as a treatment against impaired leptin signaling or leptin resistance in obesity. Front Endocrinol (Lausanne). 2015; 6:119.
26. Blevinds, J. E., Ho, J.M. Role of oxytocin signaling in the regulation of body weight. Rev Endocr Metab Disord. 2013; 14:311-329.
27. Wondmkun, Y.T. Obesity, insulin resistance, and type 2 diabetes: Associations and therapeutic implications. Diabetes Metab Syndr Obes. 2020;13:3611-3616.